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Twenty-year trend of hypertension prevalence in Yi people of China: The Yi migrant study, 1996 to 2015

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Title:

Twenty-year trend of hypertension prevalence in Yi people of China: The Yi migrant study, 1996 to 2015

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ABSTRACT:

Objective To explore the trend of hypertension prevalence and related factors in Yi people from 1996 to 2015.

Methods Three successive cross-sectional surveys were conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007 and 2015, respectively. A total of 8448 participants aged 20-80 years (5040 Yi farmers, 3408 Yi migrants) were included in final analysis.

Results Overall, the age-standardized prevalence of hypertension in migrants was significantly higher than farmers'. Furthermore, the age-standardized prevalence rates increased from 10.1% to 19.6% in Yi migrants and from 4.0% to 13.1% in Yi farmers during 1996 to 2015. The highest 2015-to-1996 ratio of age-standardized hypertension prevalence was in male farmers (ratio=4.30), whereas despite the highest prevalence of hypertension, the equivalent figure in male migrants was 1.57. The older age, overweight, and obesity were persistently risk factors of hypertension in three periods. After adjusted for age and body mass index, the difference of hypertension prevalence between 1996 and 2015 then vanished in male migrants (odds ratio=1.335; 95% confidence interval: 0.884, 2.015) and female farmers (odds ratio=1.267; 95% confidence interval: 0.590, 2.719). The disparities of hypertension prevalence between Yi migrants and farmers were not statistically significant in all subgroups when adjusted for age, body mass index, and education.

Conclusions Over the past two decades, the hypertension prevalence in Yi people has significantly increased. Yi migrants were more likely to be hypertensive than Yi

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farmers, which was predominantly drove by the discrepancy of body mass index between them.

Key words: obesity; hypertension; migrant; trend; Yi people

ARTICLE SUMMARY

1. It is the first time to explore the hypertension prevalence trend of Yi people by such a long time span and in such a large scale, which could facilitate the promotion of health status of ethnic minorities in China.

2. These three successive Yi migrant studies were almost completed by one stable team, only a few students renewed, and this high consistency guarantees the comparability between different periods.

3. Under the context of rapid urbanization, we conducted migrant study to explore the effect on hypertension of rural-urban migration and its time effect, especially for the Yi people who used to live in high-mountain areas and mountainside areas and began to migrate into counties and cities since 1950s.

4. It might seem unpersuasive to identify causal effect between body mass index and hypertension with cross-sectional study, therefore, conducting prospective cohort study in Yi people is fairly necessary.

5. This study did not analyze the Han people who resided at the same urban areas with Yi migrants in the same period, consequently, the comparison to determine which is relatively important between environment and gene is not able to be accomplished.

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INTRODUCTION

Hypertension, also known as high or raised blood pressure, is the predominant risk factor of heart disease, stroke, and renal failure which are leading causes of death.[1-3] The increasing trends of hypertension prevalence can be observed both in developed countries [4, 5] and developing countries.[6-8]

We live in a rapidly changing environment. Throughout the world, human health is being shaped by the same powerful forces: demographic ageing, rapid urbanization, and the globalization of unhealthy lifestyles. In general, rural–urban migration, as part of urbanization, is considered a promoting factor for chronic diseases [9] and evidence shows that urbanization is estimated to raise the blood pressure of residents.[10] In contemporary China, socioeconomic transformation at the beginning of twenty-first century has led to rapid urbanization and accelerated rural-urban migration [11] along with the phenomenon of increased mean blood pressure that has been described among Chinese population.[12-14]

It is reported that hypertension prevalence in ethnic minorities is significantly higher than in Han.[15] However, Yi people resided in Liangshan Yi Autonomous Prefecture located in Sichuan Province, southwestern China used to be renowned for its low mean blood pressure and prevalence of hypertension [16] and had been undergoing immense scale rural-urban migration.[17] Although a host of investigations about hypertension prevalence of Han people have been carried out, [18-20] the data about

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trend of hypertension prevalence in Yi people is insufficient. Therefore, it is of great necessity to conduct relevant research to acknowledge the situation of hypertension in Yi people. Additionally, as the dramatic health transition resulted from rapid rural-urban migration, Yi people may encounter higher hypertension prevalence than before.

Accordingly, we conducted the Yi migrant study to assess the prevalence of hypertension by migration status and period; the association of hypertension with individual characteristics; the related factors that accounting for the discrepancy of hypertension prevalence among subgroups and periods.

METHODS

Study Design and participants

The Yi people is a minority in China living in Liangshan Yi Autonomous Prefecture in Southern China, an area that covers about 60,000 kilometers and has roughly 5 million residents in which 52.5% are Yi people. The Yi people usually live in remote mountain districts at or above 1,500 meters above sea level. Their main occupation is agriculture, and they are one of the most primitive societies in China. The Yi Migrant Study includes three cross□sectional studies conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007, and 2015, respectively. The sampling procedures have been published previously in detail.[21, 22] In the two previous periods, stratified cluster sampling was used to select participants from Xichang city, Butuo, Zhaojue, Jinyang, Puge and Xide counties. Due to the inevitably restrained accessibility, we only conducted our survey in Xichang city and Puge county in 2015.

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The Yi farmers were defined as those whose parents are Yi people and had been lived in countryside since birth. There are one to four county seats in each county. The Yi farmers were selected by stratified cluster sampling from areas around each county seat. Four villages were randomly selected from each area. In the last sampling stage, all the Yi farmers aged 20 years or over in the selected villages were surveyed. There are two types of Yi migrants, one are those who were born in countryside and then migrated into county or city for more than 1 year, the other are Yi people who were born in county or city and lived there until the survey. All Yi migrants' parents are Yi people. And because the number of the Yi migrants was relatively small, all of the Yi migrants (20 years of age and over) found in the selected counties and Xichang city were all enrolled into the study.

Isolated from the outside world, the Yi farmers who live in high-mountain areas and mountainside areas have their own language and primitive life-style. There are only extremely steep and narrow paths leading to these villages, which are several hours walking distance apart. Their mainly nutritional source are staple food such as potato, oat, and buckwheats, and the living conditions are greatly backward, there even no table for eating, almost all Yi farmers squat down to eat in 2015. The Yi migrants who live in the county or city with Han people have a much more western life style. It is relatively convenient for them to acquire meat, fresh fruits, and vegetables. And there is a great extent improvement in their living conditions compared with Yi farmers. As the Jiang He's study[23] described that the Yi farmers began to migrate into counties and cities from remote mountain districts since 1950s.

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Patient and Public Involvement

In three periods, the number of participants were 1664, 3768 and 3317 respectively. After excluded those who were out of age-bracket or lacking of key variables such as blood pressure and migration status, there were a total of 8448 Yi people in the final analysis (Figure 1). Informed consent was obtained from all of the participants, and all surveys were approved by the Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences ((No. 033-2012), Beijing.

Data were collected by trained medical staff using standardized methods and identical examinations in 1996 to 2015, including questionnaire for assessment of demographic characteristics and anthropometrical measurements. The results of survey were disseminated to study participants by physical examination reports in 1996 and 2007, and in 2015 we developed an application which could allow participants to search their results at any time using mobile phones.

Measurements

Both body height and weight were measured with the participants in light clothing and without shoes after an overnight fast. Body mass index (BMI) was defined as measured weight in kilograms divided by squared height in meters. There were 4 BMI categories: underweight defined as a BMI <18.5 kg/m^2; normal weight, 18.5 to 23.9kg/m^2; overweight, 24 to 27.9kg/m^2; and obese, ≥28 kg/m^2.

Education was categorized as low (received only primary education or no education), middle (finished secondary school or high school) and high (graduated from college or university).

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Physical activity was divided into three categories: (1) light: e.g., office worker, salesperson, and house worker; (2) Middle: e.g., driver, electrician, and latheman; (3) Heavy: e.g., manual worker, steel worker, and mineworker.

Smoking status was classified as never-smokers and ever-smokers, which included current smokers (having been regularly smoking at least one cigarette per day during the previous six months) and ex-smokers (once smoked but had quitted smoking for six months or longer). Alcohol consumption was divided into never drinker and ever drinker those who drank at least twice per month (more than 640 ml beer or 100 ml Chinese liquor, about 57 g alcohol), and had lasted for at least 6 months or stopped drinker.

After an overnight fast, blood pressure (BP) were measured by trained physicians using mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device (HEM-907) in 2007 and 2015. Appropriate blood pressure cuff sizes were used for participants based on measurement of midarm circumference. BP was measured in the sitting position and on the right arm after a rest of at least 10 min and had not smoked, exercised, or eaten. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded. The mean of three measurements was used for all analyses. The definition for hypertension was as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.[24]

Statistical analysis

Summary results are presented as percentages (with numbers) for categorical

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variables and mean (and standard deviations, SD) for continuous variables. Comparisons of the differences in mean age and male percentage between 1996 and 2015 were performed using t test and chi-square test, respectively. As for other continuous variable and categorical variables, applying covariance analysis and logistic regression to adjust age and sex, respectively.

Direct standardization was performed using China population age structure from the Sixth National Population Census in 2010 by SAS 9.4 using 'stdrate' commend. And the geometric progression method was used to predict age-standardized prevalence of hypertension in Yi people by 2030.

To explore related factors of hypertension in each period, we used multiple logistic regression model to calculate odds ratio (OR) and the 95% confidence interval (CI); in which age was continuous variable while sex, BMI groups, education, activities, smoking, and drinking were categorical variables.

Finally, we developed a set of logistic regression models to identify reasons behind disparities between different periods and different migration status. P values <0.05 were considered statistically significant. All statistical analyses were conducted by SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Study Population Characteristics

Table 1 displays the characteristics of Yi people and the unadjusted prevalence of hypertension within time periods by migration status. Over the 3 study periods, the prevalence of obesity rose from 0.4% to 7.1% in Yi farmers, and from 4.6% to 17.4%

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in Yi migrants. By 2015, the crude prevalence of hypertension had increased by 9.5% in farmers, and by almost 16% in migrants.

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Table 1. Characteristics of participants by migration status and period, Yi migrant study, 1996-2015

Variable	Farmers				Migrants			
	1996 N=723	2007 N=2351	2015 N=1966	*P* for 1996 vs. 2015[a]	1996 N=679	2007 N=1393	2015 N=1336	*P* for 1996 vs. 2015[a]
Mean age, y (SD)	35.0 (12.7)	39.4 (12.0)	45.3 (12.8)	<.0001	37.9 (11.2)	39.6 (12.0)	48.3 (14.4)	<.0001
Mean BMI (SD)	20.3 (2.1)	21.4 (2.6)	22.3 (3.6)	<.0001[b]	22.4 (3.0)	23.5 (3.7)	24.4 (3.8)	<.0001[b]
Male, % (N)	63.5 (459)	47.1 (1107)	33.8 (664)	<.0001	57.1 (388)	57.3 (798)	33.1 (442)	<.0001
BMI categories, % (N)				<.0001[b]				<.0001[b]
Underweight (BMI<18.5)	15.3 (110)	9.4 (220)	12.8 (249)		8.3 (56)	7.2 (100)	5.0 (66)	
Normal weight (BMI18.5-23.9)	81.8 (588)	78.4 (1837)	58.3 (1133)		63.4 (428)	51.6 (718)	42.3 (560)	
Overweight (BMI24-27.9)	2.5 (18)	10.6 (248)	21.8 (423)		23.7 (160)	30.1 (418)	35.4 (468)	
Obesity (BMI≥28)	0.4 (3)	1.7 (39)	7.1 (138)		4.6 (31)	11.1 (155)	17.4 (230)	
Education, % (N)				<.0001[b]				<.0001[b]
Low	92.3 (658)	91.5 (2109)	88.4 (1738)		19.2 (130)	24.2 (329)	49.3 (658)	
Middle	7.0 (50)	7.6 (175)	10.4 (204)		62.3 (421)	38.6 (524)	32.4 (432)	
High	0.7 (5)	0.9 (21)	1.2 (24)		18.5 (125)	37.1 (504)	18.4 (245)	
Physical activity, % (N)				<.0001[b]				<.0001[b]
Light	4.6 (33)	3.4 (79)	28.4 (557)		62.5 (422)	73.2 (1018)	78.0 (1042)	
Moderate	9.7(70)	7.2 (168)	6.2 (122)		36.7(248)	17.4 (241)	14.3 (191)	
Heavy	85.7 (618)	89.4 (2094)	65.4 (1286)		0.8 (5)	9.4 (131)	7.7 (103)	
Smoking, % (N)	49.4 (357)	41.8 (983)	32.8 (644)	0.0247[b]	46.2(314)	42.6 (593)	32.0 (427)	0.9709[b]
Drinking, % (N)	40.7 (294)	30.3 (712)	37.5 (736)	<.0001[b]	44.8 (304)	51.5 (718)	44.8 (598)	<.0001[b]
Hypertension,% (N)[C]	3.5 (25)	5.5 (130)	13.0 (255)	<.0001	8.0 (54)	14.8 (206)	23.7 (316)	<.0001

Abbreviations: BMI, body mass index.

[a] P value for test of difference between 1996 and 2015.

[b] P-values were calculated after adjusted for age and gender.

[c] Crude prevalence of hypertension; Hypertension was defined as a systolic blood pressure ⩾140 mm Hg, diastolic blood pressure ⩾ 90 mm Hg or the use of antihypertensive drugs.

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Age-standardized prevalence of hypertension

Figure 2 shows the trends of age-standardized hypertension prevalence and predicted prevalence of hypertension over the 20-year period. It is noticeable that the prevalence of hypertension in male migrants was by far the highest among these four groups in each period, from 14.3% to 22.5% (P<0.0001), while the equivalent figure for female farmers was from 4.4% to 10.2% (P<0.0001) which almost the lowest hypertension prevalence in each period (Figure 2-A). Overall, from 1996 to 2015, these four groups saw a statistically increase in prevalence of hypertension (P<0.0001 for all groups).

And the biggest 2015-to-1996 ratio of age-standardized prevalence of hypertension was in male farmers (ratio=4.30), which means this group had the fastest pace of hypertension increase, followed by female migrants (ratio=2.81) and female farmers (ratio=2.32). Interestingly, despite the highest prevalence of hypertension, the 2015-to-1996 ratio of age-standardized prevalence of hypertension in male migrants was 1.57 and it's the lowest growth rate. Accordingly, we predicted that, if the growth rates stayed steadily, male farmers would overtake male migrants to become the most prevalent hypertensive group in 2021 and female migrants would overtake male migrants in 2025 to become the second most prevalent hypertensive group (Figure 2-B).

Related factors of hypertension and hypertensive discrepancy

Figure 3 provides odds ratios for hypertension related factors in each period. Across three period, the higher hypertensive share traits such as much older and having

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higher BMI, but only in 2015 those who acquired high school education or higher were more likely to have hypertension than those whose education level were maximum to primary school (OR=1.524, 95% CI: 1.038, 2.236).

Table 2 shows odds ratios of time period by different models. In model 1, both 2007 and 2015 had significantly higher risk of hypertension versus 1996 among all subgroups. Model 3 in table2 adjusted for age and BMI, the effect of period turned to be not significant in male migrants (OR=1.335, 95% CI: 0.884, 2.015) and female farmers (OR=1.267, 95% CI: 0.590, 2.719), indicating that the increase of hypertension prevalence in these two groups over this 20-year period could be totally explained by the population ageing and upward trend of BMI. While, the residual significant difference among period in female migrants (OR=3.158, 95% CI: 1.474, 6.765) and male farmers (OR=2.287, 95% CI: 1.307, 4.000) suggested that ageing and increasing BMI just accounted for a portion of hypertension prevalence rise.

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Table 2. Odds for hypertension in 2015, 2007 relative to Odds for hypertension in 1996, by Migration Status and Gender

Model		Male		Female	
		Odds Ratio	95% CI	Odds Ratio	95% CI
Migrants					
Model1[a]	1996	1		1	
	2007	1.749	1.227-2.495	3.530	1.657 -7.520
	2015	3.411	2.362-4.925	8.731	4.243 -17.966
Model2[b]	1996	1			
	2007	1.716	1.190 -2.475	2.852	1.321 - 6.158
	2015	1.822	1.226 -2.708	3.982	1.895 -8.368
Model3[c]	1996	1		1	
	2007	1.350	0.923 -1.974	2.661	1.205 -5.874
	2015	1.335	0.884 -2.015	3.158	1.474 -6.765
Farmers					
Model1[a]	1996	1		1	
	2007	2.385	1.405 -4.047	0.981	0.452 -2.131
	2015	5.561	3.293 -9.391	3.793	1.836 -7.835
Model2[b]	1996	1		1	
	2007	2.100	1.232 -3.578	0.776	0.353 -1.703
	2015	3.753	2.193 -6.421	2.252	1.074 -4.725
Model3[c]	1996	1		1	
	2007	1.763	1.025 -3.032	0.544	0.245 -1.210
	2015	2.287	1.307 -4.000	1.267	0.590 -2.719

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age.

[c] Model3 adjusted for age and BMI.

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In order to investigate the reason behind discrepancy in hypertension prevalence between migrants and farmers, Table 3 shows odds ratio of migrant status (migrants vs. farmers) by different models. Form model 1 we noticed that migrants were more likely had higher risk of hypertension among all subgroups except the female in 1996 (OR=0.905, 95% CI: 0.335, 2.445). Model 3 in table3 adjusted for age and BMI, and there were no significant difference between migrants and farmers for males in 2007 (OR=1.097, 95% CI: 0.782, 1.539) and 2015 (OR=0.992, 95% CI: 0.674, 1.460), and for females in 2015 (OR=1.126, 95% CI: 0.834, 1.521). After adjusted for age, BMI and education, the discrepancy between migrants and farmers in males in 1996 (OR=1.753, 95% CI: 0.729, 4.217) and females in 2007 (OR=1.295, 95% CI: 0.711, 2.357) had disappeared. Therefore, we may conclude that for males in 2007 and 2015 and females in 2015, the higher risk of hypertension in migrants was resulted from ageing and increasing BMI, whereas for males in 1996 and females in 2007, not only these two factors mentioned above but also the education contributed to the remainder higher risk of hypertension in migrants.

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Table 3. Odds for hypertension in migrants relative to Odds for hypertension in farmers, by Gender and Period

Model	1996		2007		2015	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Male						
Model1[a]	3.497	1.970 -6.207	2.565	1.946 -3.382	2.145	1.616 -2.847
Model2[b]	3.027	1.694 -5.410	2.486	1.874 -3.296	1.729	1.283 -2.329
Model3[c]	1.944	1.026 -3.684	1.097	0.782 -1.539	1.151	0.828 -1.600
Model4[d]	1.753	0.729 -4.217	0.807	0.513 -1.271	0.992	0.674 -1.460
Female						
Model1[a]	0.905	0.335 -2.445	3.257	2.118 -5.008	2.082	1.636 -2.650
Model2[b]	1.048	0.375 -2.931	3.637	2.342 -5.647	1.869	1.447 -2.414
Model3[c]	0.505	0.142 -1.799	2.359	1.473 -3.778	1.222	0.927 -1.611
Model4[d]	0.829	0.195 -3.518	1.295	0.711 -2.357	1.126	0.834 -1.521

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age.

[c] Model3 adjusted for age and BMI.

[d] Model4 adjusted for age, BMI, and education.

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DISCUSSION

Rising migrants number, coupled with population aging, have elicited major concern over the consequences of lifestyle changes for chronic diseases. Recent increases in longevity may not accompanied by a compression of morbidity, resulting in more years spent in an unhealthy state.[25] Our prior work have showed that the mean blood pressure of Yi farmers didn't rise or rarely rise with age after puberty, and essential hypertension was absent.[16] In this study, we investigated whether this unusually hypertensive profile of Yi people has continued.

We found that the prevalence of hypertension in Yi people had seen a dramatically increase over the past twenty-year period, but still lower than the whole country when compared with studies which used the same standardized population structure.[26-29] What is noteworthy is that Yi migrants had higher risk of hypertension than Yi farmers in each period, while the discrepancy in prevalence of hypertension between migrants and farmers is narrowing. Jiajia Li and her colleagues had found that the urban-rural gaps in hypertension prevalence gradually narrowed during the period 1993–2011,[30] which might be attributed to the suboptimal hypertension detection and preventive care service utilization in rural adults.[31] The Third National Health Services Survey in China[32] indicates that rural minority Chinese use significantly less health services, includes visiting physicians and hospital utilization, than urban minority Chinese. And the result that hypertension was much more prevalent in Yi migrants than Yi farmers was also consistent with many other research. The Kenyan Luo migration study conducted by Poulter et al[33] confirmed that the blood pressure of

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migrants who left a traditional rural community to settle in an urban one were significantly higher than that of control. In addition, as our country has witnessed numerous rural-urban migration,[34] there are quantitative relation between the migration and hypertension. Similarly, India is a rapidly urbanizing country which encountered the same problems as China. A cross-sectional study [35] of neo-migrants and settled-migrants (at least 10 years residence) in the city of Delhi found that settled-migrants had higher prevalence of hypertension than neo-migrants.

In our study, we detected that ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Higher BMI definitely increase the risk of hypertension,[36] and even the impact of overweight and obesity on hypertension had raised significantly over time.[37] The crude prevalence of overweight and obesity undoubtedly increased across the twenty-year period in Yi people, which was consistent with Prof. Shan's study, and revealed that both Yi migrants and Yi farmers had a distinct increase in prevalence of overweight and obesity during 1996 to 2007.[22] A cross-sectional study indicated that Yi people in China exhibited a strikingly lower prevalence of overweight and obesity than that observed in populations of Western countries, and overweight and obesity figures were 21.7% and 7.1% in 2008, respectively.[38] Additionally, The disparity in the prevalence of overweight/obesity between urban and rural areas was narrowing since 2000,[39] which could also interpret the declining trend of gap in hypertension between Yi migrants and Yi farmers. However, even though adjusted age and BMI, there still have significant difference of hypertension

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prevalence between 2015 and 1996 in female migrants and male farmers. It might seem that some uninvolved factors, such as diet and economy, are responsible for the remaining risk of hypertension in these two groups. China Health and Nutrition Survey indicated that there was a dramatic change in dietary pattern in the past two decades, especially the steep increase of the "Modern" pattern, while the "Traditional" pattern was stable over the study period, which means that now days people more likely to consume processed food that with refined carbohydrates, added salt and sweetener, edible oils, animal-resource foods, but the average intake of cereal, fresh fruits, and vegetables had decreased.[40, 41] Yi farmers who preserved their own language and primitive life-style rarely eat meat except during the Yi New Year in December, and their main crops are potatoes, oats, and buckwheats.[16] With economic growth and large-scale migration, Yi people consume more modern foods which contain high level of sugar, salt and fat, especially in Yi migrants.[42] Therefore, we suppose that changes in Yi people's diet probably account for a part of hypertensive risk.

Distinguish from other research, these three successive Yi migrant studies were almost completed by one stable team, only a few students renewed. And this high consistency guarantees the comparability between different periods. Furthermore, it is the first time to explore the hypertension prevalence trend of Yi people by such a long time span and in such a large scale. We also investigated the reasons of hypertension discrepancy both between different periods and different groups, which will provide local government with relatively practical recommendations for the prevention and

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treatment of hypertension.

There are several limitations that merit comment. At first, our study did not analyze the Han people who resided at the same urban areas with Yi migrants in the same period. Thus, the comparison to determine which is relatively important between environment and gene is not able to be accomplished. Furthermore, the tool of measuring blood pressure is not consistent among three periods. We used the mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device in 2007 and 2015. It might have slightly bias among the measurements, but the automatic device had been calibrated with the mercury sphygmomanometer before measurements. And there are studies had validated the accuracy and validation of Omron HEM-907.[43-45] At last, our research belong to cross-sectional study. It might seem unpersuasive to identify causal effect between BMI and hypertension, and selection bias probably decrease the comparability between different periods. Therefore, it is fairly necessary to conduct prospective cohort study in Yi people to investigate the association between increased BMI and the rise of hypertension. As for selection bias, we used standardized prevalence of hypertension and adjusted the 'year' by logistic regression model to eliminate the difference of demographic characteristics among three surveys and improve the comparability.

In conclusion, China has undergone unprecedented-scale urbanization and rural-urban migration which accompanied with rigorous challenges of public health during the past two decades. As the rapid increase of hypertension prevalence both in Yi migrants and farmers, effective prevention, detection, treatment, and control of

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hypertension continue to be important goals for health policy, public health, and medical care decision makers, as well as individuals who have higher risk of hypertension. We should be noted that although Yi migrants were more likely to be hypertensive than Yi farmers in each period, the growth rates of these two groups were exactly reverse. In general, ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Nevertheless, it is necessary to conduct cohort study in rural-urban migrants to explore the causal effect. These results put the onus on the governments and assist the government to tailor prevention and treatment programs for high risk population in Yi people.

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AUTHOR CONTRIBUTIONS

JZ participated in the data collection and drafted the manuscript. SW, WY, FY, ZL participated in the data collection. BZ, FD, LP, HG, GX, GL, YL, XW, GS participated in the design of the study and undertook statistical analyses. All authors

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were involved in writing the paper and had final approval of the submitted version.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

ETHICS APPROVAL

Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (No. 033-2012), Beijing.

PROVENANCE AND PEER REVIEW

Not commissioned; externally peer reviewed.

DATA SHARING STATEMENT

No additional data are available.

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Figure 1. Flow diagram of Yi migrant study

Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

Figure 2. Age-standardized prevalence of hypertension and Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015.

A, Age-standardized prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Age-standardized prevalence of hypertension was calculated by the direct method using the Chinese population age structure form the Sixth National Population Census in 2010.

B, Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Predicted prevalence of hypertension were calculated by the Geometric Progression Method.

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015.

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The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

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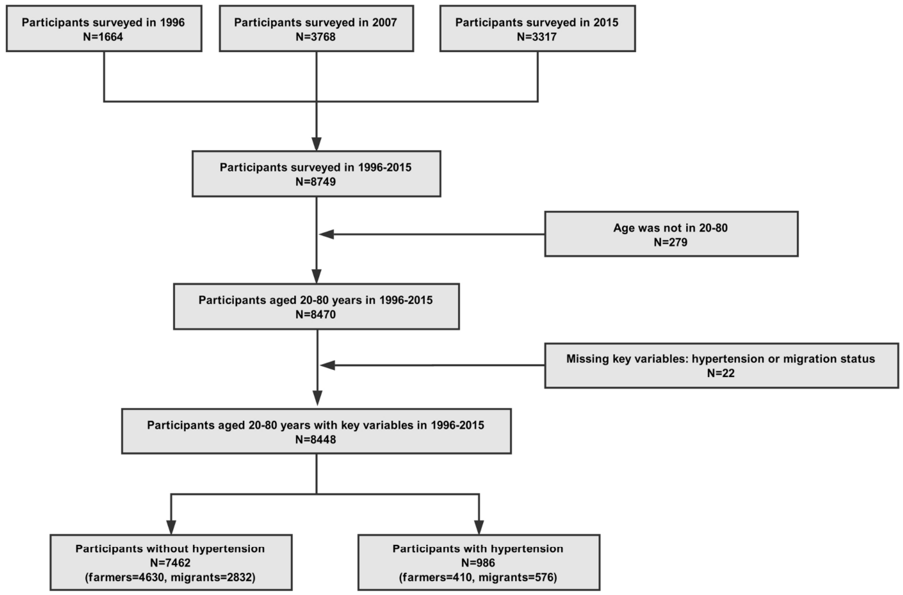

Figure 1. Flow diagram of Yi migrant study
Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

193x134mm (300 x 300 DPI)

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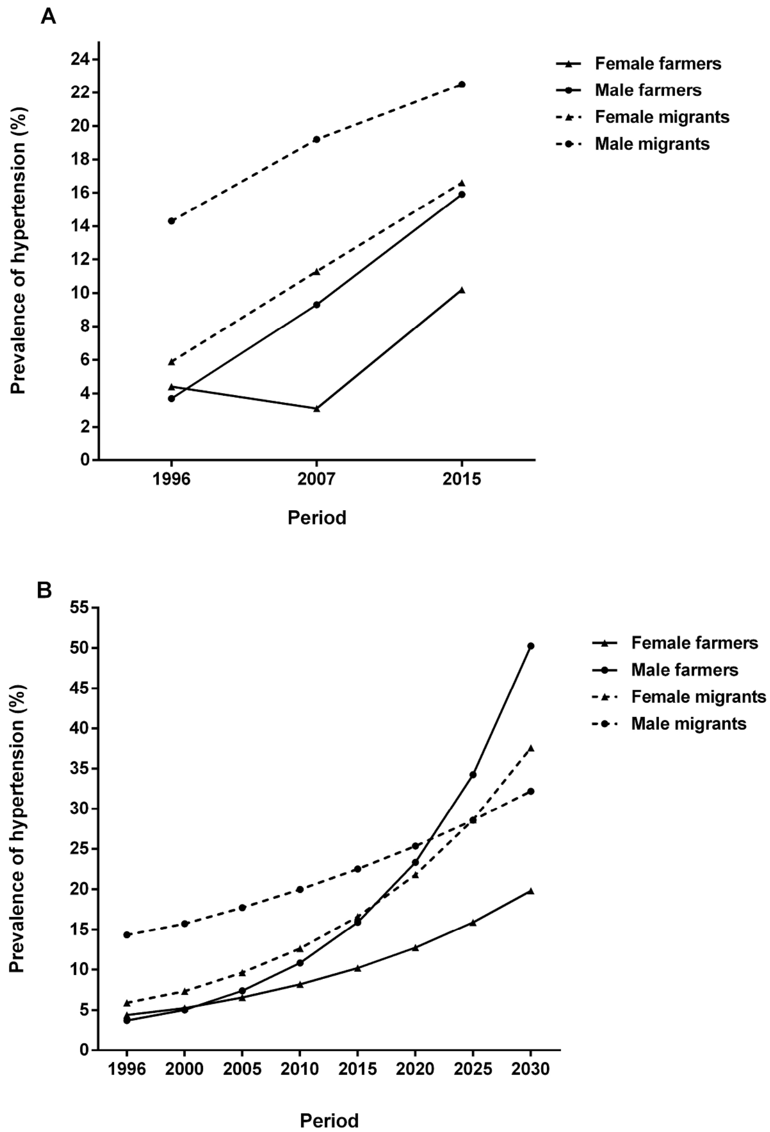

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115x165mm (600 x 600 DPI)

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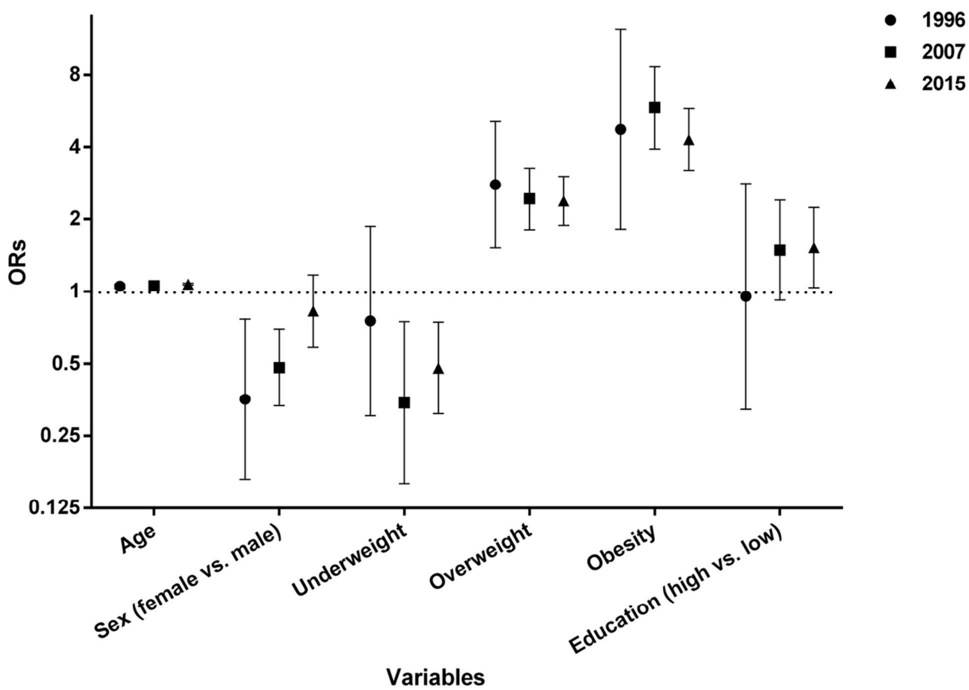

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015. The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

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The STROBE-Vet statement checklist.

	Item	STROBE-Vet recommendation	Page #
Title and Abstract	1	(a) Indicate that the study was an observational study and, if applicable, use a common study design term	1
		(b) Indicate why the study was conducted, the design, the results, the limitations, and the relevance of the findings	1
Background / rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	(a) State specific objectives, including any primary or secondary prespecified hypotheses or their absence	5
		(b) Ensure that the level of organization[a] is clear for each objective and hypothesis	4
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	(a) Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
		(b) If applicable, include information at each level of organization	5-6
Participants [b]	6	(a) Describe the eligibility criteria for the owners/managers and for the animals, at each relevant level of organization	5-6
		(b) Describe the sources and methods of selection for the owners/managers and for the animals, at each relevant level of organization	5-6
		(c) Describe the method of follow-up	NA
		(d) For matched studies, describe matching criteria and the number of matched individuals per subject (e.g., number of controls per case)	NA
Variables	7	(a) Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. If applicable, give diagnostic criteria	6-8
		(b) Describe the level of organization at which each variable was measured	6-8
		(c) For hypothesis-driven studies, the putative causal-structure among variables should be described (a diagram is strongly encouraged)	NA

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Data sources / measurement	8*	(a) For each variable of interest, give sources of data and details of methods of assessment (measurement). If applicable, describe comparability of assessment methods among groups and over time	6-8
		(b) If a questionnaire was used to collect data, describe its development, validation, and administration	7
		(c) Describe whether or not individuals involved in data collection were blinded, when applicable	NA
		(d) Describe any efforts to assess the accuracy of the data (including methods used for "data cleaning" in primary research, or methods used for validating secondary data)	8
Bias	9	Describe any efforts to address potential sources of bias due to confounding, selection, or information bias	8
Study size	10	(a) Describe how the study size was arrived at for each relevant level of organization	6
		(b) Describe how non-independence of measurements was incorporated into sample-size considerations, if applicable	7
		(c) If a formal sample-size calculation was used, describe the parameters, assumptions, and methods that were used, including a justification for the effect size selected	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8-9
Statistical methods	12	(a) Describe all statistical methods for each objective, at a level of detail sufficient for a knowledgeable reader to replicate the methods. Include a description of the approaches to variable selection, control of confounding, and methods used to control for non-independence of observations	8-9
		(b) Describe the rationale for examining subgroups and interactions and the methods used	8-9
		(c) Explain how missing data were addressed	Figure 1
		(d) If applicable, describe the analytical approach to loss to follow-up, matching, complex sampling, and multiplicity of analyses	8-9
		(e) Describe any methods used to assess the robustness of the analyses (e.g., sensitivity analyses or quantitative bias assessment)	19
Participants	13*	(a) Report the numbers of owners/managers and animals at each stage of study and at each relevant level of organization - e.g., numbers eligible, included in the study, completing follow-up, and analyzed	6

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		(b) Give reasons for non-participation at each stage and at each relevant level of organization	6-7
		(c) Consider use of a flow diagram and/or a diagram of the organizational structure	Figure 1
Descriptive data on exposures and potential confounders	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders by group and level of organization, if applicable	9-10
		(b) Indicate number of participants with missing data for each variable of interest and at all relevant levels of organization	Figure 1
		(c) Summarize follow-up time (e.g., average and total amount), if appropriate to the study design	NA
Outcome data	15*	(a) Report outcomes as appropriate for the study design and summarize at all relevant levels of organization	11
		(b) For proportions and rates, report the numerator and denominator	10-11
		(c) For continuous outcomes, report the number of observations and a measure of variability	10
Main results	16	(a) Give unadjusted estimates and, if applicable, adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders and interactions were adjusted. Report all relevant parameters that were part of the model	11-15
		(b) Report category boundaries when continuous variables were categorized	10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-15
Other analyses	17	Report other analyses done,-such as sensitivity/robustness analysis and analysis of subgroups	13
Key results	18	Summarize key results with reference to study objectives	16-17
Strengths and Limitations	19	Discuss strengths and limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalizability	21	Discuss the generalizability (external validity) of the study results	19
~~Funding~~ Transparency	22	(a) Funding- 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 (b) Conflicts of interest-Describe any conflicts of interest, or lack thereof, for each author	20-21

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		(c) Describe the authors' roles- Provision of an authors' declaration of transparency is recommended (d) Ethical approval- Include information on ethical approval for use of animal and human subjects (e) Quality standards-Describe any quality standards used in the conduct of the research	

[a] Level of organization recognizes that observational studies in veterinary research often deal with repeated measures (within an animal or herd) or animals that are maintained in groups (such as pens and herds); thus, the observations are not statistically independent. This non-independence has profound implications for the design, analysis, and results of these studies.
[b] The word "participant" is used in the STROBE statement. However, for the veterinary version, it is understood that "participant" should be addressed for both the animal owner/manager and for the animals themselves.
*Give such information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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Twenty-year time trends in hypertension prevalence in Yi people of China: Three successive cross-sectional studies, 1996-2015

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Title:

Twenty-year time trends in hypertension prevalence in Yi people of China: Three successive cross-sectional studies, 1996-2015

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ABSTRACT:

Objective To explore the trend of hypertension prevalence and related factors in Yi people from 1996 to 2015.

Methods Three successive cross-sectional surveys were conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007 and 2015, respectively. A total of 8448 participants aged 20-80 years (5040 Yi farmers, 3408 Yi migrants) were included in final analysis.

Results Overall, the age-standardized prevalence of hypertension in migrants was significantly higher than farmers'. Furthermore, the age-standardized prevalence rates increased from 10.1% to 15.3% to 19.6% in Yi migrants and from 4.0% to 6.3% to 13.1% in Yi farmers during 1996 to 2007 to 2015. The highest 2015-to-1996 ratio of age-standardized hypertension prevalence was in male farmers (ratio=4.30), whereas despite the highest prevalence of hypertension, the equivalent figure in male migrants was 1.57. The older age, overweight, and obesity were persistently risk factors of hypertension in three periods. After adjusted for age and body mass index, the difference of hypertension prevalence between 1996 and 2015 then vanished in male migrants (odds ratio=1.335; 95% confidence interval: 0.884, 2.015) and female farmers (odds ratio=1.267; 95% confidence interval: 0.590, 2.719). The disparities of hypertension prevalence between Yi migrants and farmers were not statistically significant in all subgroups when adjusted for age, body mass index, and education.

Conclusions Over the past two decades, the hypertension prevalence in Yi people has significantly increased. Yi migrants were more likely to be hypertensive than Yi

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farmers, which was predominantly drove by the discrepancy of body mass index between them.

Key words: obesity; hypertension; migrant; trend; Yi people

Strengths and limitations of this study

1. The present study was first designed to explore the hypertension prevalence trend of Yi people during last two decades.

2. These three population-based successive Yi migrant studies were implemented by identical team and followed the same protocol.

3. Under the context of rapid urbanization, the rural-urban migration effect on health was estimated by comparing hypertension prevalence between Yi migrants and Yi farmers.

4. The unclear temporal relationship between body mass index and hypertension is due to inherent weakness of cross-sectional studies, and have been heatedly debated in epidemiological studies.

5. Furthermore, important confounding factors possibly associated with the increasing trend in hypertension prevalence in Yi people, such as nutrition and environmental changes, were not evaluated in the present study.

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INTRODUCTION

Hypertension, also known as high or raised blood pressure, is the predominant risk factor of heart disease, stroke, and renal failure which are leading causes of death.[1-3] The increasing trends of hypertension prevalence can be observed both in developed countries [4, 5] and developing countries.[6-8]

We live in a rapidly changing environment. Throughout the world, human health is being shaped by the same powerful forces: demographic ageing, rapid urbanization, and the globalization of unhealthy lifestyles. In general, rural–urban migration, as part of urbanization, is considered a promoting factor for chronic diseases [9] and evidence shows that urbanization is estimated to raise the blood pressure of residents.[10] In contemporary China, socioeconomic transformation at the beginning of twenty-first century has led to rapid urbanization and accelerated rural-urban migration [11] along with the phenomenon of increased mean blood pressure that has been described among Chinese population.[12-14]

It is reported that hypertension prevalence in ethnic minorities is significantly higher than in Han.[15] However, Yi people resided in Liangshan Yi Autonomous Prefecture located in Sichuan Province, southwestern China used to be renowned for its low mean blood pressure and prevalence of hypertension [16] and had been undergoing immense scale rural-urban migration.[17] Although a host of investigations about hypertension prevalence of Han people have been carried out, [18-20] the data about trend of hypertension prevalence in Yi people is insufficient. Therefore, it is of great necessity to conduct relevant research to acknowledge the situation of hypertension in

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Yi people. Additionally, as the dramatic health transition resulted from rapid rural-urban migration, Yi people may encounter higher hypertension prevalence than before.

Accordingly, we conducted the Yi migrant study to assess the prevalence of hypertension by migration status and period; the association of hypertension with individual characteristics; the related factors that accounting for the discrepancy of hypertension prevalence among subgroups and periods.

METHODS

Study Design and participants

The Yi people is a minority in China living in Liangshan Yi Autonomous Prefecture in Southern China, an area that covers about 60,000 kilometers and has roughly 5 million residents in which 52.5% are Yi people. The Yi people usually live in remote mountain districts at or above 1,500 meters above sea level. Their main occupation is agriculture, and they are one of the most primitive societies in China. The Yi Migrant Study includes three cross□sectional studies conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007, and 2015, respectively. The sampling procedures have been published previously in detail.[21, 22] In the two previous periods, stratified cluster sampling was used to select participants from Xichang city, Butuo, Zhaojue, Jinyang, Puge and Xide counties. Due to the inevitably restrained accessibility, we only conducted our survey in Xichang city and Puge county in 2015.

The Yi farmers were defined as those whose parents are Yi people and had been lived in countryside since birth. There are one to four county seats in each county. The Yi

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farmers were selected by stratified cluster sampling from areas around each county seat. Four villages were randomly selected from each area. In the last sampling stage, all the Yi farmers aged 20 years or over in the selected villages were surveyed. There are two types of Yi migrants, one are those who were born in countryside and then migrated into county or city for more than 1 year, the other are Yi people who were born in county or city and lived there until the survey. All Yi migrants' parents are Yi people. And because the number of the Yi migrants was relatively small, all of the Yi migrants (20 years of age and over) found in the selected counties and Xichang city were all enrolled into the study.

Isolated from the outside world, the Yi farmers who live in high-mountain areas and mountainside areas have their own language and primitive life-style. There are only extremely steep and narrow paths leading to these villages, which are several hours walking distance apart. Their mainly nutritional source are staple food such as potato, oat, and buckwheats, and the living conditions are greatly backward, there even no table for eating, almost all Yi farmers squat down to eat in 2015. The Yi migrants who live in the county or city with Han people have a much more western life style. It is relatively convenient for them to acquire meat, fresh fruits, and vegetables. And there is a great extent improvement in their living conditions compared with Yi farmers. As the Jiang He's study[23] described that the Yi farmers began to migrate into counties and cities from remote mountain districts since 1950s.

Patient and Public Involvement

As the involvement of participants, local centers for disease control and prevention

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were responsible for the propagation and local governments took charge of the recruitment. There were no patient involved in the recruitment to and conduct of the study. In these three periods, the number of participants were 1664, 3768 and 3317 respectively. After excluded those who were out of age-bracket or lacking of key variables such as blood pressure and migration status, there were a total of 8448 Yi people in the final analysis (Figure 1). Informed consent was obtained from all of the participants, and all surveys were approved by the Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences ((No. 033-2012), Beijing.

Data were collected by trained medical staff using standardized methods and identical examinations in 1996 to 2015, including questionnaire for assessment of demographic characteristics and anthropometrical measurements. In order to reduce the information bias, we conducted a two-stage questionnaire survey. Firstly, participants completed the questionnaire with a trained medical staff. Then, there were several group leaders audit each questionnaire by randomly extracting some items. The results of survey were disseminated to study participants by physical examination reports in 1996 and 2007, and in 2015 we developed an application which could allow participants to search their results at any time using mobile phones.

Measurements

Both body height and weight were measured with the participants in light clothing and without shoes after an overnight fast. Body mass index (BMI) was defined as measured weight in kilograms divided by squared height in meters. There were 4 BMI

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categories: underweight defined as a BMI <18.5 kg/m^2; normal weight, 18.5 to 23.9kg/m^2; overweight, 24 to 27.9kg/m^2; and obese, ≥28 kg/m^2.

Education was categorized as low (received only primary education or no education), middle (finished secondary school or high school) and high (graduated from college or university).

Physical activity was divided into three categories: (1) light: e.g., office worker, salesperson, and house worker; (2) Middle: e.g., driver, electrician, and latheman; (3) Heavy: e.g., manual worker, steel worker, and mineworker.

Smoking status was classified as never-smokers and ever-smokers, which included current smokers (having been regularly smoking at least one cigarette per day during the previous six months) and ex-smokers (once smoked but had quitted smoking for six months or longer). Alcohol consumption was divided into never drinker and ever drinker those who drank at least twice per month (more than 640 ml beer or 100 ml Chinese liquor, about 57 g alcohol), and had lasted for at least 6 months or stopped drinker.

After an overnight fast, blood pressure (BP) were measured by trained physicians using mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device (HEM-907) in 2007 and 2015. Appropriate blood pressure cuff sizes were used for participants based on measurement of midarm circumference. BP was measured in the sitting position and on the right arm after a rest of at least 10 min and had not smoked, exercised, or eaten. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded. The mean of three measurements was

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used for all analyses. The definition for hypertension was as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.[24]

Statistical analysis

Summary results are presented as percentages (with numbers) for categorical variables and mean (and standard deviations, SD) for continuous variables. As for trend analysis, simple linear regression model and Cochran-Armitage trend test were used to explore trends of age and male percentage during 1996 to 2015, respectively. For continuous variable, BMI, using multiple linear regression model to adjust for age and sex. In this model, BMI was the dependent variable and age, sex and period were independent variables. For multinomial variables with ordered categories, such as BMI categories and education, the cumulative logistic model was used to calculate the P value of trend analysis, in this model BMI categories or education was the dependent variable and age, sex and period were independent variables. For binary variable, hypertension, we fitted a binary logistic regression model, in which hypertension was the dependent variable and age, sex and period were independent variables, to conduct the trend analysis. All generalized linear model identify the period as continuous variable instead of dummy variables, and its P value in the model represent the result of trend analysis.

Direct standardization was performed using China population age structure from the Sixth National Population Census in 2010 by SAS 9.4 using ‘stdrate’ commend. And the geometric progression method was used to predict age-standardized prevalence of

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hypertension in Yi people by 2030.

To explore related factors of hypertension in each period, we used multiple logistic regression model to calculate odds ratio (OR) and the 95% confidence interval (CI); in which age was continuous variable while sex, BMI groups, education, activities, smoking, and drinking were categorical variables.

Finally, we developed a set of binary logistic regression models to identify reasons behind disparities of hypertension risk between different periods and different migration status, in period models period was treated as dummy variable and period=1996 was the reference group, in migration status models Yi farmers was the reference group. The trend analyses were realized by identifying period as continuous variable in binary logistic regression models. P values <0.05 were considered statistically significant. All statistical analyses were conducted by SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Study Population Characteristics

Table 1 displays the characteristics of Yi people and the unadjusted prevalence of hypertension within time periods by migration status. Over the 3 study periods, the prevalence of obesity rose from 0.4% to 7.1% in Yi farmers, and from 4.6% to 17.4% in Yi migrants. By 2015, the crude prevalence of hypertension had increased by 9.5% in farmers, and by almost 16% in migrants.

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Table 1. Characteristics of participants by migration status and period, Yi migrant study, 1996-2015

Variable	Farmers				Migrants			
	1996 N=723	2007 N=2351	2015 N=1966	*P* for trend	1996 N=679	2007 N=1393	2015 N=1336	*P* for trend
Mean age, years (SD)	35.0 (12.7)	39.4 (12.0)	45.3 (12.8)	<.0001[b]	37.9 (11.2)	39.6 (12.0)	48.3 (14.4)	<.0001[b]
Mean BMI, kg/m^2 (SD)	20.3 (2.1)	21.4 (2.6)	22.3 (3.6)	<.0001[c]	22.4 (3.0)	23.5 (3.7)	24.4 (3.8)	<.0001[c]
Male, % (N)	63.5 (459)	47.1 (1107)	33.8 (664)	<.0001[d]	57.1 (388)	57.3 (798)	33.1 (442)	<.0001[d]
BMI categories, % (N)[a]				<.0001[e]				<.0001[e]
Underweight (BMI<18.5)	15.3 (110)	9.4 (220)	12.8 (249)		8.3 (56)	7.2 (100)	5.0 (66)	
Normal weight (BMI18.5-23.9)	81.8 (588)	78.4 (1837)	58.3 (1133)		63.4 (428)	51.6 (718)	42.3 (560)	
Overweight (BMI24-27.9)	2.5 (18)	10.6 (248)	21.8 (423)		23.7 (160)	30.1 (418)	35.4 (468)	
Obesity (BMI≥28)	0.4 (3)	1.7 (39)	7.1 (138)		4.6 (31)	11.1 (155)	17.4 (230)	
Education, % (N)[a]				<.0001[e]				<.0001[e]
Low	92.3 (658)	91.5 (2109)	88.4 (1738)		19.2 (130)	24.2 (329)	49.3 (658)	
Middle	7.0 (50)	7.6 (175)	10.4 (204)		62.3 (421)	38.6 (524)	32.4 (432)	
High	0.7 (5)	0.9 (21)	1.2 (24)		18.5 (125)	37.1 (504)	18.4 (245)	
Hypertension,% (N)	3.5 (25)	5.5 (130)	13.0 (255)	<.0001[f]	8.0 (54)	14.8 (206)	23.7 (316)	<.0001[f]

Abbreviations: BMI, body mass index.

[a] Numbers do not sum up to the total due to missing data.

[b] P-values were calculated by simple linear regression model in which age was the dependent variable and period were independent variables.

[c] P-values were calculated by multiple linear regression model in which BMI was the dependent variable and age, sex and period were independent variables.

[d] P-values were calculated by Cochran-Armitage trend test.

[e] P-values were calculated by cumulative logistic model in which BMI categories or education was the dependent variable and age, sex and period were independent variables.

[f] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and age, sex and period were independent variables.

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Age-standardized prevalence of hypertension

Figure 2-A shows the trends of age-standardized hypertension prevalence, and Figure2-B is the predicted prevalence of hypertension using geometric progression method. It is noticeable that the prevalence of hypertension in male migrants was by far the highest among these four groups in each period, from 14.3% to 19.2% to 22.5% (for all comparison P<0.0001), while the equivalent figure for female farmers was from 4.4% to 3.1% to 10.2% (for 1996 vs 2015, and 2007 vs 2015 P<0.0001; for 1996 vs 2007 P=0.4792) which almost the lowest hypertension prevalence in each period (Figure 2-A). Overall, from 1996 to 2015, these four groups saw a statistically increase in prevalence of hypertension (P<0.0001 for all groups).

And the biggest 2015-to-1996 ratio of age-standardized prevalence of hypertension was in male farmers (ratio=4.30), which means this group had the fastest pace of hypertension increase, followed by female migrants (ratio=2.81) and female farmers (ratio=2.32). Interestingly, despite the highest prevalence of hypertension, the 2015-to-1996 ratio of age-standardized prevalence of hypertension in male migrants was 1.57 and it's the lowest growth rate. Accordingly, we predicted that, if the growth rates stayed steadily, male farmers would overtake male migrants to become the most prevalent hypertensive group in 2021 and female migrants would overtake male migrants in 2025 to become the second most prevalent hypertensive group (Figure 2-B).

Related factors of hypertension and hypertensive discrepancy

Figure 3 provides odds ratios for hypertension related factors in each period. Across

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three periods, the higher hypertensive share traits such as much older and having higher BMI, but only in 2015 those who acquired high school education or higher were more likely to have hypertension than those whose education level were maximum to primary school (OR=1.524, 95% CI: 1.038, 2.236).

Table 2 shows odds ratios of time period by different models. In model 1, the unadjusted results showed that both 2007 and 2015 had significantly higher risk of hypertension versus 1996 among all subgroups. Model 2 in table 2 adjusted for age and BMI, the effect of period turned to be not significant in male migrants (2007: OR=1.350, 95% CI: 0.923, 1.974; 2015: OR=1.335, 95% CI: 0.884, 2.015) and female farmers (2007: OR=0.544, 95% CI: 0.245, 1.210; 2015: OR=1.267, 95% CI: 0.590, 2.719), indicating that the increase of hypertension prevalence in these two groups over the 20-year period could be totally explained by the population ageing and upward trend of BMI. While, the residual significant difference among period in female migrants (2007: OR=2.661, 95% CI: 1.205, 5.874; 2015: OR=3.158, 95% CI: 1.474, 6.765) and male farmers (2007: OR=1.763, 95% CI: 1.025, 3.032; 2015: OR=2.287, 95% CI: 1.307, 4.000) suggested that ageing and increasing BMI just accounted for a portion of hypertension prevalence rise. From 1996 to 2007 to 2015, there were significant increasing trends in the risk of hypertension among all groups when didn't adjust for other variables (P<0.0001 for all groups). While, after adjusted for age and BMI, only in male migrants the trend in risk of being hypertensive was insignificant (P=0.2277).

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Table 2. Odds for hypertension in 2015, 2007 relative to Odds for hypertension in 1996, by Migration Status and Gender

Group	Model	Period	Male		*P* for trend	Female		*P* for trend
			Odds Ratio	95% CI		Odds Ratio	95% CI	
Migrants	Model1[a]	1996	1		<.0001[c]	1		<.0001[c]
		2007	1.749	1.227-2.495		3.530	1.657 -7.520	
		2015	3.411	2.362-4.925		8.731	4.243 -17.966	
	Model2[b]	1996	1		0.2277[d]	1		0.0048[d]
		2007	1.350	0.923 -1.974		2.661	1.205 -5.874	
		2015	1.335	0.884 -2.015		3.158	1.474 -6.765	
Farmers	Model1[a]	1996	1		<.0001[c]	1		<.0001[c]
		2007	2.385	1.405 -4.047		0.981	0.452 -2.131	
		2015	5.561	3.293 -9.391		3.793	1.836 -7.835	
	Model2[b]	1996	1		0.0033[d]	1		0.0007[d]
		2007	1.763	1.025 -3.032		0.544	0.245 -1.210	
		2015	2.287	1.307 -4.000		1.267	0.590 -2.719	

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age and BMI..

[c] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and period was the independent variable.

[d] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and age, BMI and period were independent variables.

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In order to investigate the reason behind discrepancy in hypertension prevalence between migrants and farmers, Table 3 shows odds ratio of migrant status (migrants vs. farmers) by different models. Form model 1, when didn't adjust for other variables, we noticed that migrants were more likely had higher risk of hypertension among all subgroups except the female in 1996 (OR=0.905, 95% CI: 0.335, 2.445). There were no significant change after adjusted for age in Model 2. Model 3 in table 3 adjusted for age and BMI, and there were no significantly different risk of hypertension between migrants and farmers for males in 2007 (OR=1.097, 95% CI: 0.782, 1.539) and 2015 (OR=0.992, 95% CI: 0.674, 1.460), and for females in 2015 (OR=1.126, 95% CI: 0.834, 1.521). In model 4, after adjusted for age, BMI and education, the discrepancy between migrants and farmers in males in 1996 (OR=1.753, 95% CI: 0.729, 4.217) and females in 2007 (OR=1.295, 95% CI: 0.711, 2.357) had disappeared. Therefore, we may conclude that for males in 2007 and 2015 and females in 2015, the higher risk of hypertension in migrants was resulted from ageing and increasing BMI, whereas for males in 1996 and females in 2007, not only these two factors mentioned above but also the education contributed to the remainder higher risk of hypertension in migrants.

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Table 3. Odds for hypertension in migrants relative to Odds for hypertension in farmers, by Gender and Period

Model	1996		2007		2015	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Male						
Model1[a]	3.497	1.970 -6.207	2.565	1.946 -3.382	2.145	1.616 -2.847
Model2[b]	3.027	1.694 -5.410	2.486	1.874 -3.296	1.729	1.283 -2.329
Model3[c]	1.944	1.026 -3.684	1.097	0.782 -1.539	1.151	0.828 -1.600
Model4[d]	1.753	0.729 -4.217	0.807	0.513 -1.271	0.992	0.674 -1.460
Female						
Model1[a]	0.905	0.335 -2.445	3.257	2.118 -5.008	2.082	1.636 -2.650
Model2[b]	1.048	0.375 -2.931	3.637	2.342 -5.647	1.869	1.447 -2.414
Model3[c]	0.505	0.142 -1.799	2.359	1.473 -3.778	1.222	0.927 -1.611
Model4[d]	0.829	0.195 -3.518	1.295	0.711 -2.357	1.126	0.834 -1.521

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age.

[c] Model3 adjusted for age and BMI.

[d] Model4 adjusted for age, BMI, and education.

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DISCUSSION

Rising migrants number, coupled with population aging, have elicited major concern over the consequences of lifestyle changes for chronic diseases. Recent increases in longevity may not accompanied by a compression of morbidity, resulting in more years spent in an unhealthy state.[25] Our prior work have showed that the mean blood pressure of Yi farmers didn't rise or rarely rise with age after puberty, and essential hypertension was absent.[16] In this study, we investigated whether this unusually hypertensive profile of Yi people has continued.

We found that the prevalence of hypertension in Yi people had seen a dramatically increase over the past twenty-year period, but still lower than the whole country when compared with studies which used the same standardized population structure.[26-29] What is noteworthy is that Yi migrants had higher risk of hypertension than Yi farmers in each period, while the discrepancy in prevalence of hypertension between migrants and farmers is narrowing. Jiajia Li and her colleagues had found that the urban-rural gaps in hypertension prevalence gradually narrowed during the period 1993–2011,[30] which might be attributed to the suboptimal hypertension detection and preventive care service utilization in rural adults.[31] The Third National Health Services Survey in China[32] indicates that rural minority Chinese use significantly less health services, includes visiting physicians and hospital utilization, than urban minority Chinese. And the result that hypertension was much more prevalent in Yi migrants than Yi farmers was also consistent with many other research. The Kenyan Luo migration study conducted by Poulter et al[33] confirmed that the blood pressure of

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migrants who left a traditional rural community to settle in an urban one were significantly higher than that of control. In addition, as our country has witnessed numerous rural-urban migration,[34] there are quantitative relation between the migration and hypertension. Similarly, India is a rapidly urbanizing country which encountered the same problems as China. A cross-sectional study [35] of neo-migrants and settled-migrants (at least 10 years residence) in the city of Delhi found that settled-migrants had higher prevalence of hypertension than neo-migrants.

In our study, we detected that ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Higher BMI definitely increase the risk of hypertension,[36] and even the impact of overweight and obesity on hypertension had raised significantly over time.[37] The crude prevalence of overweight and obesity undoubtedly increased across the twenty-year period in Yi people, which was consistent with Prof. Shan's study, and revealed that both Yi migrants and Yi farmers had a distinct increase in prevalence of overweight and obesity during 1996 to 2007.[22] A cross-sectional study indicated that Yi people in China exhibited a strikingly lower prevalence of overweight and obesity than that observed in populations of Western countries, and overweight and obesity figures were 21.7% and 7.1% in 2008, respectively.[38] Additionally, The disparity in the prevalence of overweight/obesity between urban and rural areas was narrowing since 2000,[39] which could also interpret the declining trend of gap in hypertension between Yi migrants and Yi farmers. However, even though adjusted age and BMI, there still have significant difference of hypertension

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prevalence between 2015 and 1996 in female migrants and male farmers. It might seem that some uninvolved factors, such as diet and economy, are responsible for the remaining risk of hypertension in these two groups. China Health and Nutrition Survey indicated that there was a dramatic change in dietary pattern in the past two decades, especially the steep increase of the "Modern" pattern, while the "Traditional" pattern was stable over the study period, which means that now days people more likely to consume processed food that with refined carbohydrates, added salt and sweetener, edible oils, animal-resource foods, but the average intake of cereal, fresh fruits, and vegetables had decreased.[40, 41] Yi farmers who preserved their own language and primitive life-style rarely eat meat except during the Yi New Year in December, and their main crops are potatoes, oats, and buckwheats.[16] With economic growth and large-scale migration, Yi people consume more modern foods which contain high level of sugar, salt and fat, especially in Yi migrants.[42] Therefore, we suppose that changes in Yi people's diet probably account for a part of hypertensive risk.

Distinguish from other research, these three successive Yi migrant studies were almost completed by one stable team, only a few students renewed. And this high consistency guarantees the comparability between different periods. Furthermore, it is the first time to explore the hypertension prevalence trend of Yi people by such a long time span and in such a large scale. We also investigated the reasons of hypertension discrepancy both between different periods and different groups, which will provide local government with relatively practical recommendations for the prevention and

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treatment of hypertension.

There are several limitations that merit comment. At first, our study did not analyze the Han people who resided at the same urban areas with Yi migrants in the same period. Thus, the comparison to determine which is relatively important between environment and gene is not able to be accomplished. Furthermore, the tool of measuring blood pressure is not consistent among three periods. We used the mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device in 2007 and 2015. It might have slightly bias among the measurements, but the automatic device had been calibrated with the mercury sphygmomanometer before measurements. And there are studies had validated the accuracy and validation of Omron HEM-907.[43-45] At last, our research belong to cross-sectional study. It might seem unpersuasive to identify causal effect between BMI and hypertension, and selection bias probably decrease the comparability between different periods. Therefore, it is fairly necessary to conduct prospective cohort study in Yi people to investigate the association between increased BMI and the rise of hypertension. As for selection bias, we used standardized prevalence of hypertension and adjusted the 'period' by logistic regression model to eliminate the difference of demographic characteristics among three surveys and improve the comparability.

In conclusion, China has undergone unprecedented-scale urbanization and rural-urban migration which accompanied with rigorous challenges of public health during the past two decades. As the rapid increase of hypertension prevalence both in Yi migrants and farmers, effective prevention, detection, treatment, and control of

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hypertension continue to be important goals for health policy, public health, and medical care decision makers, as well as individuals who have higher risk of hypertension. We should be noted that although Yi migrants were more likely to be hypertensive than Yi farmers in each period, the growth rates of these two groups were exactly reverse. In general, ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Nevertheless, it is necessary to conduct cohort study in rural-urban migrants to explore the causal effect. These results put the onus on the governments and assist the government to tailor prevention and treatment programs for high risk population in Yi people.

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AUTHOR CONTRIBUTIONS

JZ participated in the data collection and drafted the manuscript. SW, WY, FY, ZL participated in the data collection. BZ, FD, LP, HG, GX, GL, YL, XW, GS participated in the design of the study and undertook statistical analyses. All authors

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were involved in writing the paper and had final approval of the submitted version.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

ETHICS APPROVAL

Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (No. 033-2012), Beijing.

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Not commissioned; externally peer reviewed.

DATA SHARING STATEMENT

No additional data are available.

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Figure 1. Flow diagram of Yi migrant study

Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

Figure 2. Age-standardized prevalence of hypertension and Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015.

A, Age-standardized prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Age-standardized prevalence of hypertension was calculated by the direct method using the Chinese population age structure form the Sixth National Population Census in 2010.

B, Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Predicted prevalence of hypertension were calculated by the Geometric Progression Method.

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015.

The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

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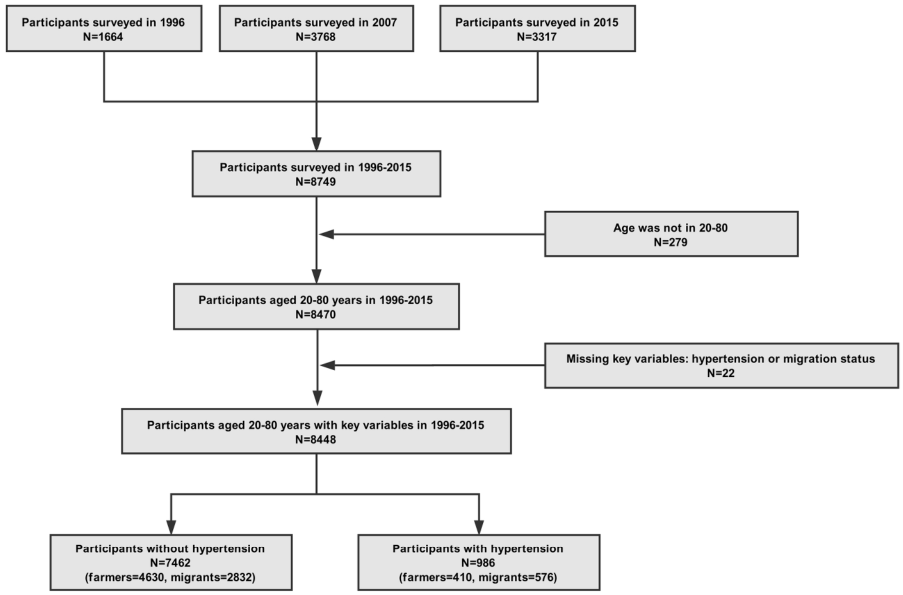

Figure 1. Flow diagram of Yi migrant study
Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

193x134mm (300 x 300 DPI)

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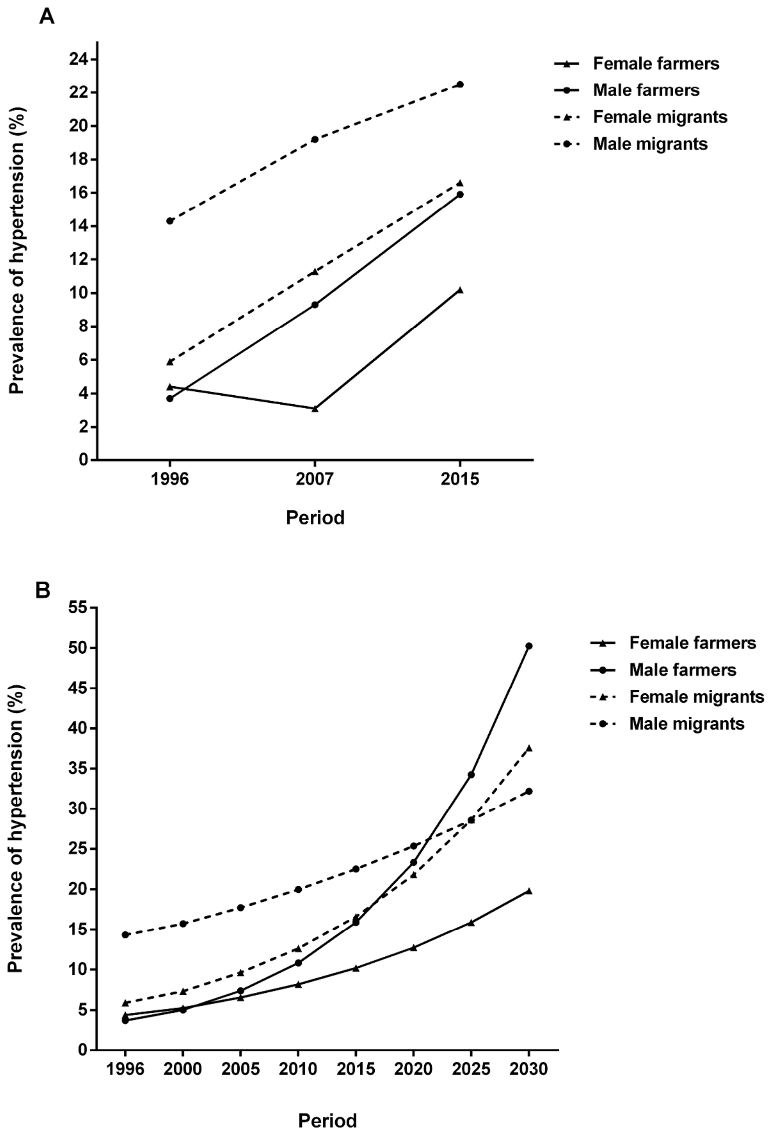

Figure 2. Age-standardized prevalence of hypertension and Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. A, Age-standardized prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Age-standardized prevalence of hypertension was calculated by the direct method using the Chinese population age structure form the Sixth National Population Census in 2010. B, Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Predicted prevalence of hypertension were calculated by the Geometric Progression Method.

115x165mm (600 x 600 DPI)

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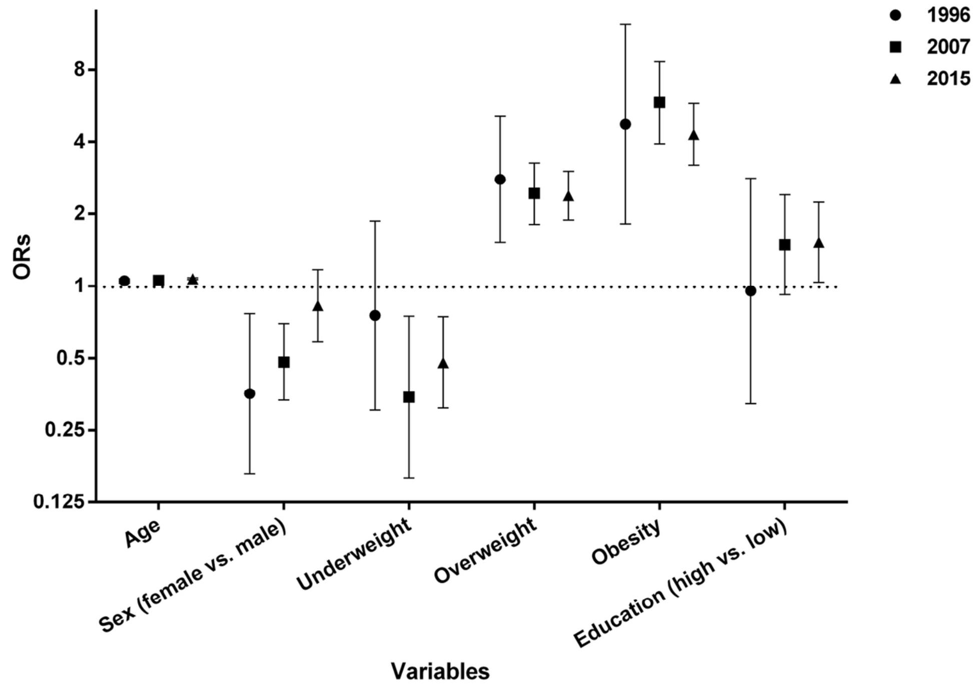

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015. The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

58x42mm (600 x 600 DPI)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			

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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	7 and Figure1
		(b) Give reasons for non-participation at each stage	7 and Figure1
		(c) Consider use of a flow diagram	Figure1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	11 (Table1)
Outcome data	15*	Report numbers of outcome events or summary measures	11 (Table1)
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	13-16
		(*b*) Report category boundaries when continuous variables were categorized	11 (Table1)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
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	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
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	22

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

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

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Twenty-year time trends in hypertension prevalence in Yi people of China: Three successive cross-sectional studies, 1996-2015

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine, Ethics, Public health
Keywords:	Hypertension < CARDIOLOGY, Obesity, migrant, trend, Yi people

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Title:

Twenty-year time trends in hypertension prevalence in Yi people of China: Three successive cross-sectional studies, 1996-2015

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ABSTRACT:

Objective To explore the trend of hypertension prevalence and related factors in Yi people from 1996 to 2015.

Methods Three successive cross-sectional surveys were conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007 and 2015, respectively. A total of 8448 participants aged 20-80 years (5040 Yi farmers, 3408 Yi migrants) were included in final analysis.

Results Overall, the age-standardized prevalence of hypertension in migrants was significantly higher than farmers'. Furthermore, the age-standardized prevalence rates increased from 10.1% to 15.3% to 19.6% in Yi migrants and from 4.0% to 6.3% to 13.1% in Yi farmers during 1996 to 2007 to 2015. The highest 2015-to-1996 ratio of age-standardized hypertension prevalence was in male farmers (ratio=4.30), whereas despite the highest prevalence of hypertension, the equivalent figure in male migrants was 1.57. The older age, overweight, and obesity were persistently risk factors of hypertension in three periods. After adjusted for age and body mass index, the difference of hypertension prevalence between 1996 and 2015 then vanished in male migrants (odds ratio=1.335; 95% confidence interval: 0.884, 2.015) and female farmers (odds ratio=1.267; 95% confidence interval: 0.590, 2.719). The disparities of hypertension prevalence between Yi migrants and farmers were not statistically significant in all subgroups when adjusted for age, body mass index, and education.

Conclusions Over the past two decades, the hypertension prevalence in Yi people has significantly increased. Yi migrants were more likely to be hypertensive than Yi

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farmers, which was predominantly drove by the discrepancy of body mass index between them.

Key words: obesity; hypertension; migrant; trend; Yi people

Strengths and limitations of this study

1. The present study was first designed to explore the hypertension prevalence trend of Yi people during last two decades.
2. These three population-based successive Yi migrant studies were implemented by identical team and followed the same protocol.
3. Under the context of rapid urbanization, the rural-urban migration effect on health was estimated by comparing hypertension prevalence between Yi migrants and Yi farmers.
4. The unclear temporal relationship between body mass index and hypertension is due to inherent weakness of cross-sectional studies, and have been heatedly debated in epidemiological studies.
5. Furthermore, important confounding factors possibly associated with the increasing trend in hypertension prevalence in Yi people, such as nutrition and environmental changes, were not evaluated in the present study.

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INTRODUCTION

Hypertension, also known as high or raised blood pressure, is the predominant risk factor of heart disease, stroke, and renal failure which are leading causes of death.[1-3] The increasing trends of hypertension prevalence can be observed both in developed countries [4, 5] and developing countries.[6-8]

We live in a rapidly changing environment. Throughout the world, human health is being shaped by the same powerful forces: demographic ageing, rapid urbanization, and the globalization of unhealthy lifestyles. In general, rural–urban migration, as part of urbanization, is considered a promoting factor for chronic diseases [9] and evidence shows that urbanization is estimated to raise the blood pressure of residents.[10] In contemporary China, socioeconomic transformation at the beginning of the twenty-first century has led to rapid urbanization and accelerated rural-urban migration [11] along with the phenomenon of increased mean blood pressure that has been described among Chinese population.[12-14]

It is reported that hypertension prevalence in ethnic minorities is significantly higher than in Han.[15] However, Yi people resided in Liangshan Yi Autonomous Prefecture located in Sichuan Province, southwestern China used to be renowned for its low mean blood pressure and prevalence of hypertension [16] and had been undergoing immense scale rural-urban migration.[17] Although a host of investigations about hypertension prevalence of Han people have been carried out, [18-20] the data about trend of hypertension prevalence in Yi people is insufficient. Therefore, it is of great necessity to conduct relevant research to acknowledge the situation of hypertension in

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Yi people. Additionally, as the dramatic health transition resulted from rapid rural-urban migration, Yi people may encounter higher hypertension prevalence than before.

Accordingly, we conducted the Yi migrant study to assess the prevalence of hypertension by migration status and period; the association of hypertension with individual characteristics; the related factors that accounting for the discrepancy of hypertension prevalence among subgroups and periods.

METHODS

Study Design and participants

The Yi people is a minority in China living in Liangshan Yi Autonomous Prefecture in Southern China, an area that covers about 60,000 kilometers and has roughly 5 million residents in which 52.5% are Yi people. The Yi people usually live in remote mountain districts at or above 1,500 meters above sea level. Their main occupation is agriculture, and they are one of the most primitive societies in China. The Yi Migrant Study includes three cross□sectional studies conducted in Liangshan Yi Autonomous Prefecture in 1996, 2007, and 2015, respectively. The sampling procedures have been published previously in detail.[21, 22] In the two previous periods, stratified cluster sampling was used to select participants from Xichang city, Butuo, Zhaojue, Jinyang, Puge and Xide counties. Due to the inevitably restrained accessibility, we only conducted our survey in Xichang city and Puge county in 2015.

The Yi farmers were defined as those whose parents are Yi people and had been lived in the countryside since birth. There are one to four county seats in each county. The

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Yi farmers were selected by stratified cluster sampling from areas around each county seat. Four villages were randomly selected from each area. In the last sampling stage, all the Yi farmers aged 20 years or over in the selected villages were surveyed. There are two types of Yi migrants, one are those who were born in countryside and then migrated into county or city for more than 1 year, the other are Yi people who were born in county or city and lived there until the survey. All Yi migrants' parents are Yi people. And because the number of the Yi migrants was relatively small, all of the Yi migrants (20 years of age and over) found in the selected counties and Xichang city were all enrolled into the study.

Isolated from the outside world, the Yi farmers who live in high-mountain areas and mountainside areas have their own language and primitive lifestyle. There are only extremely steep and narrow paths leading to these villages, which are several hours walking distance apart. Their mainly nutritional source are staple food such as potato, oat, and buckwheats, and the living conditions are greatly backward, there even no table for eating, almost all Yi farmers squat down to eat in 2015. The Yi migrants who live in the county or city with Han people have a much more western lifestyle. It is relatively convenient for them to acquire meat, fresh fruits, and vegetables. And there is a great extent of improvement in their living conditions compared with Yi farmers. As the Jiang He's study[23] described that the Yi farmers began to migrate into counties and cities from remote mountain districts since the 1950s.

As the involvement of participants, local centers for disease control and prevention were responsible for the propagation and local governments took charge of the

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recruitment. In these three periods, the number of participants were 1664, 3768 and 3317 respectively. After excluded those who were out of age-bracket or lacking of key variables such as blood pressure and migration status, there were a total of 8448 Yi people in the final analysis (Figure 1). Informed consent was obtained from all of the participants, and all surveys were approved by the Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences ((No. 033-2012), Beijing.

Data were collected by trained medical staff using standardized methods and identical examinations in 1996 to 2015, including a questionnaire for assessment of demographic characteristics and anthropometrical measurements. In order to reduce the information bias, we conducted a two-stage questionnaire survey. Firstly, participants completed the questionnaire with a trained medical staff. Then, there were several group leaders audit each questionnaire by randomly extracting some items.

Measurements

Both body height and weight were measured with the participants in light clothing and without shoes after an overnight fast. Body mass index (BMI) was defined as measured weight in kilograms divided by squared height in meters. There were 4 BMI categories: underweight defined as a BMI <18.5 kg/m^2; normal weight, 18.5 to 23.9kg/m^2; overweight, 24 to 27.9kg/m^2; and obese, ≥28 kg/m^2.

Education was categorized as low (received only primary education or no education), middle (finished secondary school or high school) and high (graduated from college or university).

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Physical activity was divided into three categories: (1) light: e.g., office worker, salesperson, and house worker; (2) Middle: e.g., driver, electrician, and latheman; (3) Heavy: e.g., manual worker, steel worker, and mineworker.

Smoking status was classified as never-smokers and ever-smokers, which included current smokers (having been regularly smoking at least one cigarette per day during the previous six months) and ex-smokers (once smoked but had quitted smoking for six months or longer). Alcohol consumption was divided into never drinker and ever drinker those who drank at least twice per month (more than 640 ml beer or 100 ml Chinese liquor, about 57 g alcohol), and had lasted for at least 6 months or stopped drinker.

After an overnight fast, blood pressure (BP) were measured by trained physicians using mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device (HEM-907) in 2007 and 2015. Appropriate blood pressure cuff sizes were used for participants based on measurement of mid-arm circumference. BP was measured in the sitting position and on the right arm after a rest of at least 10 min and had not smoked, exercised, or eaten. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded. The mean of three measurements was used for all analyses. The definition for hypertension was as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.[24]

Statistical analysis

Summary results are presented as percentages (with numbers) for categorical

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variables and mean (and standard deviations, SD) for the continuous variables. As for trend analysis, simple linear regression model and Cochran-Armitage trend test were used to explore trends of age and male percentage during 1996 to 2015, respectively. For continuous variable, BMI, using multiple linear regression model to adjust for age and sex. In this model, BMI was the dependent variable and age, sex and period were independent variables. For multinomial variables with ordered categories, such as BMI categories and education, the cumulative logistic model was used to calculate the P value of trend analysis, in this model BMI categories or education was the dependent variable and age, sex and period were independent variables. For binary variable, hypertension, we fitted a binary logistic regression model, in which hypertension was the dependent variable and age, sex and period were independent variables, to conduct the trend analysis. All generalized linear model identify the period as continuous variable instead of dummy variables, and its P value in the model represent the result of trend analysis.

Direct standardization was performed using China population age structure from the Sixth National Population Census in 2010 by SAS 9.4 using 'stdrate' commend. And the geometric progression method was used to predict the age-standardized prevalence of hypertension in Yi people by 2030.

To explore related factors of hypertension in each period, we used multiple logistic regression model to calculate the odds ratio (OR) and the 95% confidence interval (CI); in which age was continuous variable while sex, BMI groups, education, activities, smoking, and drinking were categorical variables.

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Finally, we developed a set of binary logistic regression models to identify reasons behind disparities of hypertension risk between different periods and different migration status, in period models period was treated as dummy variable and period=1996 was the reference group, in migration status models Yi farmers was the reference group. The trend analyses were realized by identifying period as continuous variable in binary logistic regression models. P values <0.05 were considered statistically significant. All statistical analyses were conducted by SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

Patient and Public Involvement

Patients were not involved in study design or conduct of the study. The results of survey were disseminated to study participants by physical examination reports in 1996 and 2007, and in 2015 we developed an application which could allow participants to search their results at any time by using mobile phones.

RESULTS

Study Population Characteristics

Table 1 displays the characteristics of Yi people and the unadjusted prevalence of hypertension within time periods by migration status. Over the 3 study periods, the prevalence of obesity rose from 0.4% to 7.1% in Yi farmers, and from 4.6% to 17.4% in Yi migrants. By 2015, the crude prevalence of hypertension had increased by 9.5% in farmers, and by almost 16% in migrants.

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Table 1. Characteristics of participants by migration status and period, Yi migrant study, 1996-2015

Variable	Farmers				Migrants			
	1996 N=723	2007 N=2351	2015 N=1966	*P* for trend	1996 N=679	2007 N=1393	2015 N=1336	*P* for trend
Mean age, years (SD)	35.0 (12.7)	39.4 (12.0)	45.3 (12.8)	<.0001[b]	37.9 (11.2)	39.6 (12.0)	48.3 (14.4)	<.0001[b]
Mean BMI, kg/m^2 (SD)	20.3 (2.1)	21.4 (2.6)	22.3 (3.6)	<.0001[c]	22.4 (3.0)	23.5 (3.7)	24.4 (3.8)	<.0001[c]
Male, % (N)	63.5 (459)	47.1 (1107)	33.8 (664)	<.0001[d]	57.1 (388)	57.3 (798)	33.1 (442)	<.0001[d]
BMI categories, % (N)[a]				<.0001[e]				<.0001[e]
Underweight (BMI<18.5)	15.3 (110)	9.4 (220)	12.8 (249)		8.3 (56)	7.2 (100)	5.0 (66)	
Normal weight (BMI18.5-23.9)	81.8 (588)	78.4 (1837)	58.3 (1133)		63.4 (428)	51.6 (718)	42.3 (560)	
Overweight (BMI24-27.9)	2.5 (18)	10.6 (248)	21.8 (423)		23.7 (160)	30.1 (418)	35.4 (468)	
Obesity (BMI≥28)	0.4 (3)	1.7 (39)	7.1 (138)		4.6 (31)	11.1 (155)	17.4 (230)	
Education, % (N)[a]				<.0001[e]				<.0001[e]
Low	92.3 (658)	91.5 (2109)	88.4 (1738)		19.2 (130)	24.2 (329)	49.3 (658)	
Middle	7.0 (50)	7.6 (175)	10.4 (204)		62.3 (421)	38.6 (524)	32.4 (432)	
High	0.7 (5)	0.9 (21)	1.2 (24)		18.5 (125)	37.1 (504)	18.4 (245)	
Hypertension,% (N)	3.5 (25)	5.5 (130)	13.0 (255)	<.0001[f]	8.0 (54)	14.8 (206)	23.7 (316)	<.0001[f]

Abbreviations: BMI, body mass index.

[a] Numbers do not sum up to the total due to missing data.

[b] P-values were calculated by simple linear regression model in which age was the dependent variable and period were independent variables.

[c] P-values were calculated by multiple linear regression model in which BMI was the dependent variable and age, sex and period were independent variables.

[d] P-values were calculated by Cochran-Armitage trend test.

[e] P-values were calculated by cumulative logistic model in which BMI categories or education was the dependent variable and age, sex and period were independent variables.

[f] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and age, sex and period were independent variables.

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Age-standardized prevalence of hypertension

Figure 2-A shows the trends of age-standardized hypertension prevalence, and Figure2-B is the predicted prevalence of hypertension using geometric progression method. It is noticeable that the prevalence of hypertension in male migrants was by far the highest among these four groups in each period, from 14.3% to 19.2% to 22.5% (for all comparison P<0.0001), while the equivalent figure for female farmers was from 4.4% to 3.1% to 10.2% (for 1996 vs 2015, and 2007 vs 2015 P<0.0001; for 1996 vs 2007 P=0.4792) which almost the lowest hypertension prevalence in each period (Figure 2-A). Overall, from 1996 to 2015, these four groups saw a statistically increase in prevalence of hypertension (P<0.0001 for all groups).

And the biggest 2015-to-1996 ratio of age-standardized prevalence of hypertension was in male farmers (ratio=4.30), which means this group had the fastest pace of hypertension increase, followed by female migrants (ratio=2.81) and female farmers (ratio=2.32). Interestingly, despite the highest prevalence of hypertension, the 2015-to-1996 ratio of age-standardized prevalence of hypertension in male migrants was 1.57 and it's the lowest growth rate. Accordingly, we predicted that, if the growth rates stayed steadily, male farmers would overtake male migrants to become the most prevalent hypertensive group in 2021 and female migrants would overtake male migrants in 2025 to become the second most prevalent hypertensive group (Figure 2-B).

Related factors of hypertension and hypertensive discrepancy

Figure 3 provides odds ratios for hypertension-related factors in each period. Across

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three periods, the higher hypertensive share traits such as much older and had higher BMI, but only in 2015 those who acquired high school education or higher were more likely to have hypertension than those whose education level were maximum to primary school (OR=1.524, 95% CI: 1.038, 2.236).

Table 2 shows odds ratios of the time period by different models. In model 1, the unadjusted results showed that both 2007 and 2015 had a significantly higher risk of hypertension versus 1996 among all subgroups. Model 2 in table 2 adjusted for age and BMI, the effect of period turned out to be not significant in male migrants (2007: OR=1.350, 95% CI: 0.923, 1.974; 2015: OR=1.335, 95% CI: 0.884, 2.015) and female farmers (2007: OR=0.544, 95% CI: 0.245, 1.210; 2015: OR=1.267, 95% CI: 0.590, 2.719), indicating that the increase of hypertension prevalence in these two groups over the 20-year period could be totally explained by the population ageing and upward trend of BMI.

While, the residual significant difference among period in female migrants (2007: OR=2.661, 95% CI: 1.205, 5.874; 2015: OR=3.158, 95% CI: 1.474, 6.765) and male farmers (2007: OR=1.763, 95% CI: 1.025, 3.032; 2015: OR=2.287, 95% CI: 1.307, 4.000) suggested that ageing and increasing BMI just accounted for a portion of hypertension prevalence rise. From 1996 to 2007 to 2015, there were significant increasing trends in the risk of hypertension among all groups when didn't adjust for other variables (P<0.0001 for all groups). While, after adjusted for age and BMI, only in male migrants the trend in risk of being hypertensive was insignificant (P=0.2277).

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Table 2. Odds for hypertension in 2015, 2007 relative to Odds for hypertension in 1996, by Migration Status and Gender

Group	Model	Period	Male		*P* for trend	Female		*P* for trend
			Odds Ratio	95% CI		Odds Ratio	95% CI	
Migrants	Model1[a]	1996	1		<.0001[c]	1		<.0001[c]
		2007	1.749	1.227-2.495		3.530	1.657 -7.520	
		2015	3.411	2.362-4.925		8.731	4.243 -17.966	
	Model2[b]	1996	1		0.2277[d]	1		0.0048[d]
		2007	1.350	0.923 -1.974		2.661	1.205 -5.874	
		2015	1.335	0.884 -2.015		3.158	1.474 -6.765	
Farmers	Model1[a]	1996	1		<.0001[c]	1		<.0001[c]
		2007	2.385	1.405 -4.047		0.981	0.452 -2.131	
		2015	5.561	3.293 -9.391		3.793	1.836 -7.835	
	Model2[b]	1996	1		0.0033[d]	1		0.0007[d]
		2007	1.763	1.025 -3.032		0.544	0.245 -1.210	
		2015	2.287	1.307 -4.000		1.267	0.590 -2.719	

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age and BMI..

[c] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and period was the independent variable.

[d] P-values were calculated by binary logistic regression model in which hypertension was the dependent variable and age, BMI and period were independent variables.

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In order to investigate the reason behind the discrepancy in hypertension prevalence between migrants and farmers, Table 3 shows the odds ratio of migrant status (migrants vs. farmers) by different models. For model 1, when didn't adjust for other variables, we noticed that migrants were more likely had a higher risk of hypertension among all subgroups except the female in 1996 (OR=0.905, 95% CI: 0.335, 2.445). There was no significant change after adjusted for age in Model 2. Model 3 in table 3 adjusted for age and BMI, and there was no significantly different risk of hypertension between migrants and farmers for males in 2007 (OR=1.097, 95% CI: 0.782, 1.539) and 2015 (OR=0.992, 95% CI: 0.674, 1.460), and for females in 2015 (OR=1.126, 95% CI: 0.834, 1.521). In model 4, after adjusted for age, BMI and education, the discrepancy between migrants and farmers in males in 1996 (OR=1.753, 95% CI: 0.729, 4.217) and females in 2007 (OR=1.295, 95% CI: 0.711, 2.357) had disappeared.

Therefore, we may conclude that for males in 2007 and 2015 and females in 2015, the higher risk of hypertension in migrants was resulted from ageing and increasing BMI, whereas for males in 1996 and females in 2007, not only these two factors mentioned above but also the education contributed to the remainder higher risk of hypertension in migrants.

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Table 3. Odds for hypertension in migrants relative to Odds for hypertension in farmers, by Gender and Period

Model	1996		2007		2015	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Male						
Model1[a]	3.497	1.970 -6.207	2.565	1.946 -3.382	2.145	1.616 -2.847
Model2[b]	3.027	1.694 -5.410	2.486	1.874 -3.296	1.729	1.283 -2.329
Model3[c]	1.944	1.026 -3.684	1.097	0.782 -1.539	1.151	0.828 -1.600
Model4[d]	1.753	0.729 -4.217	0.807	0.513 -1.271	0.992	0.674 -1.460
Female						
Model1[a]	0.905	0.335 -2.445	3.257	2.118 -5.008	2.082	1.636 -2.650
Model2[b]	1.048	0.375 -2.931	3.637	2.342 -5.647	1.869	1.447 -2.414
Model3[c]	0.505	0.142 -1.799	2.359	1.473 -3.778	1.222	0.927 -1.611
Model4[d]	0.829	0.195 -3.518	1.295	0.711 -2.357	1.126	0.834 -1.521

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] Model1 didn't adjust for other variables.

[b] Model2 adjusted for age.

[c] Model3 adjusted for age and BMI.

[d] Model4 adjusted for age, BMI, and education.

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DISCUSSION

Rising migrants number, coupled with population aging, have elicited major concern over the consequences of lifestyle changes for chronic diseases. Recent increases in longevity may not accompanied by a compression of morbidity, resulting in more years spent in an unhealthy state.[25] Our prior work have showed that the mean blood pressure of Yi farmers didn't rise or rarely rise with age after puberty, and essential hypertension was absent.[16] In this study, we investigated whether this unusually hypertensive profile of Yi people has continued.

We found that the prevalence of hypertension in Yi people had seen a dramatically increase over the past twenty-year period, but still lower than the whole country when compared with studies which used the same standardized population structure.[26-29] What is noteworthy is that Yi migrants had higher risk of hypertension than Yi farmers in each period, while the discrepancy in prevalence of hypertension between migrants and farmers is narrowing. Jiajia Li and her colleagues had found that the urban-rural gaps in hypertension prevalence gradually narrowed during the period 1993–2011,[30] which might be attributed to the suboptimal hypertension detection and preventive care service utilization in rural adults.[31] The Third National Health Services Survey in China[32] indicates that rural minority Chinese use significantly less health services, includes visiting physicians and hospital utilization, than urban minority Chinese. And the result that hypertension was much more prevalent in Yi migrants than Yi farmers was also consistent with many other research. The Kenyan Luo migration study conducted by Poulter et al[33] confirmed that the blood pressure of

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migrants who left a traditional rural community to settle in an urban one were significantly higher than that of control. In addition, as our country has witnessed numerous rural-urban migration,[34] there are quantitative relation between the migration and hypertension. Similarly, India is a rapidly urbanizing country which encountered the same problems as China. A cross-sectional study [35] of neo-migrants and settled-migrants (at least 10 years residence) in the city of Delhi found that settled-migrants had higher prevalence of hypertension than neo-migrants.

In our study, we detected that ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Higher BMI definitely increase the risk of hypertension,[36] and even the impact of overweight and obesity on hypertension had raised significantly over time.[37] The crude prevalence of overweight and obesity undoubtedly increased across the twenty-year period in Yi people, which was consistent with Prof. Shan's study, and revealed that both Yi migrants and Yi farmers had a distinct increase in prevalence of overweight and obesity during 1996 to 2007.[22] A cross-sectional study indicated that Yi people in China exhibited a strikingly lower prevalence of overweight and obesity than that observed in populations of Western countries, and overweight and obesity figures were 21.7% and 7.1% in 2008, respectively.[38] Additionally, The disparity in the prevalence of overweight/obesity between urban and rural areas was narrowing since 2000,[39] which could also interpret the declining trend of gap in hypertension between Yi migrants and Yi farmers. However, even though adjusted age and BMI, there still have significant difference of hypertension

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prevalence between 2015 and 1996 in female migrants and male farmers. It might seem that some uninvolved factors, such as diet and economy, are responsible for the remaining risk of hypertension in these two groups. China Health and Nutrition Survey indicated that there was a dramatic change in dietary pattern in the past two decades, especially the steep increase of the “Modern” pattern, while the “Traditional” pattern was stable over the study period, which means that now days people more likely to consume processed food that with refined carbohydrates, added salt and sweetener, edible oils, animal-resource foods, but the average intake of cereal, fresh fruits, and vegetables had decreased.[40, 41] Yi farmers who preserved their own language and primitive life-style rarely eat meat except during the Yi New Year in December, and their main crops are potatoes, oats, and buckwheats.[16] With economic growth and large-scale migration, Yi people consume more modern foods which contain high level of sugar, salt and fat, especially in Yi migrants.[42] Therefore, we suppose that changes in Yi people’s diet probably account for a part of hypertensive risk.

Distinguish from other research, these three successive Yi migrant studies were almost completed by one stable team, only a few students renewed. And this high consistency guarantees the comparability between different periods. Furthermore, it is the first time to explore the hypertension prevalence trend of Yi people by such a long time span and in such a large scale. We also investigated the reasons of hypertension discrepancy both between different periods and different groups, which will provide local government with relatively practical recommendations for the prevention and

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treatment of hypertension.

There are several limitations that merit comment. At first, our study did not analyze the Han people who resided at the same urban areas with Yi migrants in the same period. Thus, the comparison to determine which is relatively important between environment and gene is not able to be accomplished. Furthermore, the tool of measuring blood pressure is not consistent among three periods. We used the mercury sphygmomanometer in 1996 and Omron automatic digital BP measuring device in 2007 and 2015. It might have slightly bias among the measurements, but the automatic device had been calibrated with the mercury sphygmomanometer before measurements. And there are studies had validated the accuracy and validation of Omron HEM-907.[43-45] At last, our research belong to cross-sectional study. It might seem unpersuasive to identify causal effect between BMI and hypertension, and selection bias probably decrease the comparability between different periods. Therefore, it is fairly necessary to conduct prospective cohort study in Yi people to investigate the association between increased BMI and the rise of hypertension. As for selection bias, we used standardized prevalence of hypertension and adjusted the 'period' by logistic regression model to eliminate the difference of demographic characteristics among three surveys and improve the comparability.

In conclusion, China has undergone unprecedented-scale urbanization and rural-urban migration which accompanied with rigorous challenges of public health during the past two decades. As the rapid increase of hypertension prevalence both in Yi migrants and farmers, effective prevention, detection, treatment, and control of

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hypertension continue to be important goals for health policy, public health, and medical care decision makers, as well as individuals who have higher risk of hypertension. We should be noted that although Yi migrants were more likely to be hypertensive than Yi farmers in each period, the growth rates of these two groups were exactly reverse. In general, ageing and increasing BMI could largely accounted for the rise in prevalence of hypertension both between different periods and different migration status. Nevertheless, it is necessary to conduct cohort study in rural-urban migrants to explore the causal effect. These results put the onus on the governments and assist the government to tailor prevention and treatment programs for high risk population in Yi people.

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AUTHOR CONTRIBUTIONS

JZ participated in the data collection and drafted the manuscript. SW, WY, FY, ZL participated in the data collection. BZ, FD, LP, HG, GX, GL, YL, XW, GS participated in the design of the study and undertook statistical analyses. All authors

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were involved in writing the paper and had final approval of the submitted version.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

ETHICS APPROVAL

Bioethics Committee of the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (No. 033-2012), Beijing.

PROVENANCE AND PEER REVIEW

Not commissioned; externally peer reviewed.

DATA SHARING STATEMENT

No additional data are available.

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Figure 1. Flow diagram of Yi migrant study

Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

Figure 2. Age-standardized prevalence of hypertension and Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015.

A, Age-standardized prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Age-standardized prevalence of hypertension was calculated by the direct method using the Chinese population age structure form the Sixth National Population Census in 2010.

B, Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Predicted prevalence of hypertension were calculated by the Geometric Progression Method.

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015.

The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

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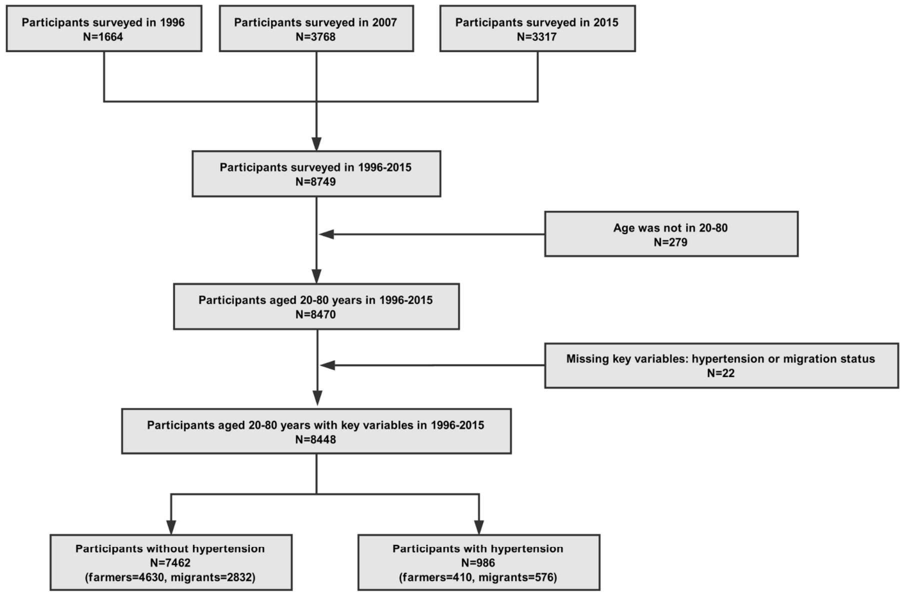

Figure 1. Flow diagram of Yi migrant study
Hypertension was defined as follows: individuals who reported having diagnosed hypertension, receiving BP-lowering treatment or had an average measured SBP at least 140 mmHg, DBP at least 90 mmHg, or both.

193x134mm (300 x 300 DPI)

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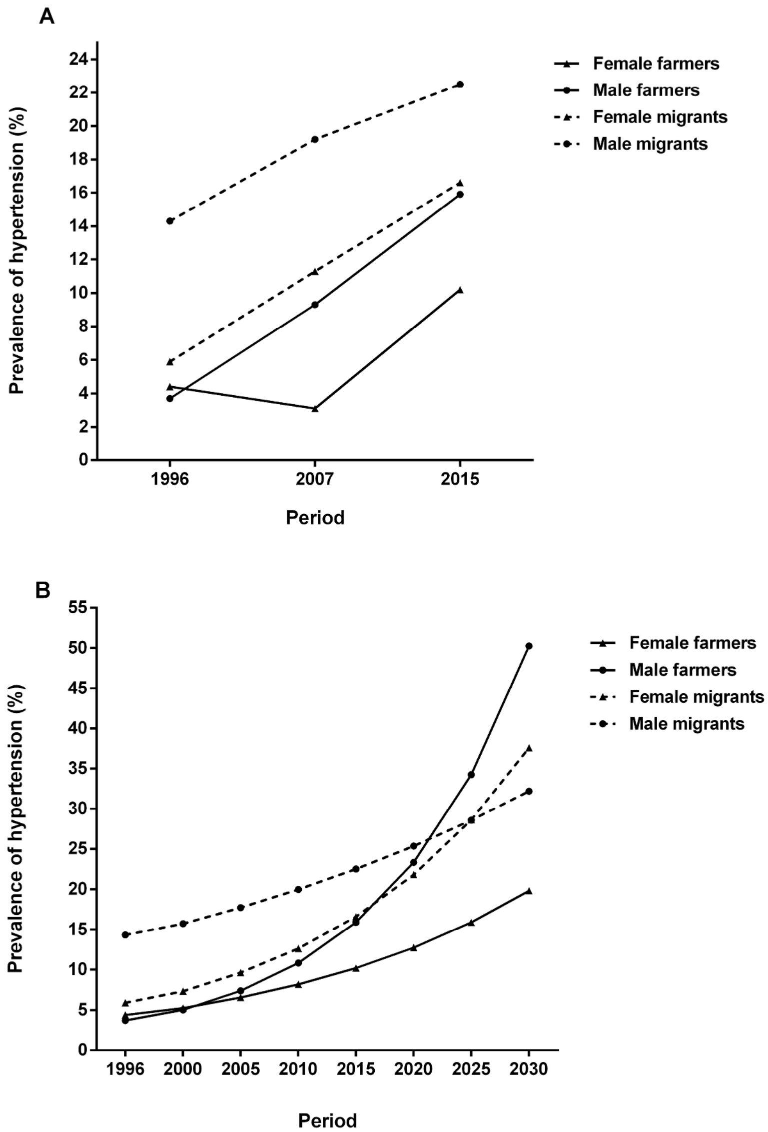

Figure 2. Age-standardized prevalence of hypertension and Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. A, Age-standardized prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Age-standardized prevalence of hypertension was calculated by the direct method using the Chinese population age structure form the Sixth National Population Census in 2010. B, Predicted prevalence of hypertension by gender and migration status, Yi migrant study, 1996-2015. Predicted prevalence of hypertension were calculated by the Geometric Progression Method.

115x165mm (600 x 600 DPI)

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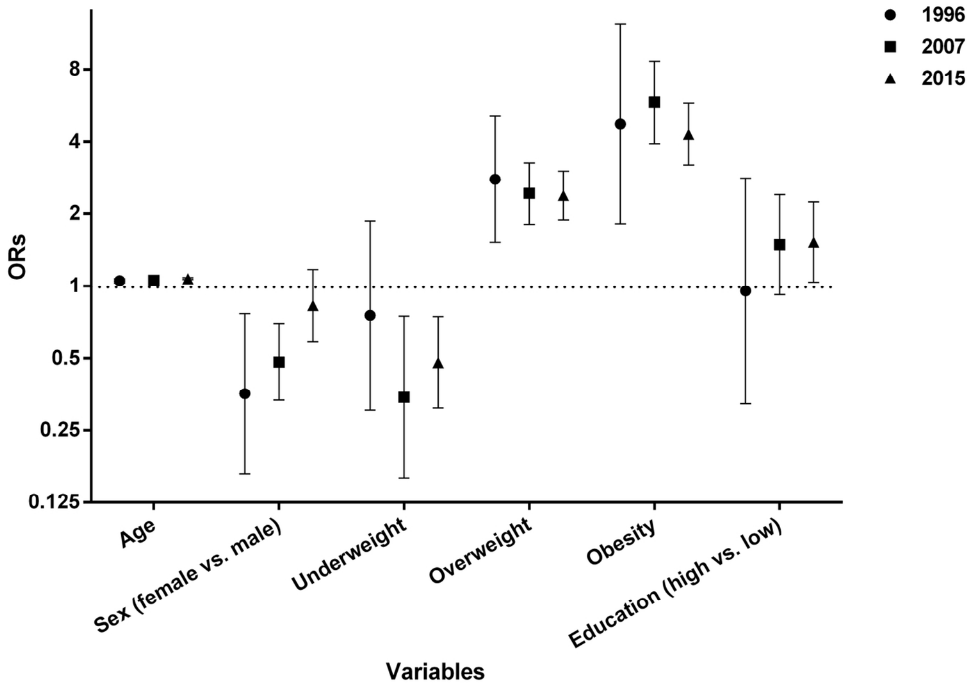

Figure 3. Relative Odds and 95%CI of hypertension related factors by Period, Yi migrant study, 1996-2015. The ORs were adjusted for age, sex, smoking, drinking, education and activities. Variables which didn't have statistical significance of hypertension in any period were not shown.

58x42mm (600 x 600 DPI)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			

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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	7 and Figure1
		(b) Give reasons for non-participation at each stage	7 and Figure1
		(c) Consider use of a flow diagram	Figure1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	11 (Table1)
Outcome data	15*	Report numbers of outcome events or summary measures	11 (Table1)
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	13-16
		(*b*) Report category boundaries when continuous variables were categorized	11 (Table1)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
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	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
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	22

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

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

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