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Long-term trends of hypertension incidence in China: Regional variations

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Title Page

Title : Long-term trends of hypertension incidence in China: Regional variations

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ABSTRACT

Objective The aim is to explore the trends of hypertension incidence and regional variations in China from 1991 to 2015.

Design A dynamic prospective cohort study.

Setting Population based study.

Participants 12 952 Chinese adults from the China Health and Nutrition Survey (CHNS).

Primary outcome measures Long-term trend of hypertension incidence in Chinese adults and risk factors for occurrence of hypertension.

Results Age-standardized hypertension incidence increased from 40.8 per 1 000 person-years (95% CI, 38.3 to 43.4) between 1993 and 1997 to 48.6 (95% CI, 46.1 to 51.0) between 2011 and 2015. The increasing trends were further supported by results from subsequent extended Cox proportional hazard model. In addition, results from the modelling analysis showed that individuals in Eastern, Central, and Northeastern China had greater risks of hypertension occurrence in comparison with their counterparts in Western China.

Conclusion Hypertension incidence increased during the study period. The growth called for more attention on the health education and health promotion of individuals with great risks.

Strengths and limitations of this study

① The dynamic cohort study-design employed individuals from diverse social and geographic contexts, which enabled us to depict the long-term trends of hypertension incidence and regional disparities in the context of China's rapid social development and population aging.

② We adopted both self-reported health outcomes and objective outcomes from physical tests, which avoided the recall bias and underestimation in underserved areas.

③ We did not employ a national-representative sample and did not include individuals from other provinces in China, which undermined the representation of our findings. As a community-based survey, CHNS excluded institutionalized individuals, which further diminished the representation of our findings among

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9 ④In addition, we did not distinguish hypertension, and future research is necessary.
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INTRODUCTION

Along with aging population, non-communicable chronic diseases, particularly stroke and ischemic heart disease, have led to great burden of disease, deaths, and years of life lost (YLLs) in both developed and developing countries.^{1 2} Connected closely with various cardiovascular diseases,^{3 4} high systolic blood pressure was ranked as the leading risk factor of risk-attributable disability-adjusted life-years (DALYs) among selected 195 countries and territories.⁵ For instance, high systolic blood pressure accounted for 2.54 million deaths and more than 5% of DALYs in China in 2017.⁶

Existing evidence has confirmed a worldwide high prevalence of hypertension.⁴⁻⁶ Countries, such as Singapore⁶ and Korea⁷, had a significant proportion of individuals with hypertension. Likewise, with the extended life expectancy,⁸ changes in lifestyle behaviors,⁹ and rapid urbanization,¹⁰ developing countries, such as China, experienced a substantial increase in the prevalence of hypertension, ranging from 13.6% in 1991 to 27.9% in 2015.¹¹

Although the increasing prevalence of hypertension provided critical information for public health practice and disease control programs, it could not accurately depict the epidemiologic transition as the incidence measure.¹² Prior studies have indicated that the increasing prevalence could coexist with the decreasing incidence in the context of healthy aging.¹³ For evidence-based health-promoting initiatives, empirical research on hypertension incidence is warranted.

However, research on the long-term trends of the incidence of hypertension from China is scarce and relatively outdated.^{14 15} This is an important knowledge gap because developing countries are experiencing unprecedented social development. Up-to-date information among developing countries could greatly

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5 contribute to depict global epidemiologic transitions. Moreover, regional disparities are a major health
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7 concern in China as a result of inequitable socio-economic development and health care resource
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9 distribution,¹⁶⁻¹⁸ while the existing research provides insufficient information regarding the regional
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11 disparities in the hypertension incidence.¹⁹⁻²¹
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16 Hence, this study aims to explore the long-term trends of hypertension incidence among Chinese from
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18 diverse social and geographic contexts. In addition, we are particularly interested in regional variations while
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20 taking the individual-level risk factors into account.
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24 25 **METHODS**

26 27 **Data source**

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29 The present study derived data from the China Health and Nutrition Survey (CHNS). CHNS has been
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31 collaboratively conducted by Carolina Population Center at the University of North Carolina at Chapel Hill
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33 and the National Institute for Nutrition and Health (NINH, former National Institute of Nutrition and Food
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35 Safety) at the Chinese Center for Disease Control and Prevention. Initiated in 1989, CHNS consisted of ten-
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37 wave data in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015, respectively. Overall, CHNS
38
39 employed a multistage random cluster method to draw the study sample, which included over 30 000
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41 individuals from three provincial-level cities and twelve provinces. Individuals in the survey came from
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43 diverse social, geographic, and cultural contexts. CHNS employed face-to-face questionnaire interviews to
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45 collect data, and the physical health examinations were conducted by well-trained investigators. Information
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47 regarding survey design, data collection, and quality control could be retrieved from the cohort profile.²²
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58 **Study design and exclusion criteria**

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The present study employed a dynamic cohort study-design as not all individuals entered the cohort at the same time. To evaluate the long-term trends of hypertension incidence, we excluded individuals (a) without individual ID and community ID; (b) aged under 18 because of the low incidence of hypertension among children and teenagers; (c) with hypertension in his/her first investigation; (d) with only one observation or only one record of hypertension status; and (e) were pregnant during the study period to exclude gestational hypertension. Furthermore, we excluded observations after the diagnosis of hypertension (figure 1).

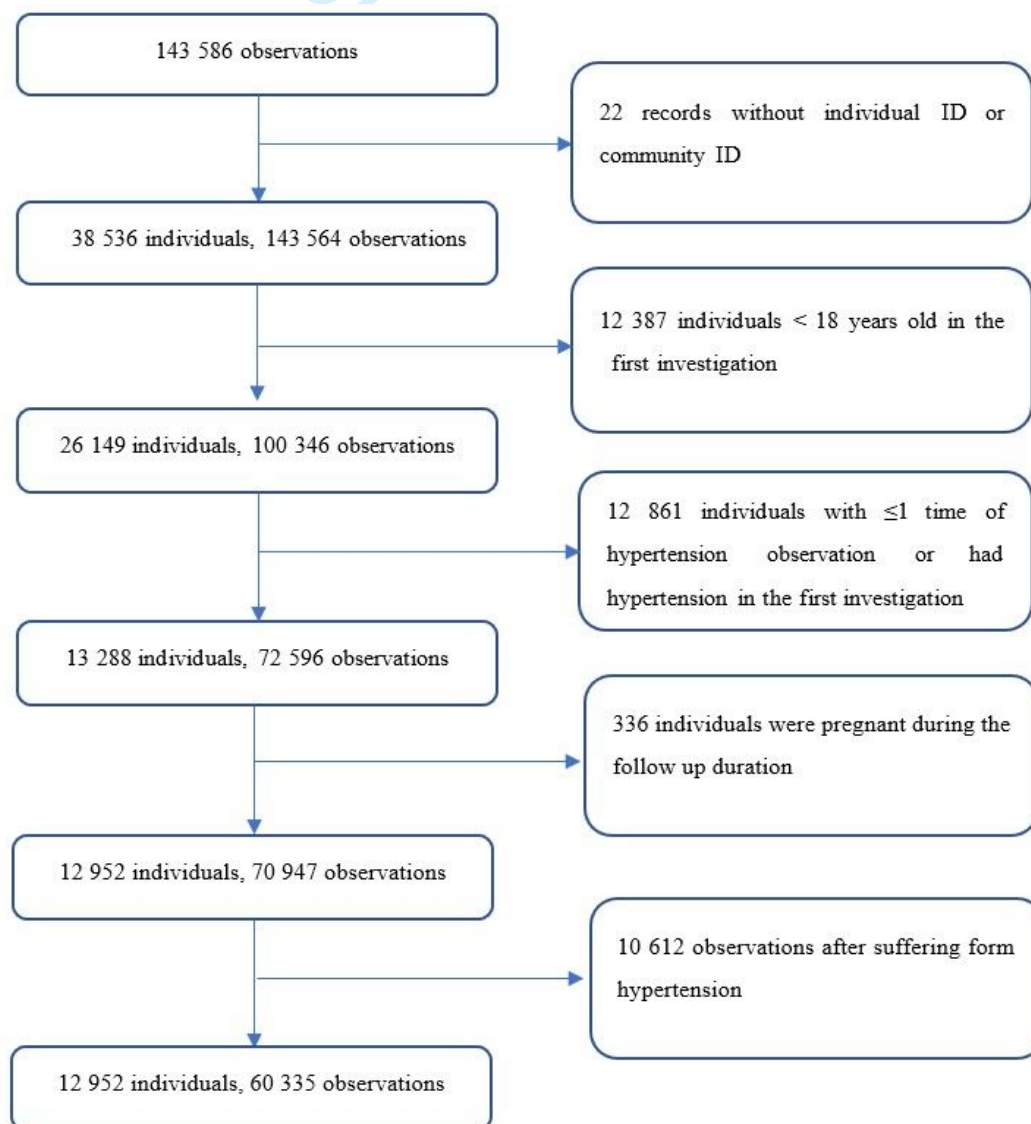


Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of

hypertension incidence in China

Exposure

The primary exposure variable of this study were time entering the cohort and geographic regions. For modeling analyses, it was not feasible to treat the waves as continuous variables, and therefore we respectively grouped the individuals entering the cohort from (a) 1991, 1993, and 1997; (b) 2000, 2004, 2006, and 2009; and (c) 2011 and 2015. In this case, two dummies were introduced in the model with individuals from 1991 to 1997 as the reference group. Geographic regions were defined according to the bulletin of the National Bureau of Statistics of China. Specifically, we grouped individuals from (a) Beijing, Shanghai, Jiangsu Province, Zhejiang Province, and Shandong Province as Eastern China; (b) Henan Province, Hubei Province, and Hunan Province as Central China; (c) Liaoning Province and Heilongjiang Province as Northeastern China; and (d) Yunnan Province, Guangxi Zhuang Autonomous Region, Guizhou Province, Chongqing, and Shanxi Province as Western China.

Outcomes

We included incidence of hypertension as the primary outcome. First, we adopted self-reported hypertension, which was derived from the answer to the question, “Has a doctor ever told you that you suffer from high blood pressure?”. If individuals self-reported no hypertension history, the outcomes would be further supplemented by the blood pressure tests to avoid the recall bias and underestimation from self-reported measures. According to the criteria of the 2018 Clinical Guideline in China and the 2018 ESC/ESH HTN Guideline,²³ hypertension was confirmed with the systolic blood pressure (SBP) ≥ 140 mmHg or with the diastolic blood pressure (DBP) ≥ 90 mmHg. To guarantee the accuracy of the tests, the blood pressure was

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5 detected in triplicate by professional health workers on the same day.
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8 **Covariates**

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11 To adjust for variations in baseline characteristics, we introduced several confounding factors that may
12 influence the occurrence of hypertension. These factors included urban vs. rural settings, sociodemographic
13 characteristics (age, sex, race, marital status, educational attainment, and employment status), and lifestyle
14 attributes (BMI, smoking behaviors, alcohol consumption, and physical activity).^{15 24}
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23 **Statistical analysis**

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26 First, we performed chi-square tests and Kruskal-Wallis rank-sum tests to evaluate variations in baseline
27 characteristics over time. Second, we calculated the crude incidence of hypertension as below:²⁵
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$$32 \text{ Incidence} = \frac{\text{number of new hypertension cases}}{\text{total person - years at risk}}$$

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35 The 'person-years at risk' is the period from the first hypertension-free year to the year when the subsequent
36 hypertension is confirmed. In addition, we calculated the age-standardized incidence of hypertension by
37 employing the sample from wave 2011 and wave 2015 as the standard population. Subgroup analyses were
38 conducted by gender. To further evaluate the long-term trends of hypertension incidence, we performed an
39 extended Cox proportional hazard model while considering geographic variations. Because the effect of age
40 didn't conform to the proportional hazard assumption, we performed a time-dependent Cox regression model
41 with age as a time-dependent variable. At the same time, we introduced all covariates in the model to control
42 for the baseline variations.
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56 Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05
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was considered statistical significance.

Patient and public involvement

Neither patients nor members of the public were involved in this study.

RESULTS

Study population

Although CHNS consisted of data of 38 558 individuals with 143 586 observations from 1989 and 2015, the present study only included 12 952 individuals from 1991 to 2015 after sample selection (figure 1). Table 1 presents the distribution of observations from included individuals during the study period. For example, 5938 individuals entered the cohort in 1991, with only 912 followed-up in 2015 (table 1). Among the 12 952 participants, 5 119 suffered from hypertension during the follow-up period.

Table 1 Observation distribution of study sample from 1991 to 2015

wave	1991	1993	1997	2000	2004	2006	2009	2011	2015
1989									
1991	5938								
1993	5166	677							
1997	3313	485	1691						
2000	2658	335	1451	1009					
2004	2050	234	1037	813	837				
2006	1722	188	865	642	684	376			
2009	1378	142	385	398	413	302	692		
2011	1200	114	329	335	359	216	630	1732	
2015	912	86	250	236	231	152	353	1732	0

Table 2 presents the baseline characteristics of the study sample. Overall, variations existed in all baseline characteristics. For example, newly recruited individuals were older ($P < 0.001$), more educated ($P < 0.001$), and with a higher BMI ($P < 0.001$).

Table 2 Baseline characteristics of study individuals, $n(\%)$ *

Characteristic	Time entering the cohort			P value
	1991-1997	2000-2009	2011-2015	
Region				
Western	2256 (27.16)	611 (20.97)	523 (30.20)	<0.001
Central	2817 (33.92)	800 (27.45)	85 (4.91)	
Northeastern	1288 (15.51)	794 (27.25)	83 (4.79)	
Eastern	1945 (23.42)	709 (24.33)	1041 (60.10)	
Urban-rural				
Rural	5616 (67.61)	1717 (58.92)	777 (44.86)	<0.001
Urban	2690 (32.39)	1197 (41.08)	955 (55.14)	
Age (years)				
18-29	2374 (28.58)	695 (23.85)	221 (12.76)	<0.001
30-39	2382 (28.68)	854 (29.31)	345 (19.92)	
40-49	1752 (21.09)	621 (21.31)	424 (24.48)	
50-59	1004 (12.09)	405 (13.90)	456 (26.33)	
≥60	794 (9.56)	339 (11.63)	286 (16.51)	
Sex				
Male	3986 (47.99)	1168 (40.08)	736 (42.49)	<0.001
Female	4320 (52.01)	1746 (59.92)	996 (57.51)	
BMI (kg/m ²)				
<18.5	763 (9.27)	191 (6.60)	60 (3.46)	<0.001
18.5-23.9	6012 (73.07)	1776 (61.35)	955 (55.14)	
24.0-27.9	1238 (15.05)	760 (26.25)	545 (31.47)	

	≥28	215 (2.61)	168 (5.80)	172 (9.93)	
Race					
	Other	1038 (12.59)	340 (11.69)	72 (4.17)	<0.001
	Han	7204 (87.41)	2568 (88.31)	1656 (95.83)	
Marital status					
	Other	1183 (14.29)	341 (11.82)	192 (11.14)	<0.001
	Married	7098 (85.71)	2545 (88.18)	1531 (88.86)	
Education attainment					
	Primary school and below	4416 (53.81)	741 (26.43)	410 (23.73)	<0.001
	Middle school	2377 (28.97)	1103 (39.34)	457 (26.45)	
	High school or equivalent	1240 (15.11)	742 (26.46)	472 (27.31)	
	College and above	173 (2.11)	218 (7.77)	389 (22.51)	
Employed					
	No	1145 (13.85)	1044 (35.95)	716 (41.34)	<0.001
	Yes	7121 (86.15)	1860 (64.05)	1016 (58.66)	
Smoking					
	Never or smoking cessation	5300 (64.72)	2163 (74.97)	1326 (77.18)	<0.001
	Current smoker, cigarettes < 20/d	1481 (18.09)	370 (12.82)	205 (11.93)	
	Current smoker, cigarettes ≥ 20/d	1408 (17.19)	352 (12.20)	187 (10.88)	
Alcohol consumption					
	Never	5042 (61.82)	2037 (70.93)	1116 (65.03)	<0.001
	Not more than once per month	469 (5.75)	102 (3.55)	144 (8.39)	
	1–3 times per month	661 (8.10)	173 (6.02)	127 (7.40)	
	1–2 times per week	781 (9.58)	227 (7.90)	127 (7.40)	
	3–4 times per week	450 (5.52)	126 (4.39)	64 (3.73)	
	On a daily basis	753 (9.23)	207 (7.21)	138 (8.04)	
Physical activity					
	Very light	997 (12.56)	780 (27.73)	823 (49.46)	<0.001
	Light	1307 (16.46)	799 (28.40)	453 (27.22)	

Moderate	1291 (16.26)	461 (16.39)	209 (12.56)
Heavy or very heavy	4344 (54.71)	773 (27.48)	179 (10.76)

*Overall, we included 11 685 individuals in the modelling analyses after excluding 97 individuals without BMI, 74 without race, 62 without marital status, 214 without education attainment, 50 without employment status, 160 without smoking history, 208 without alcohol consumption, and 449 without physical activity. (Missing rate 9.78 %)

Crude and age-standardized incidence

Table 3 presents the crude and age-standardized hypertension incidence during the study period. For the calculation of hypertension incidence, we employed a full sample of 12 952 individuals with 60 335 observations. The age-standardized incidence of hypertension witnessed a significant increase, ranging from 40.8 per 1 000 person-years (95% CI: 38.3 to 43.4) between 1993 and 1997 to 48.6 per 1 000 person-years (95% CI: 46.1 to 51.0) between 2011 and 2015. The increasing pattern was also exhibited among men (1993-1997: 46.2, 95% CI: 42.1 to 50.4; 2011-2015: 55.7, 95% CI: 51.7 to 59.7) and women (1993-1997: 36.5, 95% CI: 33.2 to 39.7; 2011-2015: 43.3, 95% CI: 40.2 to 46.3).

Table 3 Crude and age-standardized incidence over time (per 1000 person-years)

Incidence	1991	1993-1997	2000-2009	2011-2015
Total				
Case (person-year)	-	1114 (35486)	2571 (70575)	1434 (29492)
Crude incidence (95% CI)	-	31.3 (29.6-33.2)	36.4 (35.0-37.8)	48.6 (46.1-51.2)
Age-standardized incidence (95% CI)	-	40.8 (38.3-43.4)	41.5 (39.9-43.2)	48.6 (46.1-51.0)
Male				
Case (person-year)	-	594 (17530)	1292 (32524)	699 (12532)
Crude incidence (95% CI)	-	33.8 (31.2-36.7)	39.7 (37.6-41.9)	55.7 (51.7-60.0)
Age-standardized incidence (95% CI)	-	46.2 (42.1-50.4)	45.7 (43.0-48.3)	55.7 (51.7-59.7)
Female				
Case (person-year)	-	520 (17956)	1279 (38051)	735 (16960)
Crude incidence (95% CI)	-	28.9 (26.5-31.5)	33.6 (31.8-35.5)	43.3 (40.3-46.5)
Age-standardized incidence (95% CI)	-	36.5 (33.2-39.7)	38.0 (35.9-40.1)	43.3 (40.2-46.3)

Extended Cox proportional hazard analysis

For the modeling analysis, we included 11 685 individuals without missing data (missing rate, 9.78%). The duration from free of hypertension to hypertension diagnosed ranged from 2 to 24 years, with a median of 9 years (table 4). The duration was most commonly seen in 2 (14.32%), 4 (11.19%), 6 (11.45%), and 9 years (13.13%).

Table 4 Unadjusted time from hypertension-free to hypertension

Time (year)	<i>n</i>	Proportion (%)
2	733	14.32
3	227	4.43
4	573	11.19
5	94	1.84
6	586	11.45
7	253	4.94
9	672	13.13
11	121	2.36
12	82	1.60
13	383	7.48
14	55	1.07
15	357	6.97
16	45	0.88
18	425	8.30
20	187	3.65
22	43	0.84
24	283	5.35
Total	5119	100.0

Table 5 presents results from extended Cox proportional hazard analysis while taking variations in baseline characteristics into account. First, the increasing trends of hypertension incidence were robust, as suggested by the modeling results. Specifically, individuals entered the cohort from 2000 to 2009 (aHR = 1.10, 95% CI: 1.01 to 1.21) and those from 2011 to 2015 (aHR = 1.19, 95% CI: 1.04 to 1.37) had a higher risk of hypertension in comparison with individuals entering the cohort from 1991 to 1997. With reference to

regional variations, individuals in Central (aHR = 1.26, 95% CI: 1.16 to 1.37), Northeastern (aHR = 1.56, 95% CI: 1.41 to 1.72), and Eastern China (aHR = 1.48, 95% CI: 1.36 to 1.63) respectively had a higher risk of hypertension occurrence relative to their counterparts in Western China.

Table 5 Extended Cox proportional hazard analysis of hypertension incidence

Characteristic	aHR (95% CI)	P value
Time to enter the cohort		
1991-1997	Ref.	
2000-2009	1.10 (1.01-1.21)	0.025
2011-2015	1.19 (1.04-1.37)	0.010
Geographic region		
Western	Ref.	
Central	1.26 (1.16-1.37)	<0.001
Northeastern	1.56 (1.41-1.72)	<0.001
Eastern	1.48 (1.36-1.63)	<0.001
Urban (vs. rural)	0.94 (0.88-1.01)	0.109
Age*		
18-29	Ref.	
30-39	1.93 (1.41-2.65)	<0.001
40-49	3.99 (2.93-5.43)	<0.001
50-59	5.16 (3.74-7.12)	<0.001
≥60	9.11 (6.50-12.77)	<0.001
Female (vs. male)	0.81 (0.74-0.88)	<0.001
BMI (kg/m ²)		
<18.5	Ref.	
18.5-23.9	1.31 (1.16-1.48)	<0.001
24.0-27.9	2.07 (1.81-2.36)	<0.001
≥28	2.82 (2.37-3.34)	<0.001

Race (Han vs. others)	1.11 (1.01-1.23)	0.032
Married (vs. others)	0.92 (0.83-1.02)	0.149
Education attainment		
Primary school and below	Ref.	
Middle school	0.91 (0.84-0.99)	0.020
High school or equivalent	0.86 (0.77-0.95)	0.002
College and above	0.82 (0.68-0.98)	0.033
Employed (yes vs. no)	0.90 (0.82-0.99)	0.036
Smoking		
Never or smoking cessation	Ref.	
Current smoker, cigarettes < 20/d	0.98 (0.89-1.07)	0.752
Current smoker, cigarettes ≥ 20/d	1.05 (0.96-1.16)	0.237
Alcohol consumption		
never	Ref.	
Not more than once per month	0.89 (0.78-1.03)	0.125
1–3 times per month	1.17 (1.04-1.32)	0.006
1–2 times per week	1.00 (0.89-1.12)	0.963
3–4 times per week	1.05 (0.92-1.21)	0.412
On a daily basis	1.18 (1.06-1.31)	0.002
Physical activity		
very light	Ref.	
light	0.92 (0.83-1.02)	0.154
moderate	0.99 (0.88-1.11)	0.930
heavy and very	0.91 (0.82-1.02)	0.118

*Estimated time effect of age, $P < 0.001$

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5 In addition, there existed no urban-rural differences in developing hypertension (table 5). Risks of incident
6 hypertension increased with age, BMI, and alcohol consumption, while it was negatively associated with
7 educational attainment. Women had a lower risk of incident hypertension compared with men (aHR = 0.81,
8 95% CI: 0.74 to 0.88). Relative to those without a job, employees had a lower risk of developing hypertension
9 (aHR = 0.90, 95% CI: 0.82 to 0.99). Han individuals were significantly associated with a higher risk (aHR =
10 1.11, 95% CI: 1.01 to 1.23) relative to the minority.
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21 **DISCUSSION**

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24 By employing a study sample of 12 925 individuals from diverse social and geographic contexts, we found
25 the age-standardized incidence of hypertension increased during the study period. The increasing pattern
26 remained even after controlling for variations in baseline characteristics. Furthermore, we found that
27 individuals in economically developed Eastern, Central, and Northeastern China had greater risks of incident
28 hypertension in comparison with those in Western China.
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39 Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence
40 measure. For example, one of the previous studies in China indicated that the prevalence of hypertension
41 rose substantially from 13.6% in 1991 to 27.9% in 2015.¹¹ The findings were further supplemented by results
42 from Lu *et al.* (2017), which suggested a higher prevalence of hypertension among those aged between 35
43 and 75 years old (44.7%).²⁶
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52 However, our focus on the incidence measure provided a more accurate reflection of the epidemiologic
53 transition of hypertension in China. In addition, our findings updated the trends of hypertension incidence
54 in comparison with that from Liang *et al.* (2014).¹⁵ Even though hypertension incidence appeared to vary
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5 across countries,²⁷⁻²⁹ the comparison is untenable because we adopted different standard populations. Further
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8 empirical research across countries is warranted.
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11 With the rapid economic development, people often change their dietary patterns from light diet to high salt
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13 and fat diet along with a secondary lifestyle.³⁰ These changes would significantly impact the prevalence and
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15 control of hypertension in China.³⁰ In addition, due to data limitation, we didn't introduce several potential
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17 risks factors, such as sodium intake or dietary pattern, parental history, psychological status, ambient air
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19 pollutants, working hours, and household income.³¹⁻³⁴ These factors may explain the residual time-effects in
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22 the model as well.
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27 Although existing evidence on the regional disparities of hypertension incidence is scant, prior research
28
29 indicates that Central, Northeastern, and Eastern China had a higher prevalence of hypertension compared
30
31 with Western China,³⁵ which is in line with our findings. In sharp contrast, prior investigators have noted
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33 that Northeastern and Central China had lower all-cause mortality rates relative to Western China.³⁶ These
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35 findings appear to suggest that individuals in China's economically developed regions are experiencing
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37 extended life expectancy with relatively unhealthy aging.¹² However, one should be aware of the possibility
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39 that although individuals in Western China had lower risks of hypertension compared with the other three
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42 regions, local public awareness and timely treatment could be a challenging issue.
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47 Differed from previous studies,^{15 37} no urban-rural disparities were observed in the present study. This may
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49 be a result of the narrow gap of lifestyle between rural and urban residents. With the rapid economic
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51 development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are
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53 approaching to those of their counterparts in urban China.^{9 10} This possibility has been further supported by
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5 the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.²⁶ Taking
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8 into account the lower treatment rate and insufficient awareness among rural residents,³⁸ one should direct
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10 more attention to rural China.

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14 Moreover, we found that smoking history was not associated with incident hypertension. The effect of
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16 smoking on the development of the chronic disease is unclear and appears to differ across life courses.³⁹⁻⁴¹

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19 In addition, prior research based on Korean has found a J-shaped association between physical activity and
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21 incident hypertension,⁴² while the present study on Chinese did not observe a similar association, which is
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23 in line with findings based on Japanese.⁴³ The effect of physical activity on the development of hypertension
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25 seems to be controversial and varies across countries. Further analyses are warranted.

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30 Consistent with the previous studies,⁴⁴⁻⁴⁷ several risk factors, including age, gender, educational attainment,
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32 race, alcohol consumption, and BMI, were confirmed by our analyses. The growing incidence of
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34 hypertension emphasizes the early prevention, education, detection, and management for hypertension.⁴⁸

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38 Mentoring aforementioned lifestyle behaviors, such as alcohol consumption, may be helpful to constrain the
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40 hypertension incidence.⁴⁹ Public health and lifestyle interventions targeting high-risk individuals, such as
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42 the elderly, men, and obese population, hold promise.

43 44 45 46 **Conclusion**

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49 Hypertension incidence increased during the study period. Individuals in Eastern, Central, and Northeastern
50
51 China had greater risks of hypertension occurrence in comparison with their counterparts in Western China.
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53 In addition, risks of incident hypertension increased with age, BMI, and alcohol consumption, while it was
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55 negatively associated with educational attainment. The growth of hypertension incidence called for more
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5 attention on the health education and health promotion of individuals with great risks.
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8 **Strengths and limitations of this study**

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10
11 The present study has two major strengths. First, the dynamic cohort study-design employed individuals
12 from diverse social and geographic contexts, which enabled us to depict the long-term trends of hypertension
13 incidence and regional disparities in the context of China's rapid social development and population aging.
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15 In addition, we adopted both self-reported health outcomes and objective outcomes from physical tests,
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17 which avoided the recall bias and underestimation in underserved areas.
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21 Nevertheless, this study is subject to several limitations. First, we did not employ a national-representative
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23 sample and did not include individuals from other provinces in China, which undermined the representation
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25 of our findings. As a community-based survey, CHNS excluded institutionalized individuals, which further
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27 diminished the representation of our findings among Chinese. In addition, we did not distinguish
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29 hypertension, and future research is necessary.
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59 **Contributors** WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical
60

analysis, and wrote the first draft of the manuscript, which P-YL and W-ZH subsequently revised. All authors read the article and approve it for publication.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval China Health and Nutrition Survey (CHNS) was approved by the ethics committee of Carolina Population Center at the University of North Carolina at Chapel Hill and the NINH at the CCDC. Informed consent was obtained from all subjects before the investigation. The present study derived data from the public domain, and therefore ethics statement and informed consents were not applicable.

Data availability statement Data are available from China Health and Nutrition Survey (<https://www.cpc.unc.edu/projects/china/data/>).

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1 Title Page

2 **Title : Long-term trends and regional variations of hypertension incidence in China: a**
3 **dynamic prospective cohort study**

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16 ABSTRACT

17 **Objective** The aim is to explore the trends of hypertension incidence and regional variations in China from
18 1991 to 2015.

19 **Design** A dynamic prospective cohort study.

20 **Setting** China Health and Nutrition Survey (CHNS) 1991-2015.

21 **Participants** 12 952 Chinese adults aged 18+.

22 **Primary outcome measures** Incident hypertension from 1993 to 2015.

23 **Results** Age-standardized hypertension incidence increased from 40.8 per 1 000 person-years (95% CI,
24 38.3 to 43.4) between 1993 and 1997 to 48.6 (95% CI, 46.1 to 51.0) between 2011 and 2015. The increasing
25 trends were further supported by results from subsequent extended Cox proportional hazard model. In
26 addition, results from the modelling analysis showed that individuals in Eastern, Central, and Northeastern
27 China had greater risks of hypertension occurrence in comparison with their counterparts in Western China.

28 **Conclusion** Hypertension incidence increased during the study period. The growth called for more
29 attention on the health education and health promotion of individuals with great risks.

31 **Strengths and limitations of this study**

32 ① The dynamic cohort study-design employed individuals from diverse social and geographic contexts,
33 which enabled us to depict the long-term trends of hypertension incidence and regional disparities in the
34 context of China's rapid social development and population aging.

35 ② According to the design of CHNS and the underestimation of self-reported data, we adopted both self-
36 reported health outcomes and objective outcomes from physical tests, which to some extent avoided the
37 recall bias and underestimation in underserved areas.

38 ③ We did not employ a national-representative sample and did not include individuals from all provinces in
39 China, which undermined the representation of our findings. As a community-based survey, CHNS excluded
40 institutionalized individuals, which further diminished the representation of our findings among Chinese.

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5 41 ④Guidelines recommend to identify hypertension cases by using blood pressure values that are measured
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8 42 in different days, while individuals' blood pressure data in the CHNS were collected on the same day in the
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10 43 CHNS, leading to unavoidable bias.

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14 44 ⑤In addition, we did not distinguish the grade of hypertension, and future research is necessary.

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For peer review only

46 INTRODUCTION

47 Along with aging population, non-communicable chronic diseases, particularly stroke and ischemic heart
48 disease, have led to great burden of disease, deaths, and years of life lost (YLLs) in both developed and
49 developing countries.^{1 2} Connected closely with various cardiovascular diseases,^{3 4} high systolic blood
50 pressure was ranked as the leading risk factor of risk-attributable disability-adjusted life-years (DALYs)
51 among selected 195 countries and territories.⁵ For instance, high systolic blood pressure accounted for 2.54
52 million deaths and more than 5% of DALYs in China in 2017.⁶

53 Existing evidence has confirmed a worldwide high prevalence of hypertension.⁴⁻⁶ Countries, such as
54 Singapore⁶ and Korea⁷, had a significant proportion of individuals with hypertension. Likewise, with the
55 extended life expectancy,⁸ changes in lifestyle behaviors,⁹ and rapid urbanization,¹⁰ developing countries,
56 such as China, experienced a substantial increase in the prevalence of hypertension, ranging from 13.6% in
57 1991 to 27.9% in 2015.¹¹

58 Although the increasing prevalence of hypertension provided critical information for public health practice
59 and disease control programs, it could not accurately depict the epidemiologic transition as the incidence
60 measure.¹² Prior studies have indicated that the increasing prevalence could coexist with the decreasing
61 incidence in the context of healthy aging.¹³ For evidence-based health-promoting initiatives, empirical
62 research on hypertension incidence is warranted.

63 However, research on the long-term trends of the incidence of hypertension from China is scare and
64 relatively outdated.^{14 15} This is an important knowledge gap because developing countries are experiencing
65 unprecedented social development. Up-to-date information among developing countries could greatly

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5 66 contribute to depict global epidemiologic transitions. Moreover, regional disparities are a major health
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8 67 concern in China as a result of inequitable socio-economic development and health care resource
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10 68 distribution,¹⁶⁻¹⁸ while the existing research provides insufficient information regarding the regional
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13 69 disparities in the hypertension incidence.¹⁹⁻²¹

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16 70 Hence, this study aims to explore the long-term trends of hypertension incidence among Chinese from
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18 71 diverse social and geographic contexts. In addition, we are particularly interested in regional variations while
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21 72 taking the individual-level risk factors into account.

22 23 24 25 73 **METHODS**

26 27 28 74 **Data source**

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31 75 The present study derived data from the China Health and Nutrition Survey (CHNS). CHNS has been
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33 76 collaboratively conducted by Carolina Population Center at the University of North Carolina at Chapel Hill
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35 77 and the National Institute for Nutrition and Health (NINH, former National Institute of Nutrition and Food
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37 78 Safety) at the Chinese Center for Disease Control and Prevention. Initiated in 1989, CHNS consisted of ten-
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41 79 wave data in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015, respectively. Overall, CHNS
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44 80 employed a multistage random cluster method to draw the study sample, which included over 30 000
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47 81 individuals from three provincial-level cities and twelve provinces. Individuals in the survey came from
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50 82 diverse social, geographic, and cultural contexts. CHNS employed face-to-face questionnaire interviews to
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53 83 collect data, and the physical health examinations were conducted by well-trained investigators. Information
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55 84 regarding survey design, data collection, and quality control could be retrieved from the cohort profile.²²

56 57 58 85 **Study design and exclusion criteria**

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5 86 The present study employed a dynamic cohort study-design as not all individuals entered the cohort at the
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8 87 same time. To evaluate the long-term trends of hypertension incidence, we excluded individuals (a) without
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11 88 individual ID and community ID; (b) aged under 18 because of the low incidence of hypertension among
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14 89 children and teenagers; (c) with hypertension in his/her first investigation; (d) with only one observation or
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16 90 only one record of hypertension status; and (e) were pregnant during the study period to exclude gestational
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19 91 hypertension. Furthermore, we excluded observations after the diagnosis of hypertension (figure 1).

92 **Exposures**

93 The primary exposure variable of this study were the timing of entering the cohort and geographic regions.
94 For modeling analyses, it was not feasible to treat the waves as continuous variables, and therefore we
95 respectively grouped the individuals entering the cohort from (a) 1991, 1993, and 1997; (b) 2000, 2004,
96 2006, and 2009; and (c) 2011 and 2015. In this case, two dummies were introduced in the model with
97 individuals from 1991 to 1997 as the reference group.

98 Geographic regions were defined according to the bulletin of the National Bureau of Statistics of China.
99 Specifically, we grouped individuals from (a) Beijing, Shanghai, Jiangsu Province, Zhejiang Province, and
100 Shandong Province as Eastern China; (b) Henan Province, Hubei Province, and Hunan Province as Central
101 China; (c) Liaoning Province and Heilongjiang Province as Northeastern China; and (d) Yunnan Province,
102 Guangxi Zhuang Autonomous Region, Guizhou Province, Chongqing, and Shanxi Province as Western
103 China.

104 **Outcomes**

105 We included incidence of hypertension as the primary outcome. First, we adopted self-reported hypertension,

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5 106 which was derived from the answer to the question, “Has a doctor ever told you that you had high blood
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8 107 pressure?”. If individuals self-reported no hypertension history, the outcomes would be further supplemented
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11 108 by the blood pressure tests to avoid the recall bias and underestimation from self-reported measures.
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13 109 According to the criteria of the 2018 Clinical Guideline in China and the 2018 ESC/ESH HTN Guideline,²³
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16 110 hypertension was confirmed with the systolic blood pressure (SBP)≥140 mmHg or with the diastolic blood
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18 111 pressure (DBP)≥90 mmHg. To guarantee the accuracy of the tests, the blood pressure was detected in
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21 112 triplicate by professional health workers on the same day.

113 **Covariates**

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27 114 To adjust for variations in baseline characteristics, we introduced several confounding factors that may
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30 115 influence the occurrence of hypertension. These factors included urban vs. rural settings, sociodemographic
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33 116 characteristics (age, sex, race, marital status, educational attainment, and employment status), and lifestyle
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35 117 attributes (BMI, smoking behaviors, alcohol consumption, and physical activity).^{15 24}

118 **Statistical analysis**

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42 119 First, we performed chi-square tests and Kruskal-Wallis rank-sum tests to evaluate variations in baseline
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44 120 characteristics over time. Second, we calculated the crude incidence of hypertension as below:²⁵

$$121 \quad \text{Incidence} = \frac{\text{number of new hypertension cases}}{\text{total person – years at risk}}$$

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51 122 The ‘person-years at risk’ is the period from the first hypertension-free year to the year when the subsequent
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53 123 hypertension is confirmed. In addition, we conducted direct standardization to calculate the age-standardized
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56 124 incidence of hypertension by using the study sample from wave 2011 and wave 2015 as the standard
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5 125 population. Subgroup analyses were conducted by sex.
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9 126 To further evaluate the long-term trends and geographic variations of incident hypertension, we performed
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11 127 an extended Cox proportional hazard model while including all covariates to control for baseline variations.
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14 128 Because the effect of age didn't conform to the proportional hazard assumption, we performed a time-
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16 129 dependent Cox regression model with age as a time-dependent variable. As for sensitivity analyses, we
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19 130 construct the multi-level Poisson regression indicating similar findings.
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22 131 Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05
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25 132 was considered statistical significance.
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28 133 **Patient and public involvement**

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31 134 Not applicable. Data are derived from public domain.
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34 135 **RESULTS**

36 37 38 136 **Study population**

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41 137 The CHNS consisted of data of 38 558 individuals with 143 586 observations from 1989 and 2015, and the
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44 138 present study only included 12 952 individuals from 1991 to 2015 after sample selection (figure 1). Table 1
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46 139 presents the distribution of observations from included individuals during the study period. For example, 5
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49 140 938 individuals entered the cohort in 1991, with only 912 followed-up in 2015 (table 1). Among the 12 952
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51 141 participants, 5 119 of them developed hypertension during the follow-up period.
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5 143 **Table 1** Observation distribution of study sample from 1991 to 2015

Wave	1991	1993	1997	2000	2004	2006	2009	2011	2015
1989									
1991	5938								
1993	5166	677							
1997	3313	485	1691						
2000	2658	335	1451	1009					
2004	2050	234	1037	813	837				
2006	1722	188	865	642	684	376			
2009	1378	142	385	398	413	302	692		
2011	1200	114	329	335	359	216	630	1732	
2015	912	86	250	236	231	152	353	1732	0

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145 Table 2 presents the baseline characteristics of the study sample. Overall, variations existed in all baseline
146 characteristics. Newly recruited individuals were older ($P < 0.001$) and well-educated ($P < 0.001$). They
147 were more likely to be obese ($P < 0.001$), Han ($P < 0.001$), and male ($P < 0.001$), and they were less likely
148 to be smokers ($P < 0.001$), employed ($P < 0.001$), and physically active ($P < 0.001$).

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150 **Table 2** Baseline characteristics of study individuals, *n*(%)*

Characteristic	Time entering the cohort			<i>P</i> value
	1991-1997	2000-2009	2011-2015	
Region				
Western	2256 (27.16)	611 (20.97)	523 (30.20)	<0.001
Central	2817 (33.92)	800 (27.45)	85 (4.91)	
Northeastern	1288 (15.51)	794 (27.25)	83 (4.79)	
Eastern	1945 (23.42)	709 (24.33)	1041 (60.10)	
Urban-rural				
Rural	5616 (67.61)	1717 (58.92)	777 (44.86)	<0.001
Urban	2690 (32.39)	1197 (41.08)	955 (55.14)	
Age (years)				
18-29	2374 (28.58)	695 (23.85)	221 (12.76)	<0.001
30-39	2382 (28.68)	854 (29.31)	345 (19.92)	
40-49	1752 (21.09)	621 (21.31)	424 (24.48)	
50-59	1004 (12.09)	405 (13.90)	456 (26.33)	
≥60	794 (9.56)	339 (11.63)	286 (16.51)	
Sex				
Male	3986 (47.99)	1168 (40.08)	736 (42.49)	<0.001
Female	4320 (52.01)	1746 (59.92)	996 (57.51)	
BMI (kg/m ²)				
<18.5	763 (9.27)	191 (6.60)	60 (3.46)	<0.001
18.5-23.9	6012 (73.07)	1776 (61.35)	955 (55.14)	
24.0-27.9	1238 (15.05)	760 (26.25)	545 (31.47)	
≥28	215 (2.61)	168 (5.80)	172 (9.93)	
Race				
Other	1038 (12.59)	340 (11.69)	72 (4.17)	<0.001
Han	7204 (87.41)	2568 (88.31)	1656 (95.83)	
Marital status				

Other	1183 (14.29)	341 (11.82)	192 (11.14)	<0.001
Married	7098 (85.71)	2545 (88.18)	1531 (88.86)	
Education attainment				
Primary school and below	4416 (53.81)	741 (26.43)	410 (23.73)	<0.001
Middle school	2377 (28.97)	1103 (39.34)	457 (26.45)	
High school or equivalent	1240 (15.11)	742 (26.46)	472 (27.31)	
College and above	173 (2.11)	218 (7.77)	389 (22.51)	
Employed				
No	1145 (13.85)	1044 (35.95)	716 (41.34)	<0.001
Yes	7121 (86.15)	1860 (64.05)	1016 (58.66)	
Smoking history				
Never or smoking cessation	5300 (64.72)	2163 (74.97)	1326 (77.18)	<0.001
Current smoker, cigarettes < 20/d	1481 (18.09)	370 (12.82)	205 (11.93)	
Current smoker, cigarettes ≥ 20/d	1408 (17.19)	352 (12.20)	187 (10.88)	
Alcohol consumption				
Never	5042 (61.82)	2037 (70.93)	1116 (65.03)	<0.001
Not more than once per month	469 (5.75)	102 (3.55)	144 (8.39)	
1-3 times per month	661 (8.10)	173 (6.02)	127 (7.40)	
1-2 times per week	781 (9.58)	227 (7.90)	127 (7.40)	
3-4 times per week	450 (5.52)	126 (4.39)	64 (3.73)	
On a daily basis	753 (9.23)	207 (7.21)	138 (8.04)	
Physical activity				
Very light	997 (12.56)	780 (27.73)	823 (49.46)	<0.001
Light	1307 (16.46)	799 (28.40)	453 (27.22)	
Moderate	1291 (16.26)	461 (16.39)	209 (12.56)	
Heavy or very heavy	4344 (54.71)	773 (27.48)	179 (10.76)	

151 *Overall, we included 11 685 individuals in the modelling analyses after excluding 97 individuals without

152 BMI, 74 without race, 62 without marital status, 214 without educational attainment, 50 without employment

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5 153 status, 160 without smoking history, 208 without alcohol consumption, and 449 without physical activity.

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8 154 (Missing rate 9.78 %)

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14 156 **Crude and age-standardized incidence**

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18 157 Table 3 presents the crude and age-standardized hypertension incidence during the study period. For the

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20 158 calculation of hypertension incidence, we employed the full sample of 12 952 individuals with 53 703

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23 159 observations. The age-standardized incidence of hypertension witnessed a significant increase, ranging from

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25 160 40.8 per 1 000 person-years (95% CI: 38.3 to 43.4) between 1993 and 1997 to 48.6 per 1 000 person-years

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28 161 (95% CI: 46.1 to 51.0) between 2011 and 2015. The increasing pattern was also exhibited among men (1993-

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30 162 1997: 46.2, 95% CI: 42.1 to 50.4; 2011-2015: 55.7, 95% CI: 51.7 to 59.7) and women (1993-1997: 36.5,

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33 163 95% CI: 33.2 to 39.7; 2011-2015: 43.3, 95% CI: 40.2 to 46.3).

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165 **Table 3** Crude and age-standardized incidence over time, per 1000 person-years

Incidence	1991	1993-1997	2000-2009	2011-2015
Total				
Case (person-year)	-	1114 (35486)	2571 (70575)	1434 (29492)
Crude incidence (95% CI)	-	31.3 (29.6-33.2)	36.4 (35.0-37.8)	48.6 (46.1-51.2)
Age-standardized incidence (95% CI) *	-	40.8 (38.3-43.4)	41.5 (39.9-43.2)	48.6 (46.1-51.0)
Male				
Case (person-year)	-	594 (17530)	1292 (32524)	699 (12532)
Crude incidence (95% CI)	-	33.8 (31.2-36.7)	39.7 (37.6-41.9)	55.7 (51.7-60.0)
Age-standardized incidence (95% CI) *	-	46.2 (42.1-50.4)	45.7 (43.0-48.3)	55.7 (51.7-59.7)
Female				
Case (person-year)	-	520 (17956)	1279 (38051)	735 (16960)
Crude incidence (95% CI)	-	28.9 (26.5-31.5)	33.6 (31.8-35.5)	43.3 (40.3-46.5)
Age-standardized incidence (95% CI) *	-	36.5 (33.2-39.7)	38.0 (35.9-40.1)	43.3 (40.2-46.3)

166 * Age-standardized incidence was calculated using the study sample in 2011-2015 as the standard population.

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168 **Extended Cox proportional hazard analysis**

169 For the modeling analysis, we included 11 685 individuals without missing data (missing rate, 9.78%).

170 Among the identified cases, the duration from free of hypertension to incident hypertension ranged from 2

171 to 24 years, with a median of 9 years.

172 Table 4 presents results from extended Cox proportional hazard analysis while taking variations in baseline

173 characteristics into account. First, the increasing trends of hypertension incidence were robust, as suggested

174 by the modeling results. Specifically, individuals entering the cohort from 2000 to 2009 (aHR = 1.10, 95%

175 CI: 1.01 to 1.21) and those from 2011 to 2015 (aHR = 1.19, 95% CI: 1.04 to 1.37) had a higher risk of

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5 176 hypertension in comparison with individuals entering the cohort from 1991 to 1997. With reference to
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8 177 regional variations, individuals in Central (aHR = 1.26, 95% CI: 1.16 to 1.37), Northeastern (aHR = 1.56,
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10 178 95% CI: 1.41 to 1.72), and Eastern China (aHR = 1.48, 95% CI: 1.36 to 1.63) respectively had a higher risk
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13 179 of hypertension occurrence relative to their counterparts in Western China.
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181 **Table 4** Extended Cox proportional hazard analysis of hypertension incidence

Characteristic	aHR (95% CI)	P value
Timing of entering the cohort		
1991-1997	Ref.	
2000-2009	1.10 (1.01-1.21)	0.025
2011-2015	1.19 (1.04-1.37)	0.010
Geographic region		
Western	Ref.	
Central	1.26 (1.16-1.37)	<0.001
Northeastern	1.56 (1.41-1.72)	<0.001
Eastern	1.48 (1.36-1.63)	<0.001
Urban (vs. rural)	0.94 (0.88-1.01)	0.109
Age*		
18-29	Ref.	
30-39	1.93 (1.41-2.65)	<0.001
40-49	3.99 (2.93-5.43)	<0.001
50-59	5.16 (3.74-7.12)	<0.001
≥60	9.11 (6.50-12.77)	<0.001
Female (vs. male)	0.81 (0.74-0.88)	<0.001
BMI (kg/m ²)		
<18.5	Ref.	
18.5-23.9	1.31 (1.16-1.48)	<0.001
24.0-27.9	2.07 (1.81-2.36)	<0.001
≥28	2.82 (2.37-3.34)	<0.001
Race (Han vs. others)	1.11 (1.01-1.23)	0.032
Married (vs. others)	0.92 (0.83-1.02)	0.149
Educational attainment		
Primary school and below	Ref.	
Middle school	0.91 (0.84-0.99)	0.020

High school or equivalent	0.86 (0.77-0.95)	0.002
College and above	0.82 (0.68-0.98)	0.033
Employed (yes vs. no)	0.90 (0.82-0.99)	0.036
Smoking		
Never or smoking cessation	Ref.	
Current smoker, cigarettes < 20/d	0.98 (0.89-1.07)	0.752
Current smoker, cigarettes \geq 20/d	1.05 (0.96-1.16)	0.237
Alcohol consumption		
never	Ref.	
Not more than once per month	0.89 (0.78-1.03)	0.125
1–3 times per month	1.17 (1.04-1.32)	0.006
1–2 times per week	1.00 (0.89-1.12)	0.963
3–4 times per week	1.05 (0.92-1.21)	0.412
On a daily basis	1.18 (1.06-1.31)	0.002
Physical activity		
very light	Ref.	
light	0.92 (0.83-1.02)	0.154
moderate	0.99 (0.88-1.11)	0.930
heavy and very	0.91 (0.82-1.02)	0.118

182 *Estimated time effect of age, $P < 0.001$

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184 In addition, there existed no urban-rural differences in developing hypertension (Table 4). Risks of incident
 185 hypertension increased with age, BMI, and alcohol consumption, while it was negatively associated with
 186 educational attainment. Women had a lower risk of incident hypertension compared with men (aHR = 0.81,
 187 95% CI: 0.74 to 0.88). Relative to those without a job, employees had a lower risk of developing hypertension
 188 (aHR = 0.90, 95% CI: 0.82 to 0.99). Han individuals were significantly associated with a higher risk (aHR =

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5 189 1.11, 95% CI: 1.01 to 1.23) relative to the minority.
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9 **DISCUSSION**

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12 191 By employing a study sample of 12 925 individuals from diverse social and geographic contexts, we found
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14 192 the age-standardized incidence of hypertension increased during the study period. The increasing pattern
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17 193 remained even after controlling for variations in baseline characteristics. Furthermore, we found that
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20 194 individuals in economically developed Eastern, Central, and Northeastern China had greater risks of incident
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22 195 hypertension in comparison with those in Western China.

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25 196 Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence
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28 197 measure. For example, one of the previous studies in China indicated that the prevalence of hypertension
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31 198 rose substantially from 13.6% in 1991 to 27.9% in 2015.¹¹ The findings were further supplemented by results
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34 199 from Lu *et al.* (2017), which suggested a higher prevalence of hypertension among those aged between 35
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36 200 and 75 years old (44.7%).²⁶ Compared with these earlier studies, our focus on the incidence measure
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39 201 provided a more accurate reflection of the epidemiologic transition of hypertension in China.¹² Our findings
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42 202 updated the trends of hypertension incidence in comparison with that from Liang *et al.* (2014), which
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44 203 indicated a similar pattern from 1991 to 2009.¹⁵ Even though hypertension incidence appeared to vary across
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46 204 countries,²⁷⁻²⁹ the comparison is untenable because we adopted different standard populations. Further
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49 205 empirical research across countries is warranted.

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52 206 With the rapid economic development, people often change their dietary patterns from light diet to high salt
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55 207 and fat diet along with a secondary lifestyle.³⁰ These changes would significantly impact the prevalence and
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58 208 control of hypertension in China.³⁰ In addition, due to data limitation, we were unable to introduce several
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5 209 potential risks factors, such as sodium intake or dietary pattern, parental history, psychological status,
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8 210 ambient air pollutants, working hours, and household income.³¹⁻³⁴ These factors may explain the residual
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10 211 time-effects in the model.

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14 212 Although existing evidence on the regional disparities of hypertension incidence is scant, prior research
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16 213 indicates that Central, Northeastern, and Eastern China had a higher prevalence of hypertension compared
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18 214 with Western China,³⁵ which is in line with our findings. In sharp contrast, prior investigators have noted
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20 215 that Northeastern and Central China had lower all-cause mortality rates relative to Western China.³⁶ These
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22 216 findings appear to suggest that individuals in China's economically developed regions are experiencing
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24 217 extended life expectancy with relatively unhealthy aging.¹² However, one should be aware of the possibility
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26 218 that although individuals in Western China had lower risks of hypertension compared with the other three
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28 219 regions, local public awareness and timely treatment could be a challenging issue.

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35 220 Differed from previous studies,^{15 37} no urban-rural disparities were observed in the present study. This may
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37 221 be a result of the narrowing gap of lifestyle between rural and urban residents. With the rapid economic
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39 222 development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are
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41 223 approaching to those of their counterparts in urban China.^{9 10} This possibility has been further supported by
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43 224 the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.²⁶ Taking
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45 225 into account the lower treatment rate and insufficient awareness among rural residents,³⁸ one should direct
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47 226 more attention to rural China.

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54 227 Moreover, we found that smoking history was not associated with incident hypertension. The effect of
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56 228 smoking on the development of the chronic disease is unclear and appears to differ across life courses.³⁹⁻⁴¹
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229 Prior research based on Korean has found a J-shaped association between physical activity and incident
230 hypertension,⁴² while the present study on Chinese did not observe a similar association, which is in line
231 with findings based on Japanese.⁴³ The effect of physical activity on the development of hypertension seems
232 to be controversial and varies across countries. Further analyses are warranted.

233 Consistent with the previous studies,⁴⁴⁻⁴⁷ several risk factors, including age, gender, educational attainment,
234 race, alcohol consumption, and BMI, were confirmed by our analyses. The growing incidence of
235 hypertension emphasizes the early prevention, education, detection, and management for hypertension.⁴⁸
236 Mentoring aforementioned lifestyle behaviors, such as alcohol consumption, may be helpful to constrain the
237 hypertension incidence.⁴⁹ Public health and lifestyle interventions targeting high-risk individuals, such as
238 older adults, men, and obese population, hold promise.

239 **Conclusion**

240 Hypertension incidence increased during the study period. Individuals in Eastern, Central, and Northeastern
241 China had greater risks of hypertension in comparison with their counterparts in Western China. Risks of
242 incident hypertension increased with age, BMI, and alcohol consumption, but negatively associated with
243 educational attainment. The growth of hypertension incidence calls for more attention on the health
244 education and health promotion of individuals with great risks.

245 **Strengths and limitations of this study**

246 The present study has two major strengths. First, the dynamic cohort study-design employed individuals
247 from diverse social and geographic contexts, which enabled us to depict the long-term trends of hypertension
248 incidence and regional disparities in the context of China's rapid social development and population aging.

249 In addition, we adopted both self-reported health outcomes and objective outcomes from physical tests,
250 which avoided the recall bias and underestimation in underserved areas.

251 Nevertheless, this study is subject to several limitations. First, we did not employ a national-representative
252 sample and did not include individuals from all provinces in China, which undermined the representation of
253 our findings. As a community-based survey, the CHNS excluded institutionalized individuals, which further
254 diminished the representation of our findings among Chinese. Third, 2018 Clinical Guideline in China
255 recommend to identify hypertension cases by using blood pressure values that are measured in different
256 days²³, while individuals' blood pressure data in the CHNS were collected on the same day in the CHNS,
257 leading to unavoidable bias. Last, we did not distinguish the grade of hypertension, and future research is
258 necessary.

259
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263 future surveys, and the China-Japan Friendship Hospital, Ministry of Health for support for CHNS 2009, Chinese National
264 Human Genome Center at Shanghai since 2009, and Beijing Municipal Center for Disease Prevention and Control since 2011.

265
Contributors WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical
266 analysis, and wrote the first draft of the manuscript, which P-YL and W-ZH subsequently revised. All authors read the article
267 and approve it for publication.

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271 **Competing interests** None declared.

272 **Patient consent for publication** Not required.

273 **Ethics approval** China Health and Nutrition Survey (CHNS) was approved by the ethics committee of Carolina Population
274 Center at the University of North Carolina at Chapel Hill and the NINH at the CCDC. Informed consent was obtained from
275 all subjects before the investigation. The present study derived data from the public domain, and therefore ethics statement
276 and informed consents were not applicable.

277 **Data availability statement** Data are available from China Health and Nutrition Survey
278 (<https://www.cpc.unc.edu/projects/china/data/>).

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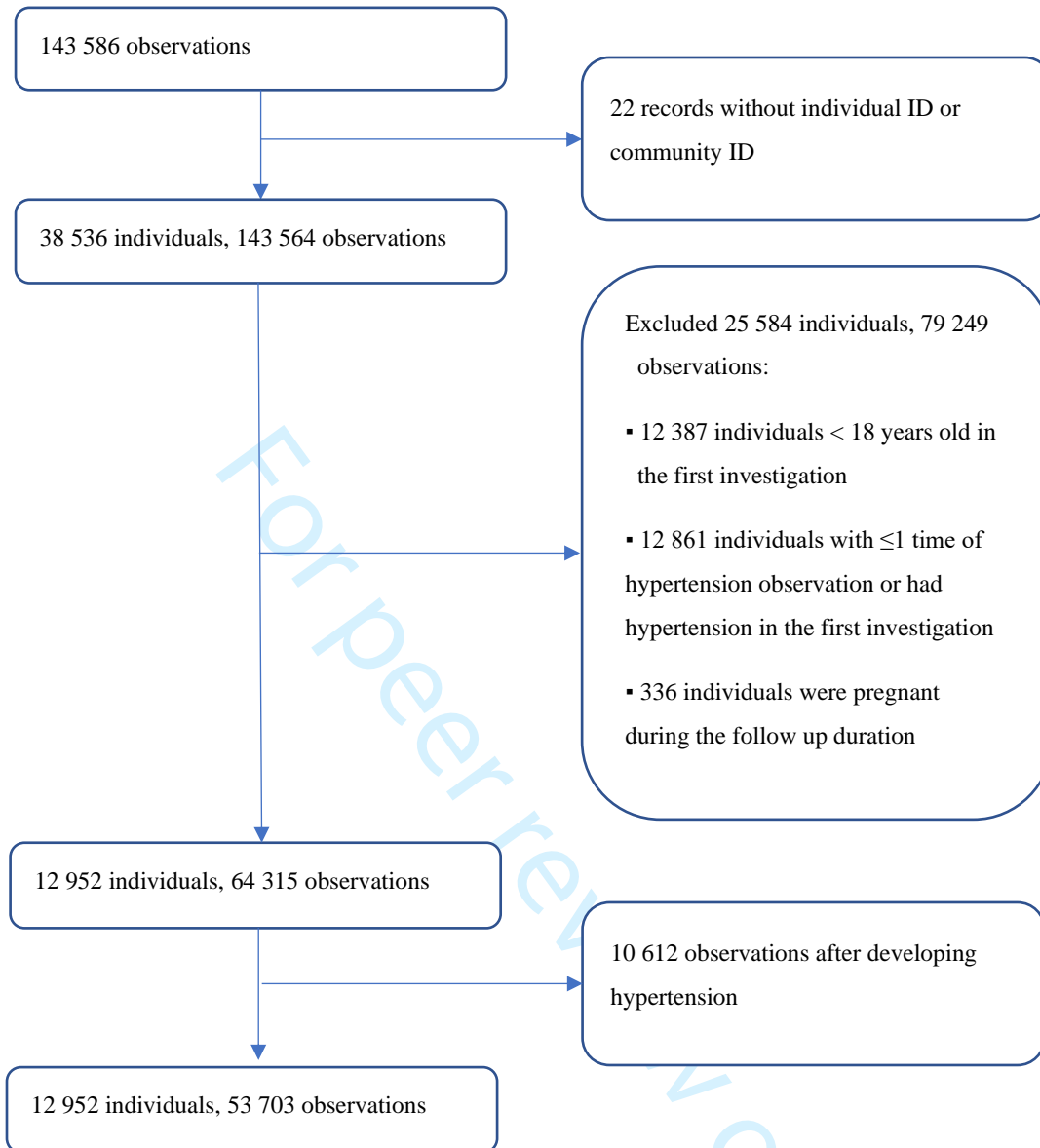
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389 Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of
390 hypertension incidence in China, with covariate information missing rate of 9.78%

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Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	page 8, figure 1, and table 1 in page 9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	page 9-11
		(b) Indicate number of participants with missing data for each variable of interest	page 11-12
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	page 13
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Cohort study: page 13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	page 13-16
		(b) Report category boundaries when continuous variables were categorized	page 15
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	page 17-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	
		Discuss both direction and magnitude of any potential bias	page 19-20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	page 19
Generalisability	21	Discuss the generalisability (external validity) of the study results	page 17-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	page 20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Title Page

Title : Long-term trends and regional variations of hypertension incidence in China: a prospective cohort study from the China Health and Nutrition Survey, 1991-2015

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ABSTRACT

Objective The aim is to explore the trends of hypertension incidence and regional variations in China from 1991 to 2015.

Design A dynamic prospective cohort study.

Setting China Health and Nutrition Survey (CHNS) 1991-2015.

21 **Participants** 12 952 Chinese adults aged 18+.

22 **Primary outcome measures** Incident hypertension from 1993 to 2015.

23 **Results** Age-standardized hypertension incidence increased from 40.8 per 1 000 person-years (95% CI,
24 38.3 to 43.4) between 1993 and 1997 to 48.6 (95% CI, 46.1 to 51.0) between 2011 and 2015. The increasing
25 trends were further supported by results from subsequent extended Cox proportional hazard model. In
26 addition, results from the modelling analysis showed that individuals in Eastern, Central, and Northeastern
27 China had greater risks of hypertension occurrence in comparison with their counterparts in Western China.

28 **Conclusion** Hypertension incidence increased during the study period. The growth called for more
29 attention on the health education and health promotion of individuals with great risks.

31 **Strengths and limitations of this study**

32 ► The dynamic cohort study-design employed individuals from diverse social and geographic contexts,
33 which enabled us to depict the long-term trends of hypertension incidence and regional disparities in
34 the context of China's rapid social development and population aging.

35 ► We adopted both self-reported health outcomes and objective outcomes from physical tests, which
36 to some extent minimized the recall bias and underestimation in underserved areas.

37 ► We did not employ a national-representative sample and did not include individuals from all
38 provinces in China, which undermined the representation of our findings.

39 ► Guidelines recommend to identify hypertension cases by using blood pressure values that are
40 measured in different days, while individuals' blood pressure data in the CHNS were collected on the
41 same day, which may lead to unavoidable bias.

42 ▶ We did not distinguish the grade of hypertension, and future research is necessary.

43

For peer review only

44 INTRODUCTION

45 Along with aging population, non-communicable chronic diseases, particularly stroke and ischemic heart
46 disease, have led to great burden of disease, deaths, and years of life lost (YLLs) in both developed and
47 developing countries.^{1 2} Connected closely with various cardiovascular diseases,^{3 4} high systolic blood
48 pressure was ranked as the leading risk factor of risk-attributable disability-adjusted life-years (DALYs)
49 among selected 195 countries and territories.⁵ For instance, high systolic blood pressure accounted for 2.54
50 million deaths and more than 5% of DALYs in China in 2017.⁶

51 Existing evidence has confirmed a worldwide high prevalence of hypertension.⁴⁻⁶ Countries, such as
52 Singapore⁶ and Korea⁷, had a significant proportion of individuals with hypertension. Likewise, with the
53 extended life expectancy,⁸ changes in lifestyle behaviors,⁹ and rapid urbanization,¹⁰ developing countries,
54 such as China, experienced a substantial increase in the prevalence of hypertension, ranging from 13.6% in
55 1991 to 27.9% in 2015.¹¹

56 Although the increasing prevalence of hypertension provided critical information for public health practice
57 and disease control programs, it could not accurately depict the epidemiologic transition as the incidence
58 measure.¹² Prior studies have indicated that the increasing prevalence could coexist with the decreasing
59 incidence in the context of healthy aging.¹³ For evidence-based health-promoting initiatives, empirical
60 research on hypertension incidence is warranted.

61 However, research on the long-term trends of the incidence of hypertension from China is scare and
62 relatively outdated.^{14 15} This is an important knowledge gap because developing countries are experiencing
63 unprecedented social development. Up-to-date information among developing countries could greatly

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5 64 contribute to depict global epidemiologic transitions. Moreover, regional disparities are a major health
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8 65 concern in China as a result of inequitable socio-economic development and health care resource
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10 66 distribution,¹⁶⁻¹⁸ while the existing research provides insufficient information regarding the regional
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13 67 disparities in the hypertension incidence.¹⁹⁻²¹

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16 68 Hence, this study aims to explore the long-term trends of hypertension incidence among Chinese from
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19 69 diverse social and geographic contexts. In addition, we are particularly interested in regional variations while
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22 70 taking the individual-level risk factors into account.

23 24 25 71 **METHODS**

26 27 28 72 **Data source**

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31 73 The present study derived data from the China Health and Nutrition Survey (CHNS). CHNS has been
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34 74 collaboratively conducted by Carolina Population Center at the University of North Carolina at Chapel Hill
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37 75 and the National Institute for Nutrition and Health (NINH, former National Institute of Nutrition and Food
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40 76 Safety) at the Chinese Center for Disease Control and Prevention. Initiated in 1989, CHNS consisted of ten-
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43 77 wave data in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015, respectively. Overall, CHNS
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46 78 employed a multistage random cluster method to draw the study sample, which included over 30 000
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49 79 individuals from three provincial-level cities and twelve provinces. Individuals in the survey came from
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52 80 diverse social, geographic, and cultural contexts. CHNS employed face-to-face questionnaire interviews to
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55 81 collect data, and the physical health examinations were conducted by well-trained investigators. Information
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58 82 regarding survey design, data collection, and quality control could be retrieved from the cohort profile.²²

59 60 83 **Study design and exclusion criteria**

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5 84 The present study employed a dynamic cohort study-design as not all individuals entered the cohort at the
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8 85 same time. To evaluate the long-term trends of hypertension incidence, we excluded individuals (a) without
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11 86 individual ID and community ID; (b) aged under 18 because of the low incidence of hypertension among
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14 87 children and teenagers; (c) with hypertension in his/her first investigation; (d) with only one observation or
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16 88 only one record of hypertension status; and (e) were pregnant during the study period to exclude gestational
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19 89 hypertension. Furthermore, we excluded observations after the diagnosis of hypertension (figure 1). As death
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21 90 data were not available in CHNS, censoring could be for death or lost to follow up.
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24 91 **Exposures**

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27 92 The primary exposure variable of this study were the timing of entering the cohort and geographic regions.
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30 93 For modeling analyses, it was not feasible to treat the waves as continuous variables, and therefore we
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33 94 respectively grouped the individuals entering the cohort from (a) 1991, 1993, and 1997; (b) 2000, 2004,
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36 95 2006, and 2009; and (c) 2011 and 2015. In this case, two dummies were introduced in the model with
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38 96 individuals from 1991 to 1997 as the reference group.
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41 97 Geographic regions were defined according to the bulletin of the National Bureau of Statistics of China.
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44 98 Specifically, we grouped individuals from (a) Beijing, Shanghai, Jiangsu Province, Zhejiang Province, and
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47 99 Shandong Province as Eastern China; (b) Henan Province, Hubei Province, and Hunan Province as Central
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49 100 China; (c) Liaoning Province and Heilongjiang Province as Northeastern China; and (d) Yunnan Province,
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52 101 Guangxi Zhuang Autonomous Region, Guizhou Province, Chongqing, and Shanxi Province as Western
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54 102 China.
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57 103 **Outcomes**

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5 104 We included incidence of hypertension as the primary outcome. First, we adopted self-reported hypertension,
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8 105 which was derived from the answer to the question, “Has a doctor ever told you that you had high blood
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10 106 pressure?”. If individuals self-reported no hypertension history, the outcomes would be further supplemented
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13 107 by the blood pressure tests to avoid the recall bias and underestimation from self-reported measures.
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15 108 According to the criteria of the 2018 Clinical Guideline in China and the 2018 ESC/ESH HTN Guideline,²³
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17 109 hypertension was confirmed with the systolic blood pressure (SBP)≥140 mmHg or with the diastolic blood
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19 110 pressure (DBP)≥90 mmHg. To guarantee the accuracy of the tests, the blood pressure was detected in
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22 111 triplicate by professional health workers on the same day.
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25 26 27 112 **Covariates**

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30 113 To adjust for variations in baseline characteristics, we introduced several confounding factors that may
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32 114 influence the occurrence of hypertension. These factors included urban vs. rural settings, sociodemographic
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34 115 characteristics (age, sex, race, marital status, educational attainment, and employment status), and lifestyle
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36 116 attributes (BMI, smoking behaviors, alcohol consumption, and physical activity).^{15 24}
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41 117 **Statistical analysis**

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44 118 First, we performed chi-square tests and Kruskal-Wallis rank-sum tests to evaluate variations in baseline
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46 119 characteristics over time. Second, we calculated the crude incidence of hypertension as below:²⁵
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$$\text{Incidence} = \frac{\text{number of new hypertension cases}}{\text{total person - years at risk}}$$

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53 121 The ‘person-years at risk’ is the period from the first hypertension-free year to the year when the subsequent
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55 122 hypertension is confirmed. In addition, we conducted direct standardization to calculate the age-standardized
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5 123 incidence of hypertension by using the study sample from wave 2011 and wave 2015 as the standard
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8 124 population. Subgroup analyses were conducted by sex.
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11 125 To further evaluate the long-term trends and geographic variations of incident hypertension, we performed
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14 126 an extended Cox proportional hazard model while including all covariates to control for baseline variations.
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16 127 Because the effect of age didn't conform to the proportional hazard assumption, we performed a time-
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19 128 dependent Cox regression model with age as a time-dependent variable. As for sensitivity analyses, we
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22 129 construct the multi-level Poisson regression indicating similar findings.
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25 130 Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05
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28 131 was considered statistical significance.
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30 31 132 **Patient and public involvement statement** 32

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34 133 Patients and the public were not involved in the research.
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36 37 134 **RESULTS** 38

39 40 41 135 **Study population** 42

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44 136 The CHNS consisted of data of 38 558 individuals with 143 586 observations from 1989 and 2015, and the
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47 137 present study only included 12 952 individuals from 1991 to 2015 after sample selection (figure 1). Table 1
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50 138 presents the distribution of observations from included individuals during the study period. For example, 5
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53 139 938 individuals entered the cohort in 1991, with only 912 followed-up in 2015 (table 1). Among the 12 952
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56 140 participants, 5 119 of them developed hypertension during the follow-up period.
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5 142 **Table 1** Observation distribution of study sample from 1991 to 2015

Wave	1991	1993	1997	2000	2004	2006	2009	2011	2015
1989									
1991	5938								
1993	5166	677							
1997	3313	485	1691						
2000	2658	335	1451	1009					
2004	2050	234	1037	813	837				
2006	1722	188	865	642	684	376			
2009	1378	142	385	398	413	302	692		
2011	1200	114	329	335	359	216	630	1732	
2015	912	86	250	236	231	152	353	1732	0

143

144 Table 2 presents the baseline characteristics of the study sample. Overall, variations existed in all baseline
 145 characteristics. Newly recruited individuals were older ($P < 0.001$) and well-educated ($P < 0.001$). They
 146 were more likely to be obese ($P < 0.001$), Han ($P < 0.001$), and male ($P < 0.001$), and they were less likely
 147 to be smokers ($P < 0.001$), employed ($P < 0.001$), and physically active ($P < 0.001$).

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149 **Table 2** Baseline characteristics of study individuals, *n*(%)*

Characteristic	Time entering the cohort			P value
	1991-1997	2000-2009	2011-2015	
Region				
Western	2256 (27.16)	611 (20.97)	523 (30.20)	<0.001
Central	2817 (33.92)	800 (27.45)	85 (4.91)	
Northeastern	1288 (15.51)	794 (27.25)	83 (4.79)	
Eastern	1945 (23.42)	709 (24.33)	1041 (60.10)	
Urban-rural				
Rural	5616 (67.61)	1717 (58.92)	777 (44.86)	<0.001
Urban	2690 (32.39)	1197 (41.08)	955 (55.14)	
Age (years)				
18-29	2374 (28.58)	695 (23.85)	221 (12.76)	<0.001
30-39	2382 (28.68)	854 (29.31)	345 (19.92)	
40-49	1752 (21.09)	621 (21.31)	424 (24.48)	
50-59	1004 (12.09)	405 (13.90)	456 (26.33)	
≥60	794 (9.56)	339 (11.63)	286 (16.51)	
Sex				
Male	3986 (47.99)	1168 (40.08)	736 (42.49)	<0.001
Female	4320 (52.01)	1746 (59.92)	996 (57.51)	
BMI (kg/m ²)				
<18.5	763 (9.27)	191 (6.60)	60 (3.46)	<0.001
18.5-23.9	6012 (73.07)	1776 (61.35)	955 (55.14)	
24.0-27.9	1238 (15.05)	760 (26.25)	545 (31.47)	
≥28	215 (2.61)	168 (5.80)	172 (9.93)	
Race				
Other	1038 (12.59)	340 (11.69)	72 (4.17)	<0.001
Han	7204 (87.41)	2568 (88.31)	1656 (95.83)	
Marital status				

Other	1183 (14.29)	341 (11.82)	192 (11.14)	<0.001
Married	7098 (85.71)	2545 (88.18)	1531 (88.86)	
Education attainment				
Primary school and below	4416 (53.81)	741 (26.43)	410 (23.73)	<0.001
Middle school	2377 (28.97)	1103 (39.34)	457 (26.45)	
High school or equivalent	1240 (15.11)	742 (26.46)	472 (27.31)	
College and above	173 (2.11)	218 (7.77)	389 (22.51)	
Employed				
No	1145 (13.85)	1044 (35.95)	716 (41.34)	<0.001
Yes	7121 (86.15)	1860 (64.05)	1016 (58.66)	
Smoking history				
Never or smoking cessation	5300 (64.72)	2163 (74.97)	1326 (77.18)	<0.001
Current smoker, cigarettes < 20/d	1481 (18.09)	370 (12.82)	205 (11.93)	
Current smoker, cigarettes ≥ 20/d	1408 (17.19)	352 (12.20)	187 (10.88)	
Alcohol consumption				
Never	5042 (61.82)	2037 (70.93)	1116 (65.03)	<0.001
Not more than once per month	469 (5.75)	102 (3.55)	144 (8.39)	
1-3 times per month	661 (8.10)	173 (6.02)	127 (7.40)	
1-2 times per week	781 (9.58)	227 (7.90)	127 (7.40)	
3-4 times per week	450 (5.52)	126 (4.39)	64 (3.73)	
On a daily basis	753 (9.23)	207 (7.21)	138 (8.04)	
Physical activity				
Very light	997 (12.56)	780 (27.73)	823 (49.46)	<0.001
Light	1307 (16.46)	799 (28.40)	453 (27.22)	
Moderate	1291 (16.26)	461 (16.39)	209 (12.56)	
Heavy or very heavy	4344 (54.71)	773 (27.48)	179 (10.76)	

150 *Overall, we included 11 685 individuals in the modelling analyses after excluding 97 individuals without

151 BMI, 74 without race, 62 without marital status, 214 without educational attainment, 50 without employment

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5 152 status, 160 without smoking history, 208 without alcohol consumption, and 449 without physical activity.

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8 153 (Missing rate 9.78 %)

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15 155 **Crude and age-standardized incidence**

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18 156 Table 3 presents the crude and age-standardized hypertension incidence during the study period. For the

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20 157 calculation of hypertension incidence, we employed the full sample of 12 952 individuals with 53 703

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23 158 observations. The age-standardized incidence of hypertension witnessed a significant increase, ranging from

24
25 159 40.8 per 1 000 person-years (95% CI: 38.3 to 43.4) between 1993 and 1997 to 48.6 per 1 000 person-years

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28 160 (95% CI: 46.1 to 51.0) between 2011 and 2015. The increasing pattern was also exhibited among men (1993-

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30 161 1997: 46.2, 95% CI: 42.1 to 50.4; 2011-2015: 55.7, 95% CI: 51.7 to 59.7) and women (1993-1997: 36.5,

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33 162 95% CI: 33.2 to 39.7; 2011-2015: 43.3, 95% CI: 40.2 to 46.3).

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164 **Table 3** Crude and age-standardized incidence over time, per 1000 person-years

Incidence	1991	1993-1997	2000-2009	2011-2015
Total				
Case (person-year)	-	1114 (35486)	2571 (70575)	1434 (29492)
Crude incidence (95% CI)	-	31.3 (29.6-33.2)	36.4 (35.0-37.8)	48.6 (46.1-51.2)
Age-standardized incidence (95% CI) *	-	40.8 (38.3-43.4)	41.5 (39.9-43.2)	48.6 (46.1-51.0)
Male				
Case (person-year)	-	594 (17530)	1292 (32524)	699 (12532)
Crude incidence (95% CI)	-	33.8 (31.2-36.7)	39.7 (37.6-41.9)	55.7 (51.7-60.0)
Age-standardized incidence (95% CI) *	-	46.2 (42.1-50.4)	45.7 (43.0-48.3)	55.7 (51.7-59.7)
Female				
Case (person-year)	-	520 (17956)	1279 (38051)	735 (16960)
Crude incidence (95% CI)	-	28.9 (26.5-31.5)	33.6 (31.8-35.5)	43.3 (40.3-46.5)
Age-standardized incidence (95% CI) *	-	36.5 (33.2-39.7)	38.0 (35.9-40.1)	43.3 (40.2-46.3)

165 * Age-standardized incidence was calculated using the study sample in 2011-2015 as the standard population.

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167 **Extended Cox proportional hazard analysis**

168 For the modeling analysis, we included 11 685 individuals without missing data (missing rate, 9.78%).

169 Among the identified cases, the duration from free of hypertension to incident hypertension ranged from 2
170 to 24 years, with a median of 9 years.

171 Table 4 presents results from extended Cox proportional hazard analysis while taking variations in baseline
172 characteristics into account. First, the increasing trends of hypertension incidence were robust, as suggested
173 by the modeling results. Specifically, individuals entering the cohort from 2000 to 2009 (aHR = 1.10, 95%
174 CI: 1.01 to 1.21) and those from 2011 to 2015 (aHR = 1.19, 95% CI: 1.04 to 1.37) had a higher risk of

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5 175 hypertension in comparison with individuals entering the cohort from 1991 to 1997. With reference to
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8 176 regional variations, individuals in Central (aHR = 1.26, 95% CI: 1.16 to 1.37), Northeastern (aHR = 1.56,
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10 177 95% CI: 1.41 to 1.72), and Eastern China (aHR = 1.48, 95% CI: 1.36 to 1.63) respectively had a higher risk
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13 178 of hypertension occurrence relative to their counterparts in Western China.
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180 **Table 4** Extended Cox proportional hazard analysis of hypertension incidence

Characteristic	aHR (95% CI)	P value
Timing of entering the cohort		
1991-1997	Ref.	
2000-2009	1.10 (1.01-1.21)	0.025
2011-2015	1.19 (1.04-1.37)	0.010
Geographic region		
Western	Ref.	
Central	1.26 (1.16-1.37)	<0.001
Northeastern	1.56 (1.41-1.72)	<0.001
Eastern	1.48 (1.36-1.63)	<0.001
Urban (vs. rural)	0.94 (0.88-1.01)	0.109
Age*		
18-29	Ref.	
30-39	1.93 (1.41-2.65)	<0.001
40-49	3.99 (2.93-5.43)	<0.001
50-59	5.16 (3.74-7.12)	<0.001
≥60	9.11 (6.50-12.77)	<0.001
Female (vs. male)	0.81 (0.74-0.88)	<0.001
BMI (kg/m ²)		
<18.5	Ref.	
18.5-23.9	1.31 (1.16-1.48)	<0.001
24.0-27.9	2.07 (1.81-2.36)	<0.001
≥28	2.82 (2.37-3.34)	<0.001
Race (Han vs. others)	1.11 (1.01-1.23)	0.032
Married (vs. others)	0.92 (0.83-1.02)	0.149
Educational attainment		
Primary school and below	Ref.	
Middle school	0.91 (0.84-0.99)	0.020

High school or equivalent	0.86 (0.77-0.95)	0.002
College and above	0.82 (0.68-0.98)	0.033
Employed (yes vs. no)	0.90 (0.82-0.99)	0.036
Smoking		
Never or smoking cessation	Ref.	
Current smoker, cigarettes < 20/d	0.98 (0.89-1.07)	0.752
Current smoker, cigarettes \geq 20/d	1.05 (0.96-1.16)	0.237
Alcohol consumption		
never	Ref.	
Not more than once per month	0.89 (0.78-1.03)	0.125
1–3 times per month	1.17 (1.04-1.32)	0.006
1–2 times per week	1.00 (0.89-1.12)	0.963
3–4 times per week	1.05 (0.92-1.21)	0.412
On a daily basis	1.18 (1.06-1.31)	0.002
Physical activity		
very light	Ref.	
light	0.92 (0.83-1.02)	0.154
moderate	0.99 (0.88-1.11)	0.930
heavy and very	0.91 (0.82-1.02)	0.118

181 *Estimated time effect of age, $P < 0.001$

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183 In addition, there existed no urban-rural differences in developing hypertension (Table 4). Risks of incident
 184 hypertension increased with age, BMI, and alcohol consumption, while it was negatively associated with
 185 educational attainment. Women had a lower risk of incident hypertension compared with men (aHR = 0.81,
 186 95% CI: 0.74 to 0.88). Relative to those without a job, employees had a lower risk of developing hypertension
 187 (aHR = 0.90, 95% CI: 0.82 to 0.99). Han individuals were significantly associated with a higher risk (aHR =

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5 188 1.11, 95% CI: 1.01 to 1.23) relative to the minority.
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9 189 **DISCUSSION**

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12 190 By employing a study sample of 12 925 individuals from diverse social and geographic contexts, we found
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14 191 the age-standardized incidence of hypertension increased during the study period. The increasing pattern
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16 192 remained even after controlling for variations in baseline characteristics. Furthermore, we found that
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18 193 individuals in economically developed Eastern, Central, and Northeastern China had greater risks of incident
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20 194 hypertension in comparison with those in Western China.
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25 195 Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence
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27 196 measure. For example, one of the previous studies in China indicated that the prevalence of hypertension
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29 197 rose substantially from 13.6% in 1991 to 27.9% in 2015.¹¹ The findings were further supplemented by results
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31 198 from Lu *et al.* (2017), which suggested a higher prevalence of hypertension among those aged between 35
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33 199 and 75 years old (44.7%).²⁶ Compared with these earlier studies, our focus on the incidence measure
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35 200 provided a more accurate reflection of the epidemiologic transition of hypertension in China.¹² Our findings
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37 201 updated the trends of hypertension incidence in comparison with that from Liang *et al.* (2014), which
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39 202 indicated a similar pattern from 1991 to 2009.¹⁵ Even though hypertension incidence appeared to vary across
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41 203 countries,²⁷⁻²⁹ the comparison is untenable because we adopted different standard populations. Further
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43 204 empirical research across countries is warranted.
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52 205 With the rapid economic development, people often change their dietary patterns from light diet to high salt
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54 206 and fat diet along with a secondary lifestyle.³⁰ These changes would significantly impact the prevalence and
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56 207 control of hypertension in China.³⁰ In addition, due to data limitation, we were unable to introduce several
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5 208 potential risks factors, such as sodium intake or dietary pattern, parental history, psychological status,
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8 209 ambient air pollutants, working hours, and household income.³¹⁻³⁴ These factors may explain the residual
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10 210 time-effects in the model.

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14 211 Although existing evidence on the regional disparities of hypertension incidence is scant, prior research
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16 212 indicates that Central, Northeastern, and Eastern China had a higher prevalence of hypertension compared
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19 213 with Western China,³⁵ which is in line with our findings. In sharp contrast, prior investigators have noted
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21 214 that Northeastern and Central China had lower all-cause mortality rates relative to Western China.³⁶ These
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24 215 findings appear to suggest that individuals in China's economically developed regions are experiencing
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26 216 extended life expectancy with relatively unhealthy aging.¹² However, one should be aware of the possibility
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29 217 that although individuals in Western China had lower risks of hypertension compared with the other three
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32 218 regions, local public awareness and timely treatment could be a challenging issue.

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35 219 Differed from previous studies,^{15 37} no urban-rural disparities were observed in the present study. This may
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38 220 be a result of the narrowing gap of lifestyle between rural and urban residents. With the rapid economic
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41 221 development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are
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43 222 approaching to those of their counterparts in urban China.^{9 10} This possibility has been further supported by
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46 223 the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.²⁶ Taking
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48 224 into account the lower treatment rate and insufficient awareness among rural residents,³⁸ one should direct
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51 225 more attention to rural China.

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54 226 Moreover, we found that smoking history was not associated with incident hypertension. The effect of
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57 227 smoking on the development of the chronic disease is unclear and appears to differ across life courses.³⁹⁻⁴¹
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228 Prior research based on Korean has found a J-shaped association between physical activity and incident
229 hypertension,⁴² while the present study on Chinese did not observe a similar association, which is in line
230 with findings based on Japanese.⁴³ The effect of physical activity on the development of hypertension seems
231 to be controversial and varies across countries. Further analyses are warranted.

232 Consistent with the previous studies,⁴⁴⁻⁴⁷ several risk factors, including age, gender, educational attainment,
233 race, alcohol consumption, and BMI, were confirmed by our analyses. The growing incidence of
234 hypertension emphasizes the early prevention, education, detection, and management for hypertension.⁴⁸
235 Mentoring aforementioned lifestyle behaviors, such as alcohol consumption, may be helpful to constrain the
236 hypertension incidence.⁴⁹ Public health and lifestyle interventions targeting high-risk individuals, such as
237 older adults, men, and obese population, hold promise.

238 **Conclusion**

239 Hypertension incidence increased during the study period. Individuals in Eastern, Central, and Northeastern
240 China had greater risks of hypertension in comparison with their counterparts in Western China. Risks of
241 incident hypertension increased with age, BMI, and alcohol consumption, but negatively associated with
242 educational attainment. The growth of hypertension incidence calls for more attention on the health
243 education and health promotion of individuals with great risks.

244 **Strengths and limitations of this study**

245 The present study has two major strengths. First, the dynamic cohort study-design employed individuals
246 from diverse social and geographic contexts, which enabled us to depict the long-term trends of hypertension
247 incidence and regional disparities in the context of China's rapid social development and population aging.

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5 248 In addition, we adopted both self-reported health outcomes and objective outcomes from physical tests,
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8 249 which avoided the recall bias and underestimation in underserved areas.
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11 250 Nevertheless, this study is subject to several limitations. First, we did not employ a national-representative
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13 251 sample and did not include individuals from all provinces in China, which undermined the representation of
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16 252 our findings. As a community-based survey, the CHNS excluded institutionalized individuals, which further
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19 253 diminished the representation of our findings among Chinese. Third, 2018 Clinical Guideline in China
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21 254 recommend to identify hypertension cases by using blood pressure values that are measured in different
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24 255 days²³, while individuals' blood pressure data in the CHNS were collected on the same day in the CHNS,
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27 256 leading to unavoidable bias. Last, we did not distinguish the grade of hypertension, and future research is
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30 257 necessary.
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45
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48
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51
52 265 **Contributors** WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical
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54
55 266 analysis, and wrote the first draft of the manuscript, which P-YL and W-ZH subsequently revised. All authors read the article
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58 267 and approve it for publication.
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60

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270 **Competing interests** None declared.

271 **Patient consent for publication** Not required.

272 **Ethics approval** China Health and Nutrition Survey (CHNS) was approved by the ethics committee of Carolina Population
273 Center at the University of North Carolina at Chapel Hill and the NINH at the CCDC. Informed consent was obtained from
274 all subjects before the investigation.

275 **Data availability statement** Data are available from China Health and Nutrition Survey
276 (<https://www.cpc.unc.edu/projects/china/data/>).

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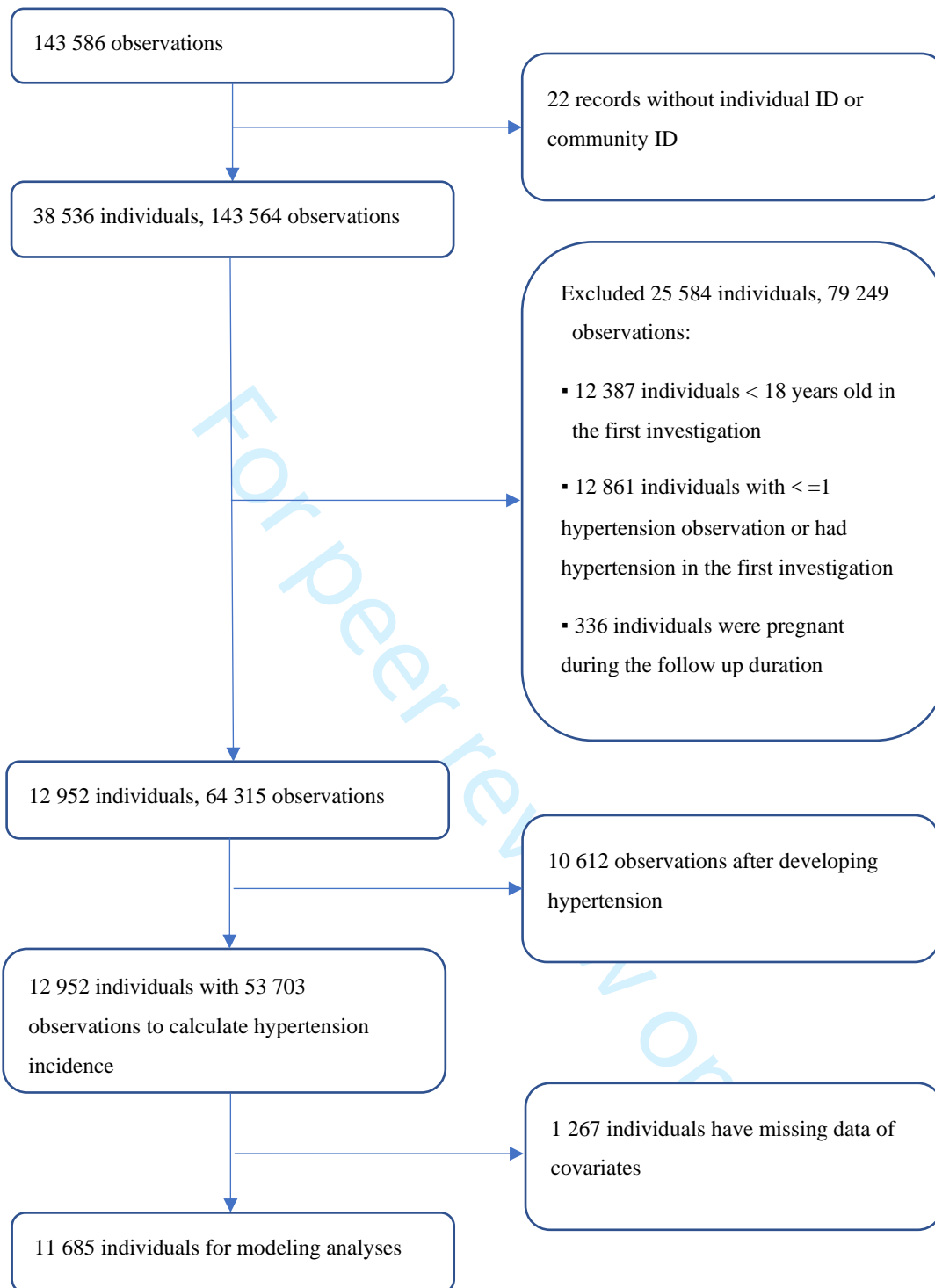
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387 Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of
388 hypertension incidence in China, with covariate information missing rate of 9.78%

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Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	page 8, figure 1, and table 1 in page 9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	page 9-11
		(b) Indicate number of participants with missing data for each variable of interest	page 11-12
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	page 13
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Cohort study: page 13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	page 13-16
		(b) Report category boundaries when continuous variables were categorized	page 15
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	page 17-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	
		Discuss both direction and magnitude of any potential bias	page 19-20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	page 19
Generalisability	21	Discuss the generalisability (external validity) of the study results	page 17-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	page 20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.