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

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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.

③We 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

Chinese.

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

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 Singapore[6] and Korea[7], 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 scare 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

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

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

METHODS

Data source

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

Study design and exclusion criteria

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).

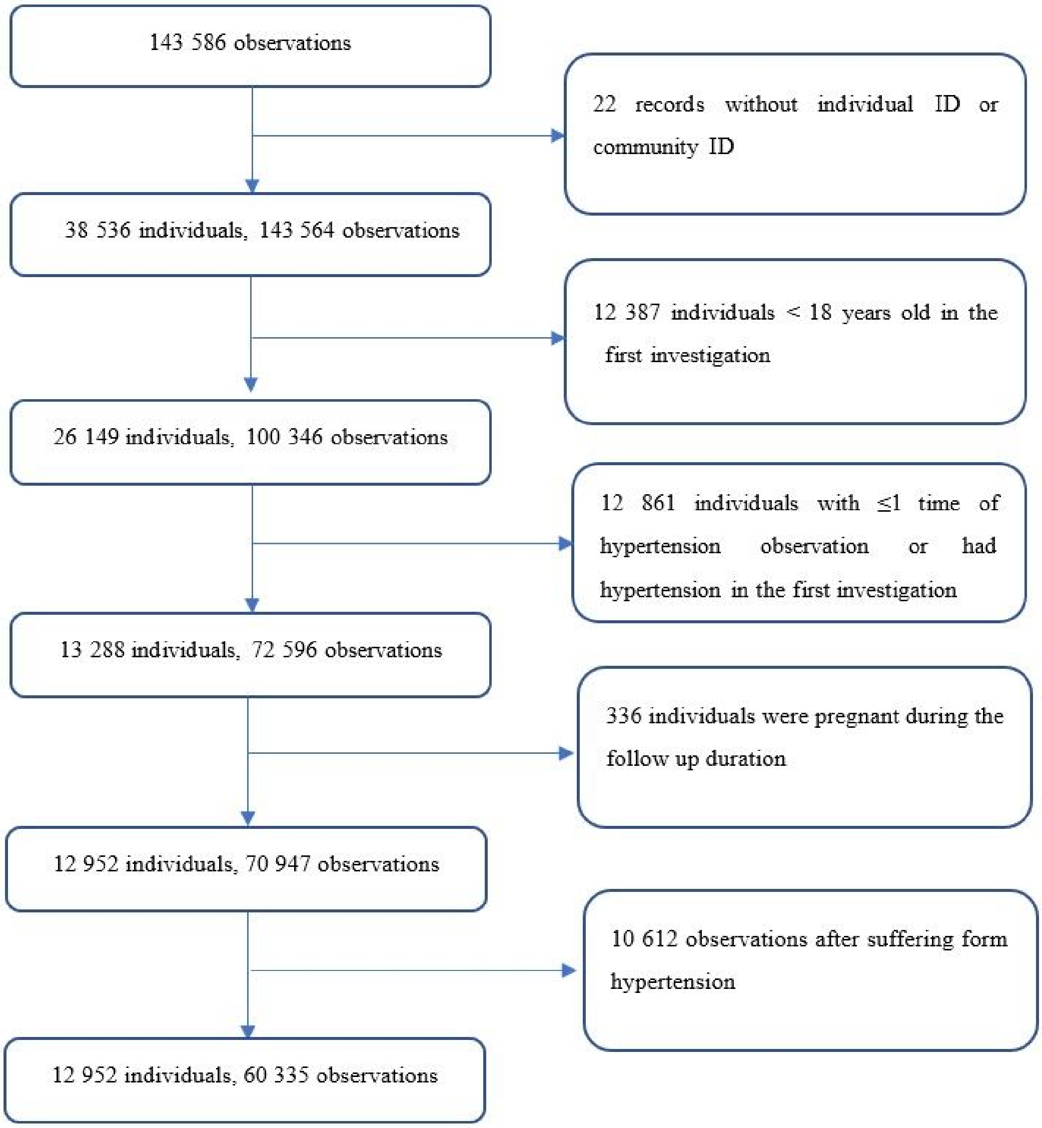

Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of

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 detected in triplicate by professional health workers on the same day.

Covariates

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

Statistical analysis

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

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

The 'person-years at risk' is the period from the first hypertension-free year to the year when the subsequent hypertension is confirmed. In addition, we calculated the age-standardized incidence of hypertension by employing the sample from wave 2011 and wave 2015 as the standard population. Subgroup analyses were conducted by gender. To further evaluate the long-term trends of hypertension incidence, we performed an extended Cox proportional hazard model while considering geographic variations. Because the effect of age didn't conform to the proportional hazard assumption, we performed a time-dependent Cox regression model with age as a time-dependent variable. At the same time, we introduced all covariates in the model to control for the baseline variations.

Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05

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)	*n*	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, $P<0.001$

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

DISCUSSION

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

Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence measure. For example, one of the previous studies in China indicated that the prevalence of hypertension rose substantially from 13.6% in 1991 to 27.9% in 2015.[11] The findings were further supplemented by results from Lu *et al*. (2017), which suggested a higher prevalence of hypertension among those aged between 35 and 75 years old (44.7%).[26]

However, our focus on the incidence measure provided a more accurate reflection of the epidemiologic transition of hypertension in China. In addition, our findings updated the trends of hypertension incidence in comparison with that from Liang *et al*. (2014).[15] Even though hypertension incidence appeared to vary across countries,[27-29] the comparison is untenable because we adopted different standard populations. Further empirical research across countries is warranted.

With the rapid economic development, people often change their dietary patterns from light diet to high salt and fat diet along with a secondary lifestyle.[30] These changes would significantly impact the prevalence and control of hypertension in China.[30] In addition, due to data limitation, we didn't introduce several potential risks factors, such as sodium intake or dietary pattern, parental history, psychological status, ambient air pollutants, working hours, and household income.[31-34] These factors may explain the residual time-effects in the model as well.

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

Differed from previous studies,[15 37] no urban-rural disparities were observed in the present study. This may be a result of the narrow gap of lifestyle between rural and urban residents. With the rapid economic development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are approaching to those of their counterparts in urban China.[9 10] This possibility has been further supported by the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.[26] Taking into account the lower treatment rate and insufficient awareness among rural residents,[38] one should direct more attention to rural China.

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

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

Conclusion

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

Strengths and limitations of this study

The present study has two major strengths. First, 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. In addition, we adopted both self-reported health outcomes and objective outcomes from physical tests, which avoided the recall bias and underestimation in underserved areas.

Nevertheless, this study is subject to several limitations. First, 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 Chinese. In addition, we did not distinguish hypertension, and future research is necessary.

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Contributors WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical 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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Long-term trends and regional variations of hypertension incidence in China: a dynamic prospective cohort study

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Title Page

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

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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.

Participants 12 952 Chinese adults aged 18+.

Primary outcome measures Incident hypertension from 1993 to 2015.

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

③ We did not employ a national-representative sample and did not include individuals from all 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 Chinese.

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

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

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 Singapore[6] and Korea[7], 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 scare 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

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

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

METHODS

Data source

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

Study design and exclusion criteria

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).

Exposures

The primary exposure variable of this study were the timing of 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 had 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 detected in triplicate by professional health workers on the same day.

Covariates

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

Statistical analysis

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

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

The 'person-years at risk' is the period from the first hypertension-free year to the year when the subsequent hypertension is confirmed. In addition, we conducted direct standardization to calculate the age-standardized incidence of hypertension by using the study sample from wave 2011 and wave 2015 as the standard population. Subgroup analyses were conducted by sex.

To further evaluate the long-term trends and geographic variations of incident hypertension, we performed an extended Cox proportional hazard model while including all covariates to control for baseline variations. Because the effect of age didn't conform to the proportional hazard assumption, we performed a time-dependent Cox regression model with age as a time-dependent variable. As for sensitivity analyses, we construct the multi-level Poisson regression indicating similar findings.

Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05 was considered statistical significance.

Patient and public involvement

Not applicable. Data are derived from public domain.

RESULTS

Study population

The CHNS consisted of data of 38 558 individuals with 143 586 observations from 1989 and 2015, and 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, 5 938 individuals entered the cohort in 1991, with only 912 followed-up in 2015 (table 1). Among the 12 952 participants, 5 119 of them developed hypertension during the follow-up period.

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

144

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).

149

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

Characteristic	Time entering the cohort			*P* value
	1991-1997	2000-2009	2011-2015	
Region				<0.001
Western	2256 (27.16)	611 (20.97)	523 (30.20)	
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				<0.001
Rural	5616 (67.61)	1717 (58.92)	777 (44.86)	
Urban	2690 (32.39)	1197 (41.08)	955 (55.14)	
Age (years)				<0.001
18-29	2374 (28.58)	695 (23.85)	221 (12.76)	
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				<0.001
Male	3986 (47.99)	1168 (40.08)	736 (42.49)	
Female	4320 (52.01)	1746 (59.92)	996 (57.51)	
BMI (kg/m^2)				<0.001
<18.5	763 (9.27)	191 (6.60)	60 (3.46)	
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				<0.001
Other	1038 (12.59)	340 (11.69)	72 (4.17)	
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)	

*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 educational 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 the full sample of 12 952 individuals with 53 703 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)

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

Extended Cox proportional hazard analysis

For the modeling analysis, we included 11 685 individuals without missing data (missing rate, 9.78%). Among the identified cases, the duration from free of hypertension to incident hypertension ranged from 2 to 24 years, with a median of 9 years.

Table 4 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 entering 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.

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 ≥ 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, $P<0.001$

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

1.11, 95% CI: 1.01 to 1.23) relative to the minority.

DISCUSSION

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

Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence measure. For example, one of the previous studies in China indicated that the prevalence of hypertension rose substantially from 13.6% in 1991 to 27.9% in 2015.[11] The findings were further supplemented by results from Lu *et al*. (2017), which suggested a higher prevalence of hypertension among those aged between 35 and 75 years old (44.7%).[26] Compared with these earlier studies, our focus on the incidence measure provided a more accurate reflection of the epidemiologic transition of hypertension in China.[12] Our findings updated the trends of hypertension incidence in comparison with that from Liang *et al*. (2014), which indicated a similar pattern from 1991 to 2009.[15] Even though hypertension incidence appeared to vary across countries,[27-29] the comparison is untenable because we adopted different standard populations. Further empirical research across countries is warranted.

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

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

Differed from previous studies,[15 37] no urban-rural disparities were observed in the present study. This may be a result of the narrowing gap of lifestyle between rural and urban residents. With the rapid economic development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are approaching to those of their counterparts in urban China.[9 10] This possibility has been further supported by the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.[26] Taking into account the lower treatment rate and insufficient awareness among rural residents,[38] one should direct more attention to rural China.

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

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

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

Conclusion

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

Strengths and limitations of this study

The present study has two major strengths. First, 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.

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

Nevertheless, this study is subject to several limitations. First, we did not employ a national-representative sample and did not include individuals from all provinces in China, which undermined the representation of our findings. As a community-based survey, the CHNS excluded institutionalized individuals, which further diminished the representation of our findings among Chinese. Third, 2018 Clinical Guideline in China recommend to identify hypertension cases by using blood pressure values that are measured in different days[23], while individuals' blood pressure data in the CHNS were collected on the same day in the CHNS, leading to unavoidable bias. Last, we did not distinguish the grade of hypertension, and future research is necessary.

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Contributors WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical 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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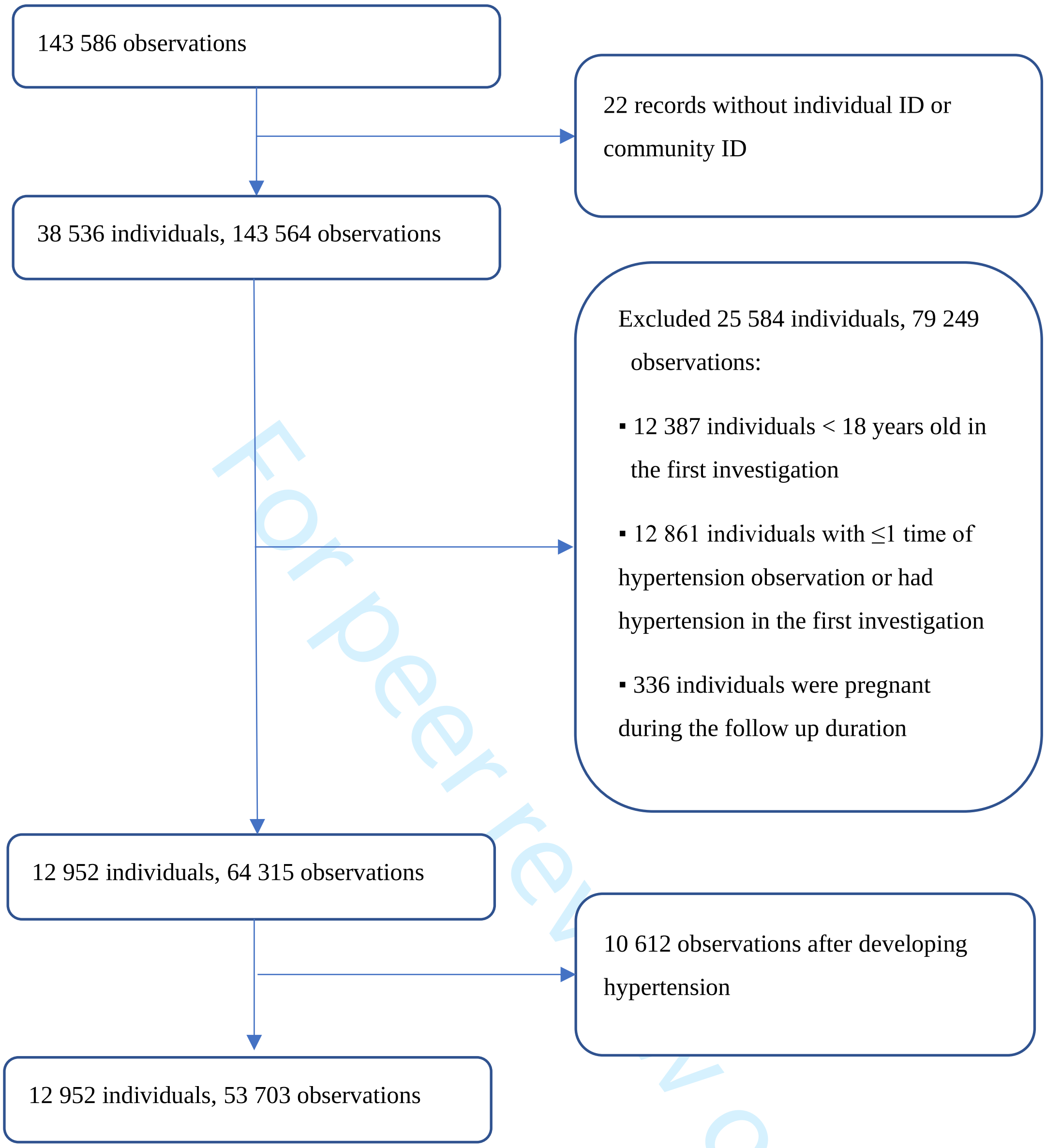
Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of hypertension incidence in China, with covariate information missing rate of 9.78%


143 586 observations
22 records without individual ID or community ID
38 536 individuals, 143 564 observations
Excluded 25 584 individuals, 79 249 observations:
▪ 12 387 individuals < 18 years old in the first investigation
▪ 12 861 individuals with ≤1 time of hypertension observation or had hypertension in the first investigation
▪ 336 individuals were pregnant during the follow up duration
12 952 individuals, 64 315 observations
10 612 observations after developing hypertension
12 952 individuals, 53 703 observations

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	page 5
Methods			
Study design	4	Present key elements of study design early in the paper	page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	page 6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	(Cohort study) page 6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	(Cohort study) NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	page 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	page 5-7
Bias	9	Describe any efforts to address potential sources of bias	page 2 and 7
Study size	10	Explain how the study size was arrived at	page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	page 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	page 7-8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(<u>*e*</u>) Describe any sensitivity analyses	

Continued on next page

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	page 8, figure 1, and table 1 in page 9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
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) *Cohort study*—Summarise follow-up time (eg, average and total amount)	page 13
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Cohort study: page 13
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—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.

BMJ Open

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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Primary Subject Heading:	Public health
Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	Hypertension < CARDIOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

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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.

Participants 12 952 Chinese adults aged 18+.

Primary outcome measures Incident hypertension from 1993 to 2015.

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 individualss with great risks.

Strengths and limitations of this study

- ►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.
- ►We adopted both self-reported health outcomes and objective outcomes from physical tests, which to some extent minimized the recall bias and underestimation in underserved areas.
- ►We did not employ a national-representative sample and did not include individuals from all provinces in China, which undermined the representation of our findings.
- ►Guidelines recommend to identify hypertension cases by using blood pressure values that are measured in different days, while individuals' blood pressure data in the CHNS were collected on the same day, which may lead to unavoidable bias.

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

43

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 Singapore[6] and Korea[7], 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 scare 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

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

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

METHODS

Data source

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

Study design and exclusion criteria

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). As death data were not available in CHNS, censoring could be for death or lost to follow up.

Exposures

The primary exposure variable of this study were the timing of 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 had 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 detected in triplicate by professional health workers on the same day.

Covariates

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

Statistical analysis

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

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

The 'person-years at risk' is the period from the first hypertension-free year to the year when the subsequent hypertension is confirmed. In addition, we conducted direct standardization to calculate the age-standardized incidence of hypertension by using the study sample from wave 2011 and wave 2015 as the standard population. Subgroup analyses were conducted by sex.

To further evaluate the long-term trends and geographic variations of incident hypertension, we performed an extended Cox proportional hazard model while including all covariates to control for baseline variations. Because the effect of age didn't conform to the proportional hazard assumption, we performed a time-dependent Cox regression model with age as a time-dependent variable. As for sensitivity analyses, we construct the multi-level Poisson regression indicating similar findings.

Data analyses were performed with Stata 15.0 (StataCorp, TX, USA). A two-tailed *P* value of less than 0.05 was considered statistical significance.

Patient and public involvement statement

Patients and the public were not involved in the research.

RESULTS

Study population

The CHNS consisted of data of 38 558 individuals with 143 586 observations from 1989 and 2015, and 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, 5 938 individuals entered the cohort in 1991, with only 912 followed-up in 2015 (table 1). Among the 12 952 participants, 5 119 of them developed hypertension during the follow-up period.

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)	

*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 educational 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 the full sample of 12 952 individuals with 53 703 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).

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.

166

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

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.

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 ≥ 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

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

1.11, 95% CI: 1.01 to 1.23) relative to the minority.

DISCUSSION

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

Instead of focusing on the incidence measure, the vast majority of prior studies focused on the prevalence measure. For example, one of the previous studies in China indicated that the prevalence of hypertension rose substantially from 13.6% in 1991 to 27.9% in 2015.[11] The findings were further supplemented by results from Lu *et al*. (2017), which suggested a higher prevalence of hypertension among those aged between 35 and 75 years old (44.7%).[26] Compared with these earlier studies, our focus on the incidence measure provided a more accurate reflection of the epidemiologic transition of hypertension in China.[12] Our findings updated the trends of hypertension incidence in comparison with that from Liang *et al*. (2014), which indicated a similar pattern from 1991 to 2009.[15] Even though hypertension incidence appeared to vary across countries,[27-29] the comparison is untenable because we adopted different standard populations. Further empirical research across countries is warranted.

With the rapid economic development, people often change their dietary patterns from light diet to high salt and fat diet along with a secondary lifestyle.[30] These changes would significantly impact the prevalence and control of hypertension in China.[30] In addition, due to data limitation, we were unable to introduce several

208 potential risks factors, such as sodium intake or dietary pattern, parental history, psychological status, 209 ambient air pollutants, working hours, and household income.[31-34] These factors may explain the residual 210 time-effects in the model.

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

219 Differed from previous studies,[15 37] no urban-rural disparities were observed in the present study. This may 220 be a result of the narrowing gap of lifestyle between rural and urban residents. With the rapid economic 221 development and urbanization in the past few decades, the lifestyle and dietary pattern of rural residents are 222 approaching to those of their counterparts in urban China.[9 10] This possibility has been further supported by 223 the fact that the prevalence of hypertension in rural China exceeded that of urban China in 2015.[26] Taking 224 into account the lower treatment rate and insufficient awareness among rural residents,[38] one should direct 225 more attention to rural China.

226 Moreover, we found that smoking history was not associated with incident hypertension. The effect of 227 smoking on the development of the chronic disease is unclear and appears to differ across life courses.[39-41]

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

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

Conclusion

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

Strengths and limitations of this study

The present study has two major strengths. First, 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.

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

Nevertheless, this study is subject to several limitations. First, we did not employ a national-representative sample and did not include individuals from all provinces in China, which undermined the representation of our findings. As a community-based survey, the CHNS excluded institutionalized individuals, which further diminished the representation of our findings among Chinese. Third, 2018 Clinical Guideline in China recommend to identify hypertension cases by using blood pressure values that are measured in different days[23], while individuals' blood pressure data in the CHNS were collected on the same day in the CHNS, leading to unavoidable bias. Last, we did not distinguish the grade of hypertension, and future research is necessary.

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Contributors WZ designed this study and revised the manuscript. Y-ML, FX, and X-XY performed data clean, statistical 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.

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

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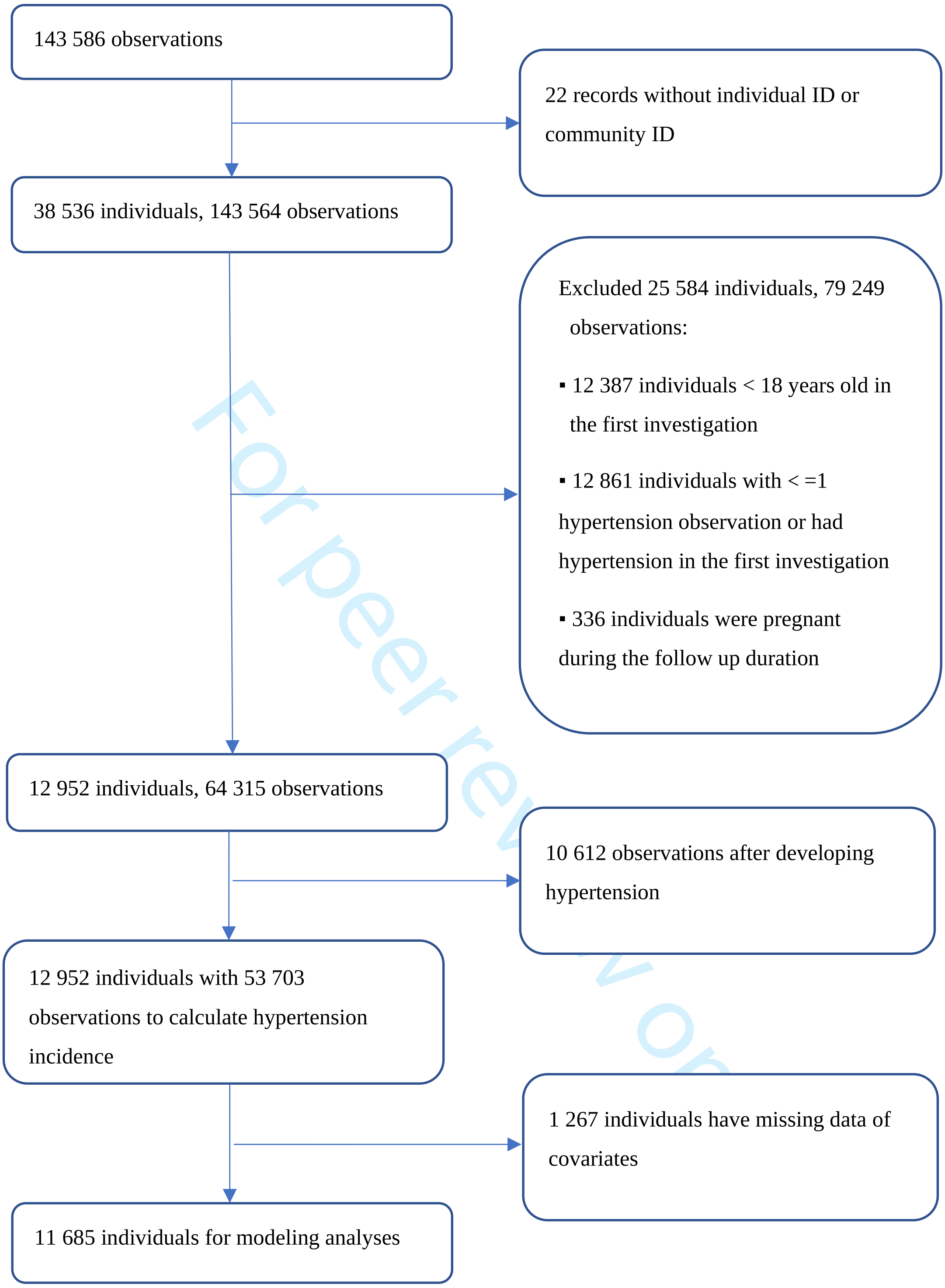
Figure 1 Flowchart showing the selection of the subjects who were included in the final analysis of hypertension incidence in China, with covariate information missing rate of 9.78%


143 586 observations
22 records without individual ID or community ID
38 536 individuals, 143 564 observations
Excluded 25 584 individuals, 79 249 observations:
▪ 12 387 individuals < 18 years old in the first investigation
▪ 12 861 individuals with < =1 hypertension observation or had hypertension in the first investigation
▪ 336 individuals were pregnant during the follow up duration
12 952 individuals, 64 315 observations
10 612 observations after developing hypertension
12 952 individuals with 53 703 observations to calculate hypertension incidence
1 267 individuals have missing data of covariates
11 685 individuals for modeling analyses

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	page 5
Methods			
Study design	4	Present key elements of study design early in the paper	page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	page 6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	(Cohort study) page 6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	(Cohort study) NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	page 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	page 5-7
Bias	9	Describe any efforts to address potential sources of bias	page 2 and 7
Study size	10	Explain how the study size was arrived at	page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	page 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	page 7-8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

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	page 8, figure 1, and table 1 in page 9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
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) *Cohort study*—Summarise follow-up time (eg, average and total amount)	page 13
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Cohort study: page 13
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—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.