# Cardiovascular risk factors in China: a nationwide population-based cohort study 

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#### Abstract

Summary Background It is estimated that 4 million deaths are due to cardiovascular diseases each year in China. Comprehensive understanding about modifiable risk factors and how the risk differs across regions is needed to inform public health policies. We aimed to examine the geographical profile of cardiovascular disease risk across China.

Methods In this study, we analysed data from a nationwide, population-based screening project, which covered 152 rural counties and 100 urban districts from 31 provinces in China. Between Sept 1, 2015, and Nov 30, 2019, standardised measurements were taken from participants aged 35-75 years who had lived in the region for at least 6 of the preceding 12 months to collect information on blood pressure, blood lipids, blood glucose, physical activity, tobacco smoking, alcohol use, overweight or obesity, and intake frequencies of fruits, vegetables, whole grains, legumes, and red meat. Individuals with a high risk of cardiovascular disease were identified according to medical history and WHO risk prediction charts.


Findings 983476 individuals were included in this study. Among the participants included, $\mathbf{1 0} \cdot \mathbf{3 \%}$ ( $95 \%$ CI 10•2-10•3) had a high cardiovascular disease risk after standardising age and sex, with a range of $3 \cdot 1-24 \cdot 9 \%$ across counties or districts. Among the seven regions in mainland China, the prevalence of high risk of cardiovascular disease was relatively high in northeast China ( $12 \cdot 6 \%$ [12.4-12.8]) and north China ( $11 \cdot 4 \%$ [ $11 \cdot 3-11 \cdot 6]$ ), whereas it was low in south China $(8 \cdot 0 \%$ [7•8-8.2]). The geographical profiles of the 12 major cardiovascular disease risk factors were different. We found that the regions with high cardiovascular disease risk were facing challenges such as obesity and high blood pressure (north China) and consumption of unhealthy non-staple food (low intake of fruits and vegetables or high intake of red meat; northeast China). By contrast, south China-the region with the lowest cardiovascular disease risk-had the highest prevalence of unhealthy staple food (low intake of whole grains and beans), abnormal metabolism (glucose and lipid), and low physical activity in the country.

Interpretation Risk for cardiovascular diseases varies geographically, and the major contributing risk factors are different across regions in China. Hence, geographically targeted interventions are needed to mitigate the risk and reduce the burden in such a vast country.

Funding Ministry of Science and Technology, Ministry of Finance, and National Health Commission of China.

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## Introduction

In China, there is an increasing prevalence of cardiovascular diseases, which caused almost 4 million deaths in 2016 in the country. ${ }^{1}$ According to the Global Burden of Disease Study, each of the top modifiable risk factors of cardiovascular disease—namely, high systolic blood pressure, high low-density lipoprotein cholesterol, tobacco smoking, high body-mass index (BMI), and high fasting plasma glucose-is accountable for $0 \cdot 5-2 \cdot 4$ million deaths due to cardiovascular disease per year in China. ${ }^{2}$ In an effort to mitigate the risk and reduce the burden of cardiovascular disease in such a vast country with diverse geographical settings, it is important to understand that the population risk varies geographically, ${ }^{1}$ but also appreciate that the major risk factors could differ across regions.
However, comprehensive evidence on the geographical profiles of cardiovascular disease risk in China is
insufficient. The Global Burden of Disease Study identified a wide geographical variation in the mortality rate of cardiovascular diseases, ${ }^{1}$ but with respect to population risk of cardiovascular disease, findings from previous studies have included small sample sizes, have had incomplete regional coverage, or have focused on a narrow spectrum of risk factors. ${ }^{3-6}$ Additionally, to tailor targeted strategies for cardiovascular disease control, it is also crucial to identify which risk factors often occur simultaneously and could be reduced altogether in the population, and how these clusters are associated with regional characteristics. Using data from the China Patient-centered Evaluative Assessment of Cardiac Events Million Persons Project (PEACE MPP), we aimed to compare the population risk of cardiovascular diseases among different regions across China, and to describe the geographical distributions of cardiovascular disease risk factors and their clusters throughout the nation.

Lancet Public Health 2020; 5: e672-81
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For the Chinese translation of the abstract see Online for appendix 1

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## Research in context

Evidence before this study
We searched PubMed for literature published in English before May 1, 2019, using the terms "CVD risk factor cluster", "CVD risk factor pattern", "geographical/regional disparity/difference/ variation", "lifestyle", or "nationwide". We excluded studies with less than 10000 samples or studies done in a single province. We identified 43 articles (with participants enrolled between 1991 and 2017) that showed the distribution or association of major risk factors of cardiovascular disease in China. Of these studies, 17 included more than 100000 participants, 20 covered all 31 provinces, 12 studied more than seven risk factors, and none reported the geographical discrepancies of clusters of major cardiovascular disease risk factors.

## Added value of this study

To our knowledge, this study is the largest population-based report of major risk factors of cardiovascular disease across all 31 provinces in mainland China. We evaluated geographical variations in cardiovascular disease risk and multiple cardiovascular risk factors. We found differences in the
prevalence of high risk of cardiovascular disease across areas. Also, among the regions with similarly high population risk, the major contributing factors were not the same, and among regions with middle or even low risk, there were still some risk factors posing severe threats to population health. This study identified several clear classifications for the major risk factors of cardiovascular disease in the Chinese population; these risk factors occurred simultaneously and could be reduced to some clusters. These findings provided a detailed risk atlas, which highlights not only the high-risk areas, but also-more importantly-the priority factors.

## Implications of all the available evidence

The geographical profile of cardiovascular disease risk in China is complex, with a large variation in population prevalence and in contributor factors across regions. In view of the clustering of risk factors of cardiovascular disease in populations reported in this study, strategies and policies need to be targeted and based on comprehensive and practical data for delivering interventions.

## Methods

## Study design and participants

The PEACE MPP is a government-funded public health programme focusing on cardiovascular disease risk in China. Details of the project's design have been described previously.' Briefly, from Sept 1, 2015, to Nov 30, 2019, we sampled 252 sites ( 152 rural counties, 100 urban districts) across China, which covered $55 \%$ of prefectural-level municipalities in mainland China. For each of the 31 provinces, about eight counties or districts were selected using a typical case sampling design, to provide diversity in geographical distribution, economic development, and population structure (appendix $2 \mathrm{pp} 2-3$ ). Participants aged $35-75$ years who had lived in the region for at least 6 of the preceding 12 months were invited to the study by local community workers via extensive publicity campaigns on television and in the newspapers. Individuals who provided written consent were asked to go into clinics to have measurements taken. The overall response rate was $30 \%$, although it was higher among female and older residents (appendix 2 pp 22-23). Among the 2.9 million people screened in PEACE MPP, those whose serial project ID number ended with 1, 3, 5, or 7 were selected to provide detailed information on multiple cardiovascular disease risk factors, which formed the population of this study (appendix $2 \mathrm{pp} 16-17,24]$ ). The central ethics committee at the China National Center for Cardiovascular Diseases approved this project. All enrolled participants provided written informed consent.

## Procedures

We assessed 12 leading risk factors related to cardiovascular diseases, which have been outlined by the Global

Burden of Disease Study ${ }^{2,8}$ and the World Health Report 2002.' First, in the clinics, we measured pathophysiological risk factors, such as high blood pressure ( $\geq 140 / 90 \mathrm{~mm}$ Hg; Omron HEM-7430, Omron Corporation, Japan), high total cholesterol $(\geq 5.0 \mathrm{mmol} / \mathrm{L}$; CardioChek PA Analyzer, Polymer Technology Systems, USA), high blood glucose ( $\geq 7.0 \mathrm{mmol} / \mathrm{L}$; BeneCheck BK6-20M Multi-Monitoring System, Suzhou Pu Chun Tang Biotechnology, China), and overweight or obesity (BMI $\geq 25 \mathrm{~kg} / \mathrm{m}^{2}$ ), with standardised devices and procedures. Second, we collected information on lifestyle risk factors, such as tobacco smoking, alcohol use, factors related to unhealthy diet (ie, low frequency of fruits, vegetables, whole grains, and legumes, and high frequency of red meat), and lack of physical activity, through standardised in-person interviews using electronic questionnaires with real-time logical check function.
In addition to prevalence, we computed quantitative assessment of risk factor exposure. For tobacco smoking, we used the daily cigarette amount as a quantitative indicator, a score of 0 meant that the individual is not a current smoker. For alcohol use, frequency of drinking and daily number of standard drinks were combined to measure the amount of alcohol consumption. For diet, a food frequency questionnaire was used to collect the intake frequency over the previous year, with response options ranging from "daily" to "never or almost never". For physical activity, we multiplied the hours per day spent on occupation-related activities, leisure activities, transportation-related activities, and housework activities by the MET value of each activity separately, and we then summed the values for each activity together (appendix $2 \mathrm{pp} 4-6) .{ }^{10}$

|  | Overall $(\mathrm{n}=983476)$ | Participants in rural areas ( $\mathrm{n}=596360$ ) | Participants in urban areas ( $\mathrm{n}=387116$ ) | Standardised mean difference between rural and urban areas |
| :---: | :---: | :---: | :---: | :---: |
| Cardiovascular disease risk |  |  |  |  |
| High cardiovascular disease risk | 16470 (16.6\%) | 103761 (17.2\%) | 60709 (15.7\%) | 0.0418 |
| Demographic and socioeconomic characteristics |  |  |  |  |
| Gender |  |  |  |  |
| Female | 590779 (60.1\%) | 355364 (59.6\%) | 235415 (60.8\%) | -0.0250 |
| Male | 392697 (39.9\%) | 240996 (40.4\%) | 151701 (39.2\%) | 0.0250 |
| Age, years | $55 \cdot 9$ (9.9) | 55.9 (9.8) | $55 \cdot 9$ (9.9) | 0.0055 |
| Occupation: farmer | 475785 (48.4\%) | 388613 (65.2\%) | 87172 (22.5\%) | 0.9518 |
| Education: high school or higher | 223785 (22.8\%) | 86279 (14.5\%) | 137506 (35.5\%) | -0.5013 |
| Household income: $¥ 50000$ per year or higher | 172840 (17.6\%) | 73088 (12.3\%) | 99752 (25.8\%) | -0.3496 |
| Social medical insurance | 963896 (98.0\%) | 588371 (98.7\%) | 375525 (97.0\%) | 0.1138 |
| Disease history |  |  |  |  |
| Myocardial infarction | 13074 (1.3\%) | 7660 (1.3\%) | 5414 (1.4\%) | -0.0099 |
| Stroke | 24193 (2.5\%) | 14368 (2.4\%) | 9825 (2.5\%) | -0.0083 |
| Ischaemic stroke | 17478 (1.8\%) | 10366 (1.7\%) | 7112 (1.8\%) | -0.0075 |
| Diabetes* | 77144 (7.8\%) | 42326 (7.1\%) | 34818 (9.0\%) | -0.0698 |
| Risk factors |  |  |  |  |
| Blood pressure $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$ | 405776 (41.3\%) | 259995 (43.6\%) | 145781 (37.7\%) | 0.1211 |
| Systolic blood pressure, mm Hg | $136 \cdot 1$ (20.3) | $137 \cdot 2$ (20.7) | 134.4 (19.7) | 0.1410 |
| Diastolic blood pressure, mm Hg | 81.1 (11.3) | 81.6 (11.4) | $80 \cdot 3$ (11.1) | 0.1122 |
| Total cholesterol $\geq 5.0 \mathrm{mmol} / \mathrm{L}$ | 304407 (31.0\%) | 186005 (31.2\%) | 118402 (30.6\%) | 0.0061 |
| Total cholesterol, mmol/L | 4.6 (1.1) | $4 \cdot 6$ (1.1) | $4 \cdot 6$ (1.1) | 0.0107 |
| Blood glucose $\geq 7.0 \mathrm{mmol} / \mathrm{L}$ | 167480 (17.0\%) | 100916 (16.9\%) | 66564 (17.2\%) | -0.0072 |
| Blood glucose, mmol/L | 6.2 (1.7) | 6.2 (1.7) | 6.2 (1.7) | 0.0105 |
| Body-mass index $\geq 25 \mathrm{~kg} / \mathrm{m}^{2}$ | 433479 (44.1\%) | 260732 (43.7\%) | 172747 (44.6\%) | -0.0174 |
| Body-mass index, $\mathrm{kg} / \mathrm{m}^{2}$ | 24.8 (3.4) | 24.7 (3.5) | 24.8 (3.3) | -0.0318 |
| Waist circumference, cm | 83.9 (9.7) | 83.6 (9.8) | 84.3 (9.5) | -0.0658 |
| Smoking | 196438 (20.0\%) | 127889 (21.4\%) | 68549 (17.7\%) | 0.0935 |
| Number of cigarettes per day $\dagger$ | 18.2 (9.4) | 18.7 (9.5) | $17 \cdot 3$ (9.2) | 0.1461 |
| Alcohol use | 77009 (7.8\%) | 50387 (8.4\%) | 26622 (6.9\%) | 0.0585 |
| Low intake of whole grains | 691276 (70.3\%) | 436593 (73.2\%) | 254683 (65.8\%) | 0.1548 |
| Low intake of fruits | 493129 (50.1\%) | 345967 (58.0\%) | 147162 (38.0\%) | 0.4072 |
| Low intake of vegetables | 172524 (17.5\%) | 118609 (19.9\%) | 53915 (13.9\%) | 0.1572 |
| Low intake of beans | 751529 (76.4\%) | 483441 (81.1\%) | 268088 (69.3\%) | 0.2719 |
| High intake of red meat | 177276 (18.0\%) | 93494 (15.7\%) | 83782 (21.6\%) | -0.1589 |
| Low physical activity | 218925 (22.3\%) | 128944 (21.6\%) | 89981 (23.2\%) | -0.0527 |
| Metabolic equivalent task, h per day | 16.3 (12.6) | 16.7 (12.8) | 15.6 (12.1) | 0.0834 |
| Data are $\mathrm{n}(\%)$ or mean (SD). *Defined as self-reported history of diagnosis or use of antidiabetic drugs. †Only among smokers. |  |  |  |  |
| Table 1: Basic characteristics and risk factors |  |  |  |  |

We defined individuals with high risk of cardiovascular disease as those with a predicted 10 -year risk of cardiovascular disease greater than $20 \%$, according to the 2019 cardiovascular disease risk charts for east Asia by WHO (appendix 2 p 25), ${ }^{11}$ or those with previous myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, or stroke. ${ }^{12}$
We compared the risk profiles between rural counties and urban districts and between seven regions, including northeast China, north China, east China, central China, south China, northwest China, and southwest China,
which were classified on the basis of geographical divisions of China (appendix 2 p 3). We also searched grey literature, including statistical yearbooks, for information on the annual average ambient temperature, average altitude, and per capita gross domestic product (GDP) in 2017, to define environmental and socioeconomic characteristics of each study site.

## Statistical analysis

For participant characteristics and risk factors, we calculated the frequencies and percentages for categorical


Figure 1: Geographical disparity in the rate of high risk of cardiovascular disease, standardised by age and sex p value of Kruskal-Wallis test was less than 0.0001 for the seven-region comparison. The small circles represent outliers. Grey colour means no data were available in this study.
variables, and means and standard deviations or medians (with IQR) for continuous variables. We computed standardised mean differences to compare differences between rural counties and urban districts. An absolute value of the standardised mean difference smaller than 0.2 can be interpreted as a small difference. ${ }^{13}$ To describe county-level variation of measures, we computed the median odds ratio by applying multilevel models with random effect. We used box plots and Kruskal-Wallis tests to visualise and test for differences between the seven regions. Using factor analysis, we generated clusters that characterised variations of the 12 risk factors to explore how these risk factors clustered in the population. Mathematically, all observed risk factors can be expressed as linear combinations of common factors. First, we transformed the 12 risk factors into standardised normal distribution with a mean value of 0 and a standard
deviation of 1 , to treat all variables as equally important. For healthy food and physical activities, we took the opposite value of their quantitative measures (ie, intake frequency and daily MET) in the analyses, to ensure the same direction with other risk factors-the higher value, the higher the risk. Second, we examined the correlation matrix of these normally standardised risk factor variables. The factor analysis was done with the principal component method and the assumption that all initial communalities are equal to 1 . We retained factors as clusters of risk factors according to the Kaiser rule (ie, we retained factors with eigenvalues greater than $1 \cdot 0$ ), and we applied varimax orthogonal rotation to help interpret the salience of the factors. Finally, we computed factor scores for all retained factors for each observation, and the mean score of a population was used to reflect its relative importance. Considering the possible gender difference, we also repeated the factor analysis for male and female participants separately.
We constructed maps for the rate of the populations with high cardiovascular disease and for the score of risk factor clusters, which had been standardised according to the 2010 population census of China. To show county-level or district-level distributions, we included 236 counties or districts after excluding those with less than 1000 eligible participants enrolled. Additionally, we generated prevalence or scores of each province by averaging the values of their corresponding counties or districts. Scatterplots and fitting lines were used to show the correlations of the risk factor clusters with environmental and socioeconomic characteristics across counties or districts, and Fisher z-transformation was applied to test the heterogeneity of correlation coefficients between rural and urban areas.
The proportion of participants missing data was $14.9 \%$ for MET, $3.8 \%$ for the number of cigarettes smoked, and less than $2 \%$ for all other risk factors (appendix 2 p 8 ). We applied a multiple imputation method based on Markov Chain Monte Carlo by PROC multiple imputation procedure to impute the missing values, and the average of ten imputations was used to do the factor analysis (appendix 2 p 7 ). We repeated the factor analysis among participants without any missing value as a sensitive analysis.
All analyses were done with SAS 9.4, and the maps were constructed with R 3.4.1.

## Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Results

Among the 2.9 million people screened in PEACE MPP, 983476 individuals, as a systematic sample selected based

|  | Factor 1: obesity | Factor 2: <br> blood pressure | Factor 3: staple food | Factor 4: non-staple food | Factor 5: smoking and alcohol use | Factor 6: metabolic and physical activities |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Systolic blood pressure | 0.110 | 0.896 | 0.012 | 0.029 | 0.006 | 0.141 |
| Diastolic blood pressure | 0.159 | 0.896 | -0.011 | 0.006 | 0.075 | -0.023 |
| Total cholesterol | -0.088 | 0.096 | 0.123 | -0.183 | -0.120 | 0.689 |
| Glucose | 0.203 | 0.039 | 0.047 | -0.018 | 0.128 | 0.582 |
| Body-mass index | 0.910 | 0.143 | -0.014 | -0.022 | -0.054 | 0.049 |
| Waist circumference | 0.913 | 0.127 | -0.034 | -0.003 | 0.077 | 0.065 |
| Smoking | 0.048 | -0.021 | 0.019 | 0.010 | 0.779 | -0.095 |
| Alcohol use | -0.026 | 0.091 | 0.017 | -0.061 | 0.759 | 0.078 |
| Intake of grains | -0.015 | -0.034 | 0.787 | -0.017 | 0.015 | -0.008 |
| Intake of fruits | -0.040 | 0.080 | 0.448 | 0.579 | 0.166 | 0.070 |
| Intake of vegetables | -0.003 | -0.041 | -0.055 | 0.795 | 0.021 | -0.037 |
| Intake of beans | -0.020 | 0.020 | 0.741 | 0.263 | -0.014 | 0.058 |
| Intake of red meat | 0.001 | -0.041 | -0.185 | -0.560 | 0.150 | 0.067 |
| Physical activity (metabolic equivalent task, h per day) | -0.008 | -0.038 | -0.311 | 0.338 | -0.077 | 0.521 |
| Data are factor pattern loadings. |  |  |  |  |  |  |

on their serial project ID, were included in this study. Among the included participants, the average age was $55 \cdot 9$ years (SD 9.9), and $60 \cdot 1 \%$ were female (table 1 ). Overall, $596360(60 \cdot 6 \%)$ participants were living in rural areas, 172840 ( $17.6 \%$ ) had an annual household income of $¥ 50000$ or higher, 223785 ( $22 \cdot 8 \%$ ) had high school education or a higher education, and 963896 (98.0\%) had social health insurance. Rural participants had lower income and education levels than their urban counterparts (table 1). Additionally, rural participants had a lower intake of fruits and beans than those living in urban regions (table 1). The characteristics of participants among the seven geographical regions are displayed in appendix 2 (pp 18-20).
Among all participants, $16 \cdot 6 \%$ (95\% CI 16•6-16•7) had a high risk of cardiovascular disease, ranging from $2 \cdot 8 \%$ to $34 \cdot 2 \%$ across the counties or districts included (data not shown). After standardising age and sex using the 2010 national census data, the overall rate of high risk was $10 \cdot 3 \%(10 \cdot 2-10 \cdot 3)$, with a range of $3 \cdot 1-24 \cdot 9 \%$ among the counties or districts (figure 1). The median odds ratio of the rates of high cardiovascular disease risk at the county level or district level was 1.52 (95\% CI 1.46-1.58).
Generally, the standardised rates of participants with high risk of cardiovascular disease were high in northeast China ( $12 \cdot 6 \%$ [ $95 \%$ CI $12 \cdot 4-12 \cdot 8$ ]) and north China ( $11 \cdot 4 \%$ [11•3-11•6]), with $95 \%$ CIs higher than $11 \%$. In contrast, south China ( $8.0 \%$ [7.8-8.2]) had low standardised rates, with a $95 \%$ CI lower than $9 \%$. In between were east China ( $9 \cdot 6 \%$ [9•4-9•7]), northwest China ( $9 \cdot 6 \%$ [9.5-9.8]), southwest China ( $10 \cdot 0 \%$ [ $9 \cdot 8-10 \cdot 1]$ ), and central China ( $10 \cdot 7 \%$ [10•5-10•9]; figure 1).
In the factor analysis, six components with eigenvalues greater than 1.0 were retained. Of the total variance, the obesity factor (factor 1) accounted for $16 \cdot 2 \%$, the blood
pressure factor (factor 2) for $13 \cdot 6 \%$, the staple food factor (factor 3) for $9.5 \%$, the non-staple food factor (factor 4) for $8.8 \%$, the smoking and alcohol use factor (factor 5) for $7.9 \%$, and the metabolic and physical activities factor (factor 6) for $7.4 \%$ (table 2). After varimax orthogonal rotation, the first component, the obesity factor, had factor pattern loadings exceeding 0.9 for BMI and waist circumference. The second component, the blood pressure factor, had factor pattern loadings of nearly 0.9 for systolic blood pressure and diastolic blood pressure. The third component was termed staple food factor because it mainly included intake of whole grains (with loadings of 0.8 ) and beans ( $0 \cdot 7$ ). The fourth component was termed non-staple food factor because it mainly included intake of fruit $(0 \cdot 6)$, vegetables $(0 \cdot 8)$, and red meat $(0 \cdot 6)$. The fifth component was termed smoking and alcohol use factor because of its high loadings on these two risk factors ( 0.8 for both). The last component was termed metabolic and physical activities factor with its high loadings on blood glucose ( $0 \cdot 6$ ), blood lipid ( $0 \cdot 7$ ), and physical activity $(0 \cdot 5)$. In the separate analyses for male and female individuals, we found the same six components and similar factor patterns. The findings did not change in the sensitivity analyses that were done using data without missing imputations (appendix $2 \mathrm{pp} 9-15$ ).
Large regional variations in prevalence of major risk factors of cardiovascular diseases were observed (appendix 2 p 26). Moreover, geographical distributions of the six risk factor clusters were complex (appendix 2 p 27; figure 2). Among the high-risk regions, north China was particularly affected by the obesity factor and blood pressure factor, whereas northeast China was highest for the non-staple food factor. Nevertheless, south China, although being the region with the lowest risk, had the highest values for the staple food factor and the metabolic and physical activities factor (figure 2).

Analyses looking at annual average ambient temperature, altitude, and per capita GDP also showed differences between regions (figure 3; appendix 2 p 21). Higher per capita GDP was associated with lower risk in non-staple food factor in urban areas and higher risk in metabolic and physical activities factor in rural areas ( $\mathrm{p}<0 \cdot 05$ for both). Notably, the correlation between per
capita GDP and the smoking and alcohol use factor differed significantly between rural and urban regions ( $\mathrm{p}=0 \cdot 042$; figure 3 ).

## Discussion

We found an eight-time difference in the rate of the population at high risk for cardiovascular diseases


Figure 2: Geographical disparity of the six risk factor clusters
$p$ values of Kruskal-Wallis test were less than 0.0001 for all of the factors except for factor $4(p=0.014)$. The small circles represent outliers. Grey colour means no data were available in this study.
across counties or districts, with the highest rate in northeast China and north China, and the lowest rate in south China. Moreover, the risk factors were clustered and had uneven spatial distributions through the country. These variations could be partly explained by regional environmental and socioeconomic characteristics.
This study extends current knowledge in several ways. First, it showed geographical variation of the population risk of cardiovascular disease in more granular detail. Previous studies on individual risk indicators in China generally pointed out a higher prevalence of hypertension in the north, ${ }^{4}$ and a higher prevalence of prediabetes in the south. ${ }^{3}$ Among the studies considering multiple risk factors, the results were inconsistent. ${ }^{5.6}$ In comparison, our study provided more comprehensive and robust information by comparing almost all major risk factors for cardiovascular disease, and-importantly-by examining the overall cardiovascular disease risk in nearly 1 million people, at regional, provincial, and county level.

Second, the current study took a step forward to elucidate the geographical discrepancies in major risk factors contributing to cardiovascular disease. A study on 195 countries, published in 2019, indicated that China had the highest age-standardised rates of deaths due to diet-related cardiovascular disease. ${ }^{14}$ We further reported that the unhealthy dietary habits were associated with such risk differently according to regions of China. For example, northeast China had the highest non-staple food factor but the lowest staple food factor in the country.
Third, the current study has identified an array of clusters with the major cardiovascular risk factors and plausible pathophysiological meanings. Previous studies were focusing on whether there was a tendency for risk factors to aggregate, by comparing the rate of populations having multiple risk factors with the product of each risk factor's prevalence, ${ }^{15,16}$ here we obtain better insights on which risk factors often coexist in the population and





|  | p value for testing |
| :--- | :--- |
| Rural coefficient | 0.061 |
| Urban coefficient | 0.269 |
| Difference between | 0.042 |
| rural and urban coefficient |  |


|  | p value for testing |
| :--- | :--- |
| Rural coefficient | 0.014 |
| Urban coefficient | 0.895 |
| Difference between | 0.147 |
| rural and urban coefficient |  |



(Figure 3 continues on next page)

(Figure 3 continues on next page)
which risk factors could be controlled altogether, such as consultation on tobacco and alcohol use.
Finally, the current study revealed how cardiovascular disease risk factors were related to regional environmental and socioeconomic characteristics. In addition to previous individual-level evidence across ethnicities, ${ }^{17-19}$ our findings suggest that the associations might be more complex. Indeed, temperature was negatively associated with blood pressure and positively associated with blood glucose. Different agricultural patterns that are related to temperature (eg, more corn, beans, and livestock in north China) are likely to account for the dietary differences we observed. ${ }^{20,21}$ In contrast to previous findings showing that hypertension prevalence increases with residence altitude, ${ }^{22}$ our study did not observe the county-level association between altitude and blood pressure. However, we found rural-urban disparities in the correlations between per capita GDP and smoking or alcohol drinking. More research will be needed to better
understand such complexity in population health and behaviour.
Our findings could have strong implications for cardiovascular disease control in China, in line with what has been observed in the USA, with the so-called Stroke Belt (ie, a region in southeastern USA that had an usually high incidence of stroke and other forms of cardiovascular disease). ${ }^{23,24}$ Comprehensive populationbased risk assessments, such as population screening projects, are essential, and successful strategies for cardiovascular disease control developed in high-risk areas, such as the Daqing Model on diabetes (in northeast China) ${ }^{25}$ or the Kailuan Model on hypertension (in north China), ${ }^{26}$ can serve as references. Moreover, the clustering of cardiovascular disease risk factors suggests that effective interventions require a targeted and multifaceted approach. For such an approach, the primary care setting rather than specialty care seems more appropriate, along with social prescribing (ie, when


|  | p value for testing |
| :--- | :--- |
| Rural coefficient | 0.341 |
| Urban coefficient | 0.664 |
| Difference between | 0.349 |
| rural and urban coefficient |  |






Figure 3: Correlations of the six risk factor clusters with per capita gross domestic product, annual average ambient temperature, and average altitude, across counties or districts
health professionals refer patients to support in the community to improve their health and wellbeing) and community engagement; it will hence be crucial for future health-care reform to mitigate the gaps in access and quality of primary health care in China. ${ }^{27}$
Findings in the current study should be interpreted in the context of several potential limitations. First, some cardiovascular disease risk factors, such as sodium intake, were missing owing to absence of reliable measurement in the screening visit. However, this limitation could have little influence on our findings because we used factor analysis with potentially related but more immediate risk factors included (eg, blood pressure). Second, the study network has not been established on the basis of a random sampling design, which prohibited estimation of national or regional prevalence. Nevertheless, most of our analysis focused on the diversity rather than the average values, which might be generalisable within a particular area.

Third, as in other large-scale studies, our data on some risk factors, including physical activities, diet, tobacco smoking, and alcohol use, were collected using selfreports, which might have been influenced by recall bias and social desirability. Finally, it is notable that the WHO risk prediction algorithm, although developed and dedicated for east Asia, might not fit the heterogeneous population in China.
In conclusion, the geographical profile of cardiovascular disease risk in China is complex; the population risk levels can vary substantially across regions. Thus, China needs geographically targeted intervention strategies considering environmental and socioeconomic factors to control cardiovascular disease risk and reduce the burden of cardiovascular diseases.

## Contributors

SH and JLi conceived the China Patient-centered Evaluative Assessment of Cardiac Events Million Persons Project and take responsibility for all
aspects of it. XL and CW designed the study. XL and CW wrote the first draft of the Article, with further contributions from JLu, BC, YL, YY, JLi, and SH. CW and BC did the statistical analysis. All authors interpreted the data and approved the final version of the Article. XL, CW, JLu, BC, JLi, and SH had access to the raw data.

## Declaration of interests

We declare no competing interests.
Data sharing
The data are not publicly available.

## Acknowledgments

We acknowledge funding by the National Key Research and Development Program (2018YFC1312404, 2017YFC1310803, 2017YFC1310801) from the Ministry of Science and Technology of China, the Chinese Academy of Medical Sciences Innovation Fund for Medical Science (2017-I2M-1-003, 2017-I2M-2-002), and the Ministry of Finance of China and National Health Commission of China. We thank the contributions that have been made by study teams at the Chinese National Center for Cardiovascular Diseases, and the local sites in the collaborative network in the realms of study design and operations, particularly data collection by Jianlan Cui, Wei Xu, and Bo Gu. We thank Danwei Zhang, Aoxi Tian, and Xingyi Zhang from the Chinese National Center for Cardiovascular Diseases for their support in manuscript coordinating and editing.
Editorial note: the Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

## References

1 Liu S, Li Y, Zeng X, et al. Burden of cardiovascular diseases in China, 1990-2016: findings from the 2016 Global Burden of Disease Study. JAMA Cardiol 2019; 4: 342-52.
2 Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019; 394: 1145-58.
3 Zhao ZP, Li YC, Wang LM, et al. Geographical variation and related factors in prediabetes prevalence in Chinese adults in 2013. Zhonghua Yu Fang Yi Xue Za Zhi 2018; 52: 158-64 (in Chinese).
4 He J, Klag MJ, Wu Z, Whelton PK. Stroke in the People's Republic of China. I. Geographic variations in incidence and risk factors. Stroke 1995; 26: 2222-27.
5 Wang ZH, Zhang B, Wang HJ, Wang LS, Ding GG. Prevalence of cardio metabolic risk factors and related socio-demographic factors in adults aged 18-59 years in 15 provinces of China. Zhonghua Liu Xing Bing Xue Za Zhi 2018; 39: 904-08 (in Chinese).
6 Wu J, Cheng X, Qiu L, et al. Prevalence and clustering of major cardiovascular risk factors in China: a recent cross-sectional survey. Medicine (Baltimore) 2016; 95: e2712.
7 Lu J, Xuan S, Downing NS, et al. Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project pilot. BMJ Open 2016; 6: e010200.
8 Stanaway JD, Afshin A, Gakidou E, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018; 392: 1923-94.
9 WHO. The World Health Report 2002: reducing risks, promoting healthy life 2002. 2002. http://www.who.int/whr/2002/en/ (accessed Sept 20, 2019).

10 Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011; 43: 1575-81.
11 Kaptoge S, Pennells L, De Bacquer D, et al. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health 2019; 7: e1332-45.
12 WHO. Prevention of cardiovascular disease: guidelines for assessment and management of cardiovascular risk. Geneva: World Health Organization, 2007.
13 Cohen J. Statistical power analysis for the behavioral sciences, 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates, 1988: 1-17.
14 GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019; 393: 1958-72.
15 Wu DM, Pai L, Chu NF, et al. Prevalence and clustering of cardiovascular risk factors among healthy adults in a Chinese population: the MJ Health Screening Center Study in Taiwan. Int J Obes Relat Metab Disord 2001; 25: 1189-95.
16 Raitakari OT, Leino M, Räkkönen K, et al. Clustering of risk habits in young adults. The Cardiovascular Risk in Young Finns Study. Am J Epidemiol 1995; 142: 36-44.
17 Wang Q, Li C, Guo Y, et al. Environmental ambient temperature and blood pressure in adults: a systematic review and meta-analysis. Sci Total Environ 2017; 575: 276-86.
18 Valdés S, Doulatram-Gamgaram V, Lago A, et al. Ambient temperature and prevalence of diabetes and insulin resistance in the Spanish population: Di@bet.es study. Eur J Endocrinol 2019; 180: 273-80.
19 Blauw LL, Aziz NA, Tannemaat MR, et al. Diabetes incidence and glucose intolerance prevalence increase with higher outdoor temperature. BMJ Open Diabetes Res Care 2017; 5: e000317.
20 Li X, Liu N, You L, et al. Patterns of cereal yield growth across China from 1980 to 2010 and their implications for food production and food security. PloS One 2016; 11: e0159061.
21 Robinson TP, Wint GRW, Conchedda G, et al. Mapping the global distribution of livestock. PLoS One 2014; 9: e96084.
22 Mingji C, Onakpoya IJ, Perera R, Ward AM, Heneghan CJ. Relationship between altitude and the prevalence of hypertension in Tibet: a systematic review. Heart 2015; 101: 1054-60.
23 Lanska DJ. Geographic distribution of stroke mortality in the United States: 1939-1941 to 1979-1981. Neurology 1993; 43: 1839-51.
24 Ovbiagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. Stroke 2013; 44: 2361-75.
25 Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008; 371: 1783-89.
26 Gao F, Liu X, Wang X, et al. Changes in cardiovascular health status and the risk of new-onset hypertension in Kailuan Cohort Study. PLoS One 2016; 11: e0158869.
27 Li X, Lu J, Hu S, et al. The primary health-care system in China. Lancet 2017; 390: 2584-94.

