## Regional Disparities in the Hypertension Risk in China: A Longitudinal Study

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## Introduction

Hypertension is not only a chronic disease condition itself, but also a risk factor associated with other cardiovascular disease, osteoporosis and chronic kidney disease [1, 2]. In China, hypertension has been increasing dramatically in last several decades [3]. Prehypertension and hypertension are attributable to $51.9 \%$ and $49.1 \%$ of death in Chinese population for men and women respectively [4]. Thus, it has become one of the major public health problems that call for immediate concern from health policy maker.
Most researchers attributed the prevalence of hypertension to the fast economic development in the last three decades.

Urbanization and expansion of western fast food and lifestyle may impact the distribution of risk factors for hypertension [5]. However, the demographic variation and inequality may also have great impact on the prevalence pattern of hypertension in China. Several studies have noticed the regional disparity in the prevalence of hypertension. The prevalence in northern is significantly higher than in southern China [6, 7]. However, those studies were focused on the extreme distant area, and few studies are conducted within a longitudinal setting. The reason of this geographic effect is still unclear. A subtle description of this variation may provide essential information to understand the underlying cause. Further, it will be helpful to determine the priority of health policy and allocation of health resources in China.

We conducted a longitudinal analysis using China Health and Nutrition Survey data. We report the hypertension risk escalates from south to north of China latitudinally. This regional effect is independent to gender, rural or urban residence, age and BMI.

## Methods

## China health and nutrition survey and analysis cohort

The data of this study are from China Health and Nutrition Survey, which is an ongoing national survey conducted by the Carolina Population Center at the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety at the Chinese Center for Disease Control and Prevention [5]. The survey data is now public available. The survey used a multistage, random cluster method to sample about 4400 households with a total of 26,000 individuals from nine provinces in China. The survey was conducted for first round in 1989, then 1991, 1993, 1997, 2000, 2004, 2006 and 2009. In each year of survey, participants received detailed physical examination from trained and experienced professionals. Weight, height, arm and head circumference, mid-arm skinfold were measured. Additionally, blood pressure for people aged 7 and older were measured repeatedly for three times.
For the purpose of longitudinal analysis to this study, five waves of survey data, including 1997, 2000, 2004, 2006 and 2009 were included in analysis cohort. Liaoning province was excluded in the analysis because it didn't participate in 1997 and 2000. Eight other provinces, Heilongjiang, Shandong, Henan, Jiangsu, Hubei, Hunan, Guangxi and Guizhou, locate in east part of China including representative Northern provinces and Southern provinces.

The analysis was limited to those who were age 18 to 67 years old in 1997 and were at least followed up in one subsequent survey. 10,638 participants who participated 1997 survey and took physical exam were born before December 31, 1979, and 9,789 of them born after January 1930. However, only 7,710 participants came back in at least one more subsequent survey year. They provided totally 30,934 observations.

The survey collected nationality, education, residence in rural or urban region, and age and gender. Height and weight at each survey time were measured. For women, marital status was available. The primary outcome for this study is the measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP). The average of triplicates was used to analysis. Participants whose SBP $\geq 140 \mathrm{mmHg}$ and/or DBP $\geq 90 \mathrm{~mm} \mathrm{Hg}$ or who reported taking anti-hypertension medication or self-reported history or hypertension were defined as being hypertensive [8].

## Statistical analysis

The same individuals in the analysis cohort were followed in 12 years. This design was referred as accelerated longitudinal designs [9] or longitudinal panels design [10]. The demographic characteristics of cohort were described with frequency, percentage, mean and standard deviation accordingly. MantelHaenszel chi-square test was performed to check the trend of proportion change over survey year for those characteristics. A
generalize estimating equation (GEE) was employed to model the probability of being hypertensive as previously defined. All statistical analyses were conducted using software SAS 9.3 (SAS Institute Inc. Cary, NC) and ArcGIS 10 (Esri, Redlands, CA). The statistical significance level was at 0.05 , two-sided.

## Results

As shown in Table 1, 7,710 participants consisted of 3,918 (50.8\%) men and $3,792(49.2 \%)$ women. The majority of the population was Han Chinese ( $88.0 \%$ ). Most subjects received education at middle school level or above ( $42.0 \%$ and $6.4 \%$ respectively, compared to $40.9 \%$ and $2.3 \%$ in entire nation). The proportion of each province in the study population varied from 10.9\% (Shandong) to $13.7 \%$ (Guangxi). Urban residence was $31.2 \%$ that was comparable to national level (30.4\%, China Year Book 2009). In addition, the average age of cohort in 1997 was $41 \pm 13$ (mean $\pm$ SD) years old. Participants from province Heilongjiang were the youngest population with age of $37 \pm 12$ years old.
Response rate was $86.6 \%, 77.1 \%, 72.9 \%$ and $64.9 \%$ for 2000, 2004, 2006 and 2009 survey year respectively. The missingness may be caused by death, moving out of survey region, missing in physical exam and other un-identifiable factors. Mantel-Haenszel Chi-square tests showed that the change of composition in gender, nationality, residence and province was not significant over survey years. The changes in education and residence status over years were highly significant ( $p<0.001$ ). The rate of loss to follow up was slightly higher in urban participants. The proportion of those receiving above middle school education increased over year due to the graduation from lower grade schools.
Table 2 shows that prevalence of hypertension in this cohort increased from $15.1 \%$ in 1997 to $32.2 \%$ in 2009.

Hypertensive people who reported to have been diagnosed to have hypertension were defined as being aware of their hypertension. If they were taking antihypertensive drugs then they were considered to be treated. The treated people whose blood pressure were lower than $140 / 90 \mathrm{mmHg}$ were considered controlled [11]. The rate of awareness doubled from 1997 to 2009. The treatment rate among those being aware increased to $79 \%$. However, the control rate among those on treatment remained relatively stable over years. Only about one third of treated people were controlled. Among all hypertensive population there was only $10.1 \%$ people were controlled in 2009.
Figures 1a and 1b shows the trend of SBP and DBP changes over years for each of eight provinces in this cohort. The detail data were given in Supplementary Table 1. Overall, blood pressure in this cohort increased across 12 years. From north to south of China blood pressure showed a declining trend. BMI distribution showed similar pattern (Figure 1c). Across provinces, the distributions of age were comparable (Figure 1d).

As shown in Supplementary Table 2, bivariate analyses using GEE method showed that urban or rural residence, age, gender, BMI and province were significant predicators of hypertension outcome. Further, multivariate analyses found that the significance of these effects didn't change while adjusting for other significant effects. Adjusting for other effects, the odds

Table 1 Demographics over survey years. Data are presented as $\mathrm{N}(\%)$.

| Characteristics | $\begin{gathered} 1997 \\ (\mathrm{~N}=7710) \end{gathered}$ | $\begin{gathered} 2000 \\ (\mathrm{~N}=6677) \end{gathered}$ | $\begin{gathered} 2004 \\ (\mathrm{~N}=5946) \end{gathered}$ | $\begin{gathered} 2006 \\ (\mathrm{~N}=5621) \end{gathered}$ | $\begin{gathered} 2009 \\ (\mathrm{~N}=4974) \end{gathered}$ | P -value* |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 100\% | 86.6\% | 77.1\% | 72.9\% | 64.5\% |  |
| Gender |  |  |  |  |  | 0.164 |
| Male | 3918 (50.8) | 3272 (49.0) | 2960 (49.8) | 2763 (49.2) | 2442 (49.1) |  |
| Female | 3792 (49.2) | 3405 (51.0) | 2986 (50.2) | 2858 (50.9) | 2532 (50.9) |  |
| Nationality |  |  |  |  |  | 0.579 |
| Han | 6784 (88.0) | 5849 (87.6) | 5231 (88.0) | 4978 (88.6) | 4388 (88.2) |  |
| Others | 926 (12.0) | 828 (12.4) | 715 (12.0) | 643 (11.4) | 586 (11.8) |  |
| Residence |  |  |  |  |  | $<0.001$ |
| Urban | 2407 (31.2) | 2153 (32.3) | 1830 (30.8) | 1690 (30.1) | 1429 (28.7) |  |
| Rural | 5303 (68.8) | 4524 (67.8) | 4116 (69.2) | 3931 (69.9) | 3545 (71.3) |  |
| Education |  |  |  |  |  | $<0.001$ |
| Unknown | 2142 (27.8) | 1718 (25.7) | 1361 (22.9) | 1692 (30.1) | 1541 (31.0) |  |
| Primary School | 1835 (23.8) | 1588 (23.8) | 1555 (26.2) | 1093 (19.4) | 1060 (21.3) |  |
| Middle School | 3241 (42.0) | 2850 (42.7) | 2543 (42.8) | 2299 (40.9) | 1507 (30.3) |  |
| Above Middle School | 492 (6.4) | 521 (7.8) | 487 (8.2) | 537 (9.6) | 866 (17.4) |  |
| Province |  |  |  |  |  | 0.517 |
| Heilongjiang | 883 (11.5) | 819 (12.3) | 691 (11.6) | 662 (11.8) | 596 (12.0) |  |
| Jiangsu | 1011 (13.1) | 937 (14.0) | 740 (12.5) | 705 (12.5) | 653 (13.1) |  |
| Shandong | 842 (10.9) | 741 (11.1) | 676 (11.4) | 635 (11.3) | 547 (11.0) |  |
| Henan | 976 (12.7) | 801 (12.0) | 708 (11.9) | 653 (11.6) | 576 (11.6) |  |
| Hubei | 991 (12.9) | 832 (12.5) | 770 (13.0) | 714 (12.7) | 656 (13.2) |  |
| Hunan | 932 (12.1) | 823 (12.3) | 706 (11.9) | 702 (12.5) | 593 (12.0) |  |
| Guangxi | 1055 (13.7) | 857 (12.8) | 864 (14.5) | 807 (14.4) | 675 (13.6) |  |
| Guizhou | 1020 (13.2) | 867 (13.0) | 791 (13.3) | 743 (13.2) | 678 (13.6) |  |

Table 2 Hypertension awareness, treat and control over survey years.

|  | 1997 | 2000 | 2004 | 2006 |  |
| :--- | :---: | :---: | :---: | :---: | :---: |
| Sample size, $\mathbf{N}$ | 7710 | 6677 | 5946 | 5621 |  |
| Prevalence of Hypertension, $\mathbf{n}(\%)$ | $1162(15.1)$ | $1299(19.5)$ | $1397(23.5)$ | $1320(23.5)$ | $1600(32.2)$ |
| Awareness among hypertension, $\mathbf{n}$ (\%) | $237(20.4)$ | $398(30.6)$ | $493(35.3)$ | $527(40.0)$ |  |
| Treatment, $\mathbf{n}$ | 149 | 263 | 351 | $699(43.7)$ |  |
| Among those being aware, (\%) | $(62.9)$ | $(66.0)$ | $(71.2)$ | 591 | $(74.2)$ |
| Among all with hypertension, (\%) | $(12.8)$ | $(20.2)$ | $(25.1)$ | $(29.7)$ | $(79.0)$ |
| Control, $\mathbf{n}$ | 46 | 61 | 118 | $(34.5)$ |  |
| Among those treated, (\%) | $(30.9)$ | $(23.2)$ | $(33.6)$ | 125 | $(31.9)$ |
| Among those with hypertension, (\%) | $(4.0)$ | $(4.7)$ | $(8.5)$ | $(9.5)$ | $(29.2)$ |

ratio of male vs. female was 1.40 ( $96 \% \mathrm{Cl}: 1.29,1.52$ ). The odds ratio of urban vs. rural was 1.13 ( $95 \% \mathrm{Cl}: 1.03,1.23$ ). One unit increase in BMI increased 17\% odds of hypertension while 10 years increase in age doubled the odds of hypertension. The risk of hypertension increased with a spatial pattern in general that was in line with the south-north axis in both analyses (Figure 2). The farthest north province, Heilongjiang, corresponded to the highest risk with an adjusted OR of 2.4 ( $95 \% \mathrm{Cl}: 2.0,2.8$ ) vs. south province Guizhou.

## Discussion

The sample population of this study was not nationally representative. However, the participated provinces accounted for $40 \%$ of Chinese population and great diversity of socioeconomic development stages [5]. The gender ratio,
education status and residence status (urban / rural) of study population were comparable to the national data. Therefore the results of this study are able to provide useful perspectives in terms of hypertension risk profile in China.

The prevalence of hypertension in this cohort increased over years. A great leap occurred from 2006 to 2009. In 2009, the ages of entire cohort were above 30 years old. This may partially contribute to this jump. Although there were some improvements, the proportions of awareness, treatment and control among hypertensive population in this study in 2009 were markedly lower than same statistics in the US 10 years earlier (32.2\% / 43.7\% / 10.1\% in 2009 vs. 68.7\% / 58.2\% / 29.2\% in 1999-2000, respectively) [11].
Using multivariate GEE approach to predict the likelihood of developing hypertension, male was found to be $40 \%$ lower in


Figure 1 The trajectories of blood pressure, BMI and age over 12 years for participated provinces.
odds of having hypertension than female. The result is consistent with other studies [12-14]. It is well known that the gender effect depends on age [13]. This potential moderation can be examined further by introducing interaction term between age and gender. In this study, rural residence accounted for $12 \%$ lower odds in developing hypertension than urban residence. Studies have found that the prevalence of hypertension was lower in rural China although during recent decade rural area increased much faster than urban area [15, 16].
The most interesting result of the present study is the overall increasing trend of hypertension risk from south to north of China, along with the increase of latitude. This result is consistent with previous studies [6, 7, 15-17] in which higher salt intake with Na and $\mathrm{Na} / \mathrm{K}$, lack of physical activity during winter and heavier body mass were considered to be underlying causes. Nevertheless, this analysis is the first time to evaluate the south-north difference in such a detail that participating provinces almost lined up longitudinally in map, and there was no study that had tracked the change of risk over years within a longitudinal setting.

The reason of this spatial pattern remains uncertain in our analysis. Multivariate analyses implied that the regional disparity was independent to the BMI variation, gender and rural residence. Researchers have found that nutraceuticals and function food ingredients are able to reduce dyslipidaemia [18]. It would be responsible to assume the dietary difference might be attributable to this disparity. However, the dietary habit or life style didn't vary too much in adjacent provinces, such as Guangxi and Guizhou, Hunan and Hubei, Henan and Shandong. It implies that no single or simple underlying factor may fully account for this disparity. Interestingly, the lowest risk of Guozhou coincided with its most backward economy in the participated provinces. On the other hand, Jiansu was outstanding from the trend due to higher hypertension risk even it is north to Shandong and as same north as Henan. This province also has the highest GDP per capita in China. This may signalize the impact of socioeconomic development on the risk of hypertension in China.
The main strength of this study is its longitudinal design that


Figure 2 Risk profile of hypertension for eight participated provinces.
same individuals were followed up for years. The sample size is pretty large, and the selected eight provinces are geographically representative.

There are limitations in this study too. The loss to follow-up resulted missing data in analysis. GEE approach assumes the loss to follow up is due to missing completely at random (MCAR). Table 1 tested the variation of respondents over survey years and didn't find significance changes in the proportion of gender, ethnicity and province that had significant impact on blood pressure and hypertension incidence. Although urban residence changed statistically significantly, the magnitude was pretty small. Further, the primary aim of CNHS was not to investigate the risk of hypertension. The assumption of MCAR is fairly reasonable. Another limitation is that we didn't have data that could give us complete risk profile of hypertension, such as information of
glucose and lipid, for this cohort. Therefore it's difficult to figure out the cause of the observed disparities using current data.

We concluded that there are significant regional disparities in hypertension risk in China. The spatial pattern appears as gradually increasing risk from south to north China. This effect is not sourced from regional variation in gender, age, urban / rural residence and BMI. The further investigation into this phenomenon is warranted.

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