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**Complete List of Authors:** Xiao, Wenwen; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center
Wumaer, Aishanjiang; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center
Maimaitiwusiman, Zhuoya; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center
Liu, Jinling; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center
Xuekelati, Saiyare; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center
Wang, Hongmei; People's Hospital of Xinjiang Uygur Autonomous Region, Second Department of cadre health care center

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Heat maps of cardiovascular disease risk factor clustering among community-dwelling older people in Xinjiang: a cross-sectional study

Wenwen Xiao, Aishanjiang Wumaer, Zhuoya Maimaitiwusiman, Jinling Liu, Saiyare Xuekelati, Hongmei Wang

Second Department of Cadre Health Care Center of People’s Hospital of Xinjiang Uygur Autonomous Region, Urumqi, China

Correspondence to: Dr Hongmei Wang; whmdoctor@163.com
ABSTRACT

Objective: The clustering of multiple cardiovascular disease risk factors (CRFs) increases the risk of cardiovascular disease (CVD) prevalence and mortality. Little is known about CRF clustering among community-dwelling older people in Xinjiang. The objective of this study was to explore the prevalence of CRF clustering in this population.

Design: Cross-sectional study.

Setting: Xinjiang, China.

Participants: Multi-level random sampling was used to survey individuals aged ≥60 in six regions of Xinjiang. In total, 87,000 participants volunteered, with a response rate of 96.67%; 702 participants with incomplete data were excluded and data from 86,298 participants were analyzed.

Outcome measures: The prevalence of smoking, drinking, hypertension, diabetes, dyslipidemia and overweight/obesity was 9.4%, 5.4%, 52.1%, 16.8%, 28.6%, and 62.7%, respectively. The prevalence of CRF clusters among people of different ages, regions, and ethnic groups differed significantly. The 85.9% of the participants presented at least one CRFs and 56.9% of the participants presented clustering of CRFs. The proportion of CRF clusters tended to be higher in men, 60–69 year old group, northern Xinjiang, and the Kazakh population. After adjusting for age and sex, logistic regression analysis revealed that men, 60–69 year old group, northern Xinjiang, and the Kazakh population were more likely to have clustering of CRFs, compared with their counterparts.

Conclusions: The prevalence of CRFs in the older Xinjiang population is high and their clustering differs by age, region, and ethnicity. CRF prevention and management should be active in this population, and strategies to reduce CVD risk based on age, ethnic group, and region are warranted.
Strengths and limitations of this study

- The study is the first epidemiological investigation of CRF clustering in the older population of Xinjiang.

- Strengths included the use of multi-level random sampling, representative samples, a large sample size, strict pre-survey staff training, and standard protocols and instruments to ensure the reliability of the data.

- Cross-sectional studies cannot quantify the importance, nor can they determine the causality and temporality, of the relationship between CRF clustering and the morbidity of CVD.

- The study did not conduct an oral glucose tolerance test, which may underestimate the morbidity of diabetes.
INTRODUCTION

Because of its high prevalence and mortality rate, cardiovascular disease (CVD) has become the primary burden of global population health. Moreover, how to intervene, control, and reduce the occurrence and development of CVD is an urgent problem in need of a solution. Cardiovascular disease risk factors (CRFs) are closely related to the incidence and prevalence of CVD, and the clustering of multiple CRFs has been found to increase the risk of CVD occurrence and death.\textsuperscript{1-3} The China CVD Report 2018 showed that due to widespread CRF exposure, the prevalence of CVD in China is continuously on the rise, with an estimated 290 million CVD patients at present. The CVD mortality rate ranks first among urban and rural residents, and the total cost of hospitalization due to CVD increases annually. The growth of China’s CVD disease burden is much higher than the country’s GDP growth rate, further highlighting the urgency of CVD prevention and control.

Studies have recognized that smoking, drinking, hypertension, diabetes, dyslipidemia, and overweight/obesity are common and easily measurable CRFs.\textsuperscript{4,5} The clustering of CRFs has been found to increase the risk of CVD; individuals with more than one CRF have a greater risk of CVD than those with a single CRF.\textsuperscript{1,2} Additionally, studies have found that the prevalence of clustered CRFs in different countries, populations, regions and ethnic groups is not uniform.\textsuperscript{6-9} Therefore, understanding these differences may assist with CVD prevention and control through the targeting of CRFs unique to different regions and ethnic groups.

Xinjiang, located in northwestern China, in the hinterland of the Eurasian continent. Since ancient times, Xinjiang has been a multi-ethnic, multi-cultural, and multi-religious place. Many ethnic groups have lived in Xinjiang and migration in general is frequent. By the end of the 19th century, 13 major ethnic groups, including Uyghur, Han, Kazakh, Mongolian, Hui, Kirgiz, Manchu, Xibe, Tajik, Daur, Uzbek, Tatar, and Russian people, had settled in Xinjiang. Uyghur, Han, Kazakh, and Hui people accounted for 97.32% of the total population at this time.\textsuperscript{10} According to the Sixth National Census and Statistical Communiqué on Xinjiang’s Population Sample
Survey (2015), the population of those aged 65 years and over in 2010 was 1,350,300, accounting for 6.48% of the total population; in 2015, this percentage increased to 7.21%. The growth rate of the population aged 65 and over is much faster than that of Xinjiang's total population, highlighting this aging population. At present, there have been no large-scale surveys or analyses of the prevalence and clustering of CRFs in the older population of Xinjiang.

It is also well known that findings from the younger population may not be applicable to the older. Therefore, our research aims to provide the latest prevalence of CRFs and their clusters in the older population of Xinjiang. By understanding the differences in CRFs and their clusters among different sexes, ages, regions, and ethnic groups, we can formulate specific intervention measures against CRFs to prevent, manage, and reduce the mortality of CVD and the economic burden of medical insurance.

MATERIALS AND METHODS

Study population

The study was approved by the Ethics Committee of People's Hospital of Xinjiang Uygur Autonomous Region (Xinjiang, China). Written informed consent was obtained from all participants before data collection and measurement.

This study was a cross-sectional epidemiological survey of the older population of Xinjiang. According to natural settings and climate patterns, Xinjiang is divided into three distinct subregions (north, south, and east). A multi-stage random sampling method was used between January and December 2019 to administer surveys in this population. In the first stage, two prefectures were randomly selected from southern, northern, and eastern Xinjiang (Altai and Tacheng in northern Xinjiang, Kashgar and Hotan in southern Xinjiang, and Hami and Turpan in East Xinjiang). In the second stage, one city was randomly selected from each prefecture. In the third stage, two counties were randomly selected from each city. In the fourth stage, 7,500 people
aged ≥60 were randomly selected from each county. From this pool, a total of 90,000 participants were randomly selected. All participants met the inclusion criteria of this survey: participants were aged ≥60 with independent consciousness, who were able to understand and cooperate with investigations and sign an informed consent form. Ultimately, 87,000 participants accepted the survey, with a response rate of 96.67%; 702 participants with incomplete data were excluded and data from 86,298 people were analyzed.

Research methods

Questionnaire

A set of standardized questionnaires was completed under physician guidance. The questionnaire collected information such as age, sex, ethnic group, education, occupation, disease history, medication history, family history, drinking history, smoking history, eating habits, and other details.

Physical examination

A detailed physical examination was carried out on each subject by a physician and blood pressure, weight, and height, were measured by qualified professionals according to standard methods.

Blood pressure measurement: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the method recommended by the American Heart Federation. All participants were prohibited from smoking and drinking alcohol, tea, coffee, and other such caffeinated drinks 30 minutes before. Participants were seated and the blood pressure of their right upper arm was measured after a 10-minute rest. A specialist doctor used a desktop mercury sphygmomanometer to measure blood pressure every two minutes for three consecutive measurements, with room temperature kept above 18°C.

Weight measurement: The participants were required to have an empty stomach, take off their shoes, and wear only light clothes. A calibrated medical scale was used for
weighing. The participants were relaxed and stood upright in the middle of the scale’s chassis, with the reading being accurate to 0.1 kg.

Height measurement: A measuring ruler with a minimum scale of 1 mm was fixed vertically to the ground. The participants stood upright with both heels together and their body, hips, and shoulders close to the ruler. The examiner put a square ruler on the top of the participants' head, with one side of the right angle being near to the measuring ruler and the other side to the participants' scalp. The reading on the measuring ruler was accurate to 1 mm.

Calculation of BMI = weight (kg) / height (m)^2.

Collection of blood samples and laboratory testing

Disposable blood collection equipment was used to draw 10 ml of fasting peripheral venous blood from all participants in the morning (participants’ stomachs should have been empty for a minimum of 10 hours). Plasma (serum) was centrifugally separated from blood cells immediately and both components were stored at -80°C. Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum creatinine (sCr), serum urea nitrogen (SUN), and other biochemical indicators were examined within one month, using a Hitachi 7600 automatic biochemical analyzer at the clinical Laboratory Center of People's Hospital of Xinjiang Uyghur Autonomous Region (a Third-Grade Class A hospital).

Assessment criteria

Hypertension: SBP ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, or a previous diagnosis of hypertension with the use of antihypertensive medication.

Diabetes: Fasting plasma glucose (FPG) concentration ≥7.0 mmol/L or a previous diagnosis of diabetes with use of hypoglycemic agents.

Overweight/obesity: According to criteria listed in the Guidelines for Prevention and Control of Overweight and Obesity in Chinese Adults, a BMI of 18.5–24 kg/m^2 was
considered as normal weight, 24.0–28.0 kg/m² as overweight, and ≥28.0 kg/m² as obese.

Dyslipidemia: According to criteria from the Guidelines for Prevention and Control of Dyslipidemia in Chinese Adults (2016 Revised Edition), dyslipidemia was defined as the presence of at least one of the following: TC ≥6.2 mmol/L, TG ≥2.3 mmol/L, HDL-C <1.0 mmol/L, and LDL-C ≥4.1 mmol/L.

Smoking and drinking: According to World Health Organization standards, participants were defined as smokers if they smoked continuously or smoked for a cumulative period of at least 6 months. Participants were defined as drinkers if they drank alcohol once a week, with an alcohol consumption of 8 g per week.

The clustering of CRFs: Smoking, drinking, hypertension, diabetes, dyslipidemia, and overweight/obesity were the CRFs included in this study. Clustering referred to the same individual exposed to at least two of the above CRFs.

**Quality control**

Standard methods and unified, standardized instruments (checked and corrected by professionals) were used to collect the relevant data. In order to control observer error to the greatest extent, investigators were rigorously trained and assessed to administer the questionnaire (the questionnaire administrator was a specialist doctor), and to perform physical examination, blood sample collection, transportation, separation, preservation, marking, recording, questionnaire review, data entry, etc. Only trained and qualified individuals could administer the survey. Double blind data entry was used in which two professionals entered data in parallel and performed statistical analysis after verification.

**Statistical analysis**

Data analyses were performed using SPSS for Windows (version 19.0; SPSS Inc., Chicago, IL, USA). Values were expressed as the mean ± standard deviation (SD). Count data was shown as the number of total cases (n) or percentages (%).
Comparisons of clinical phenotypic measurement data between two groups were performed using a Student’s t-test, and categorical data were analyzed using a chi-squared test. Logistic regression analysis was used to analyze the influence of differences in sex, age, region, and ethnicity on the clustering of CRFs after adjusting for age and sex. P <0.05 indicated that the difference was statistically significant.

Patient and public involvement

Participants and the public were not involved in the design, implementation or analysis of this study.

RESULTS

Demographic and physiological characteristics of participants

As shown in table 1, a total of 86,298 participants aged ≥60 years were involved in this study, including 41,087 (47.6%) males and 45,211 (52.4%) females. Moreover, 33.5%, 6.1%, 57.3%, and 3.1% of participants were of Han, Kazakh, Uyghur, and Hui ethnicities, respectively. The DBP value of men was higher than that of women (P <0.05); smoking and drinking rates in men were also significantly higher than in women (P <0.001) The BMI, SBP, TC, TG, LDL-C, HDL-C, and FPG values of women were all higher than those of men (P <0.001). The prevalence of hypertension, diabetes, dyslipidemia, and overweight/obesity were also higher in women than in men (P <0.001).

| Characteristic | Total (n=86298) | Men (n=41087) | Women (n=45211) | t/χ² value | P value |
|---------------|----------------|--------------|----------------|------------|---------|
| Age*, years   | 73.5±6.0       | 73.6±6.1     | 73.3±5.9       | 6.46       | <0.001  |
| Ethnic group, n (%) |            |              |                | 262.14     | <0.001  |
| Han           | 28129(33.5)    | 12447(31.1)  | 15682(35.7)    |            |         |
| Kazakh        | 5132(6.1)      | 2263(5.7)    | 2869(6.5)      |            |         |
BMI*, kg/m² 25.7±4.4 25.3±4.0 26.1±4.7 -28.64 <0.001
SBP*, mmHg 135.4±20.4 134.2±20.1 136.5±20.6 -16.44 <0.001
DBP*, mmHg 77.1±12.3 77.2±12.3 76.9±12.3 2.85 0.004
TC*, mmol/L 4.8±1.2 4.6±1.1 4.9±1.2 -47.01 <0.001
TG*, mmol/L 1.5±1.0 1.4±0.9 1.6±1.0 -29.68 <0.001
LDL-C*, mmol/L 2.6±0.9 2.5±0.9 2.7±0.9 -22.21 <0.001
HDL-C*, mmol/L 1.4±0.4 1.3±0.4 1.4±0.4 -39.07 <0.001
FBG*, mmol/L 6.0±2.1 5.9±2.1 6.0±2.2 -10.57 <0.001
Smoking, n (%) 7832(9.4) 7646(18.9) 186(0.4) 8371.27 <0.001
Drinking, n (%) 4504(5.4) 4230(10.5) 274(0.6) 3946.89 <0.001
Hypertension, n (%) 44595(52.1) 20084(49.2) 24511(54.6) 248.96 <0.001
Diabetes, n (%) 14175(16.8) 6227(15.5) 7948(18) 90.61 <0.001
Dyslipidemia, n (%) 24130(28.6) 10787(26.8) 13343(30.2) 117.85 <0.001
Overweight/Obesity, n (%) 53294(62.7) 24308(60.2) 28986(65.1) 214.98 <0.001

*Mean±SD.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, serum total cholesterol; TG, triglyceride; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.

The prevalence of CRFs among different ages, regions, and ethnic groups in the older population of Xinjiang, China

The prevalence of smoking, drinking, hypertension, diabetes, dyslipidemia, and overweight/obesity among the older population of Xinjiang was 9.4%, 5.4%, 52.1%, 16.8%, 28.6%, and 62.7%. Men had more bad health-related behaviors than women, such as smoking and drinking. The prevalence of hypertension, diabetes, dyslipidemia, and overweight/obesity were higher in women than in men (table 1).
Participants were divided into five groups by age (60–69 years old, 70–79 years old, 80–89 years old, 90–99 years old, ≥100 years old). Differences in the prevalence of smoking, drinking, hypertension, diabetes, dyslipidemia, and overweight/obesity across age groups were statistically significant (P <0.05). Prevalence rates of smoking, drinking, dyslipidemia and overweight/obesity were highest in the 60–69 year old group; diabetes prevalence was highest in the 70–79 year old group; and hypertension was highest in the 80–89 year old group, thereafter showing a downward trend with age (table 2).

**Table 2** The prevalence of cardiovascular disease risk factors (CRFs) among community-dwelling older people in Xinjiang

| Category     | Smoking  | Drinking | Hypertension | Diabetes | Dyslipidemia | Overweight/Obesity |
|--------------|----------|----------|--------------|----------|--------------|--------------------|
| Age group, n (%) |          |          |              |          |              |                    |
| 60-69        | 2977(11.7)| 1598(6.3)| 12770(48.7)  | 4144(16.0)| 7491(28.8)  | 17515(67.3)        |
| 70-79        | 3809(8.7 )| 2197(5.0 )| 24105(53.5)  | 7748(17.4)| 12784(28.7) | 28021(62.6)        |
| 80-89        | 996(7.8)  | 682(5.3)  | 7139(54.6)   | 2153(16.9)| 3546(27.9)  | 7210(55.7)         |
| 90-99        | 50(4.3)   | 27(2.3)   | 560(46.7)    | 126(10.8)| 292(25.2)   | 522(43.9)          |
| ≥100         | 0(0.0)    | 0(0.0)    | 21(33.3)     | 4(6.3)   | 17(27.0)    | 29(46.0)           |
| χ² value     | 265.31    | 77.45     | 208.98       | 59.98    | 10.67        | 688.91             |
| P value      | <0.001    | <0.001    | <0.001       | <0.001   | 0.031        | <0.001             |

| Category     | Smoking  | Drinking | Hypertension | Diabetes | Dyslipidemia | Overweight/Obesity |
|--------------|----------|----------|--------------|----------|--------------|--------------------|
| Geographic region, n (%) |          |          |              |          |              |                    |
| Northern Xinjiang | 2833(11.3)| 2379(9.5)| 15419(61.4)  | 5009(20.2)| 7003(28.1)  | 17317(69.2)        |
| Eastern Xinjiang  | 1978(9.6)| 1204(5.9)| 12503(54.7)  | 3558(16.2)| 6010(27.3)  | 13456(60.2)        |
| Southern Xinjiang | 3021(8.0)| 921(2.4)| 16673(44.3)  | 5608(15.0)| 11117(29.6) | 22524(59.9)        |
| χ² value     | 195.52    | 1479.23  | 1847.79      | 281.77   | 40.63        | 634.09             |
| P value      | <0.001    | <0.001   | <0.001       | <0.001   | <0.001       | <0.001             |

| Category     | Smoking  | Drinking | Hypertension | Diabetes | Dyslipidemia | Overweight/Obesity |
|--------------|----------|----------|--------------|----------|--------------|--------------------|
| Ethnic group, n (%) |          |          |              |          |              |                    |
| Han          | 3172(11.5)| 2989(10.8)| 15438(55.2) | 5974(21.9)| 8266(30.2)  | 17840(64.8)        |
| Kazakh       | 428(8.4) | 233(4.4) | 3400(66.3)   | 490(9.7) | 1413(27.9)  | 3827(75.0)         |
| Uyghur       | 3742(8.1)| 1037(2.3)| 22877(48.0)  | 6754(14.3)| 13005(27.5) | 28206(59.5)        |
There were statistically significant differences in the prevalence of all six CRFs between northern, eastern, and southern Xinjiang (P < 0.05). The prevalence of smoking, drinking, hypertension, diabetes and overweight/obesity was highest in northern Xinjiang, followed by eastern Xinjiang and southern Xinjiang. The prevalence of dyslipidemia was highest in southern Xinjiang, followed by northern and eastern Xinjiang (table 2).

Statistically significant differences in the prevalence of the six CRFs were also found between ethnic groups (P < 0.05). Kazakh individuals had the highest prevalence of hypertension and overweight/obesity, followed by Hui and Han; Uyghurs had the lowest. However, nearly half or more than half of all participants suffered from hypertension and overweight/obesity. The prevalence of smoking, drinking, and dyslipidemia in Han individuals were higher than in other ethnic groups. The prevalence of diabetes was the highest in Hui individuals (table 2).

### Heat maps of CRF clustering among the older population of Xinjiang, China

In Xinjiang, only 14.1% of the older population did not have any CRFs. People with 1, 2, 3 or ≥4 CRFs accounted for 29.0%, 32.5%, 17.9% and 6.5% of those sampled, while those with ≥1, ≥2, ≥3 or ≥4 CRFs accounted for 85.9%, 56.9%, 24.4% and 6.5%, respectively (table 3).

| Category | None (0) | Clustering(≥1) | Clustering(≥2) | Clustering(≥3) | Clustering(≥4) | χ² value | P value |
|----------|----------|----------------|----------------|----------------|----------------|-----------|---------|
| Gender   |          |                |                |                |                |           |         |
| Men      | 5635(14.5)| 33316(85.5)    | 22515(57.8)    | 10550(27.1)    | 3454(8.9)      |          | <0.001  |
| Women    | 5690(13.7)| 35828(86.3)    | 23298(56.1)    | 9088(21.9)     | 1748(4.2)      |          |         |
### Differences in the Prevalence of the Six CRFs differed by sex, age, region, and ethnic group (P <0.05). Men had more CRF clusters than women. Furthermore, CRF clustering decreased gradually with age (Figure 5). People in northern Xinjiang with ≥1, ≥2, ≥3 or ≥4 clustered CRFs had the highest morbidity. Moreover, 90.5% of people were exposed to at least one CRF. After eastern Xinjiang, people in southern Xinjiang had the lowest morbidity. By ethnic group: Kazakhs with ≥1 or ≥2 clustered CRFs had the highest morbidity; Han with ≥3 or ≥4 clustered CRFs had the highest morbidity; and Uyghurs with ≥1, ≥2, ≥3, or ≥4 clustered CRFs had the lowest morbidity (table 3).

**Logistic regression analysis of ≥1, ≥2, ≥3 and ≥4 clustered CRFs among different sexes, ages, regions, and ethnic groups in the older population of Xinjiang**

After adjusting for age and sex, the logistic regression analysis revealed that the risk
of illness in women with ≥1, ≥2, ≥3, and ≥4 clustered CRFs was 1.061, 1.021, 0.852, and 0.499 times that of a man, respectively. Compared with people aged 60 to 69 years old, the odds ratios of CRFs clustering decreased gradually with age. Northern Xinjiang, and the Kazakh population were more likely to have clustering of CRFs (Table 4).

| Category       | ≥1 CRFs       | ≥2 CRFs       | ≥3 CRFs       | ≥4 CRFs       |
|----------------|---------------|---------------|---------------|---------------|
| Gender*        |               |               |               |               |
| Men            | Reference     | Reference     | Reference     | Reference     |
| Women          | 1.061 (1.019 to 1.104) | 1.021 (0.980 to 1.064) | 0.852 (0.813 to 0.892) | 0.499 (0.466 to 0.534) |
| Age group**    |               |               |               |               |
| 60-69          | Reference     | Reference     | Reference     | Reference     |
| 70-79          | 0.931 (0.890 to 0.975) | 0.929 (0.886 to 0.974) | 0.937 (0.888 to 0.988) | 0.871 (0.808 to 0.938) |
| 80-89          | 0.839 (0.789 to 0.893) | 0.805 (0.755 to 0.858) | 0.790 (0.735 to 0.850) | 0.723 (0.651 to 0.803) |
| 90-99          | 0.546 (0.471 to 0.634) | 0.431 (0.367 to 0.506) | 0.286 (0.230 to 0.355) | 0.179 (0.117 to 0.274) |
| ≥100           | 0.566 (0.299 to 1.071) | 0.340 (0.163 to 0.706) | 0.134 (0.038 to 0.477) | 0.000 (0.000 to) |
| Geographic region*** |           |               |               |               |
| Northern Xinjiang | Reference     | Reference     | Reference     | Reference     |
| Eastern Xinjiang | 0.600 (0.565 to 0.636) | 0.527 (0.496 to 0.560) | 0.471 (0.440 to 0.503) | 0.443 (0.405 to 0.485) |
| Southern Xinjiang | 0.501 (0.476 to 0.527) | 0.419 (0.398 to 0.442) | 0.333 (0.314 to 0.353) | 0.261 (0.241 to 0.283) |
| Ethnic group**** |               |               |               |               |
| Han            | Reference     | Reference     | Reference     | Reference     |
| Kazakh         | 1.421 (1.272 to 1.588) | 1.421 (1.269 to 1.591) | 1.121 (0.993 to 1.267) | 0.669 (0.564 to 0.794) |
| Uyghur         | 0.580 (0.554 to 0.608) | 0.489 (0.466 to 0.513) | 0.372 (0.353 to 0.393) | 0.271 (0.251 to 0.292) |
| Hui            | 0.980 (0.852 to 1.128) | 0.962 (0.833 to 1.111) | 0.904 (0.773 to 1.056) | 0.657 (0.529 to 0.816) |

A logistic regression model was used to estimate ORs with 95% CIs.

The odds ratios for gender groups were adjusted for age.
**The odds ratios for age groups were adjusted for gender.

***The odds ratios for region groups were adjusted for age and gender.

****The odds ratios for ethnic groups were adjusted for age and gender.

DISCUSSION

In this study, we investigated the epidemic characteristics of CRFs clustering among a large representative sample in the older Xinjiang population. High morbidity of clustered CRFs was presented in Xinjiang. After adjusting the confounding factors, the clustering of CRFs was associated with gender, age, region and ethnic.

This study found a high morbidity of clustered CRFs in Xinjiang; only 14.1% of the older population was not affected by any CRFs. Similarly, data collected in 2005 by InterAsia showed that 80.5% of Chinese adults aged 35 to 74 were affected by one or more CRFs (dyslipidemia, hypertension, diabetes, smoking, and overweight/obesity); the corresponding morbidities were 53.6%, 26.1%, 5.2%, 34.4% and 28.2%, respectively, and the corresponding morbidity of adults with ≥1, ≥2 and ≥3 clustered CRFs was 80.5%, 45.9% and 17.2%, respectively. In America, these figures were 93.1%, 73.0%, and 35.9%, respectively. After analysis, we found that the most common CRFs in our study were overweight/obesity (62.7%) and hypertension (52.1%). The rate of overweight/obesity was consistent with the national level. Conversely, the morbidity of hypertension and diabetes (16.8%) were higher than the national level, while the morbidity of smoking and dyslipidemia were lower; these findings are consistent with that of previous research. Additionally, the morbidity of the participants with ≥2 and ≥3 clustered CRFs was higher than the national level, and that of northeastern China, suburban areas and rural-urban fringe zones of Beijing, Qamdo, Nanjing, Guangxi, the Yangpu District in Shanghai, Malaysia, and southwest Nigeria. In contrast, the morbidity of the participants with ≥2 and ≥3 clustered CRFs was lower than that reported in the USA,
India,\textsuperscript{26} Nepal,\textsuperscript{27} Shenzhen,\textsuperscript{28} rural areas of Yunnan,\textsuperscript{29} Hubei,\textsuperscript{30} and the Panyu District of Guangzhou.\textsuperscript{31} Potential reasons for these differences may include differences in participants’ ages, the CRFs components included, and the sample size. Our study shows that the older population in Xinjiang is more likely to have clustered CRFs; thus, active public health measures should be taken to prevent and control these factors.

Consistent with our results, one systematic review of 16 studies published in 2007 and another of 101 Canadian studies published in 2015 certified that there are striking differences in the morbidity of clustered CRFs across ethnic groups.\textsuperscript{32, 33} After adjustment for age and sex, the odds ratios for the prevalence of $\geq 1$, and $\geq 2$ clustered CRFs were higher in the Kazakh population than in the Han; odds ratios in the Hui and Uyghur populations were lower than in the Han. The morbidity of overweight/obesity and hypertension in Kazakhs was higher than other ethnic groups. The morbidity of smoking, drinking, and dyslipidemia in the Han population was also higher than other ethnic groups. The prevalence of diabetes in the Hui population was higher than in other ethnic groups. However, these results are inconsistent with the conclusions drawn by Wang et al.\textsuperscript{7} and Tao et al.\textsuperscript{34} Wang et al. conducted a study from 2002 to 2008 that included 13,356 participants over 30 years old. Participants were of various ethnicities, including Uyghur, Kazakh, Mongolian, and Han, and the CRFs measured included hypertension, obesity, diabetes, dyslipidemia, and smoking. In contrast, Tao et al. conducted a study from 2007 to 2010 of 11,608 participants aged 35 to 74 years old. Participants were of different ethnicities, including Uygur, Kazakh, and Han, and the CRFs included were dyslipidemia, hypertension, obesity, diabetes, and smoking. The above inconsistency may be due to sample size, the age of participants, and the region studied. The measures taken to prevent and control CRFs as well as improvements in living standards and people’s health awareness over time also contribute.

This study also showed that among the clustered CRFs, the morbidity of smoking, drinking, hypertension, diabetes, and overweight/obesity was higher in northern
Xinjiang than in eastern and southern Xinjiang. Hypertension, diabetes, obesity, and dyslipidemia are multi-factor diseases affected by genetics and the environment. Located in northwestern China, Xinjiang spans a large latitude and longitude and has large differences in altitude, temperature (in southern and northern Xinjiang), and residents' genetic background, cultural customs, and eating habits. In northern Xinjiang, the temperature is relatively low with an average annual temperature of -4–9 °C accompanied by low precipitation. It is dominated by animal husbandry and 96.4% of the Kazakh in China live here. The Kazakh population mainly follow a nomadic lifestyle. Men often drink hard liquor and eat a simple diet of meat and salt to resist the cold, with fewer fruits and vegetables. In contrast, southern Xinjiang is a typical comprehensive zone integrating three systems: oasis, mountain, and desert. Belonging to an arid and warm temperate climate, it has low rainfall. Light and heat are abundant. Residents mainly rely on farming for their livelihood and they eat sufficient fruits and vegetables. Eastern Xinjiang is a typical continental desert climate. It is arid and hot, with a large temperature difference between day and night. The annual precipitation is low and evaporation is large. Salinization and desertification are serious. The natural environments, production, and lifestyles mentioned above may cause differences in the morbidity and clustering of CRFs. This study suggests that the morbidity and clustering of CRFs in northern, eastern, and southern Xinjiang are different, with the highest clustering of CRFs in northern Xinjiang, and a relatively low risk of CRFs clustering in southern Xinjiang and eastern Xinjiang. Therefore, it is necessary to take region-oriented CRFs prevention and control measures.

The study also found that the highest CRF exposure was in those aged 60–69 years old, and that both CRF clustering and age- and sex-adjusted CRF clustering gradually decreased with age. Numerous studies have shown that correlations between several traditional CRFs and cardiovascular events are reduced in the older adult. For individuals whose lifestyle risk factors remain the same throughout life, their lifetime risk of CVD is lower at 70 years old than at 50 years old. Similarly, a strong
relationship has been found between hypertension and the hazard of death in the older at younger ages, while a weak relationship has been found at very older ages. The risk of hypertension does not continue to increase with age. This may be because people with a high risk of CVD are more likely to have early lifetime events, and multiple clustered CRFs and competition between diseases lead to a greater risk of death. Another possible reason may be that more older survivors with one CRF are less likely to have been adversely affected by other CRFs. People with longer lifespans may either have a genetic composition resistant to CVD or have a lower burden of CRFs, which in turn reduce their risk of CVD. Moreover, the physiological changes that occur during aging may change the effects of some CRFs. One study found that a minimum cholesterol level is necessary to maintain neuronal function; a very older individual with a heavy weight in the overweight range may reflect lower weakness and less loss of physiological reserve; the optimal BMI for an older individual is considered higher than that of one who is middle-aged. In this study, it was found that the morbidity of cardiovascular CRFs was relatively low among individuals aged 100 years old and above, which is consistent with the results of Zyczkowska et al. In this study, participants ≥100 years did not smoke or drink, and had a healthier lifestyle with a low morbidity (33.3%, 6.3%, 27.0%, 46%) of hypertension, diabetes, dyslipidemia, and overweight/obesity. This explains to some extent why fewer than 4 CRFs were clustered in this age group.

This study also found that women had a higher risk than men of having at least one clustered CRF, while men had a higher risk than women of having ≥2, ≥3, and ≥4 clustered CRFs. This is in line with the study results of Zhao et al. and Wang, who found that CRF clustering occurs easily in men. The study showed that the morbidity of CVD in women was further increased in participants aged 51 years (the average menopausal age of Asian women) or older. Like in whites, the onset of menopause may further increase the risk of CVD. Furthermore, compared with pre-menopausal women, post-menopausal women have higher levels of CRF indicators (hypertension, diabetes, dyslipidemia) related to metabolism. Considering the decline of hormone
levels in post-menopausal women, the protective effect is reduced for metabolic CRFs. Meanwhile, lifestyle and eating habits are hard to change in a short time.\textsuperscript{52}

The advantages of this study were distinct. First, the results were based on a community-dwelling population with a large sample size, which made our conclusions more convincible. Second, to the best of our current knowledge, this was the first epidemiological investigation of CRF clustering specifically for older people in Xinjiang. Third, the high-quality study design, high response rate, multi-level random sampling, representative samples, strict pre-survey staff training, and standard protocols and instruments were used to ensure the reliability of the data. Despite these strengths, our study also had several limitations. The cross-sectional studies cannot quantify the importance, nor can they determine the causality and temporality, of the relationship between CRF clustering and the prevalence of CVD. Therefore, further prospective studies should be conducted. Additionally, the study did not perform an oral glucose tolerance test or check 2-hour postprandial blood glucose, which may underestimate the morbidity of diabetes.

CONCLUSIONS

In summary, the morbidity risk of CVD in the older population of Xinjiang is high, and there are differences in CRFs based on sex, age, region, and ethnic group. Some studies have found that eliminating health-threatening behavior (smoking, drinking) through the evaluation and early screening of high-risk groups contributes to the prevention of at least 80\% of CVD cases.\textsuperscript{53} Similarly, the "Million Hearts" plan in the USA has achieved good results after implementation. The results of this study suggest that in the older population in Xinjiang, it is necessary to actively carry out measures for the prevention and treatment of CRFs, and to formulate specific strategies based on sex, age, region, and ethnic group to reduce the risk of CVD.
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Contributors

HW contributed to the study design, data collection, and provided critical manuscript revisions. WX analysed the data, interpreted the results, and wrote the article. AW, ZM, JL, and SX were involved in the data collection and analysis and also provided critical manuscript revisions. All authors read and approved the submitted manuscript.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

The studies involving human participants were reviewed and approved by Ethics Committee of People’s Hospital of Xinjiang Uygur Autonomous Region (reference number: NNSFC 2016011). The participants provided their written informed consent to participate in this study.

Data availability statement

The original contributions presented in the study are included in the article, further
inquiries can be directed to the corresponding author/s.
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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                                                                                                                        | 1-2                |
|                     |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found                                                                                                |                    |
| Introduction        |        |                                                                                                                                                                                                              |                    |
| Background/rationale| 2      | Explain the scientific background and rationale for the investigation being reported                                                                                                                        | 4-5                |
| 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                                                                           | 5-6                |
| 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                                                                      | 6-8                |
| Data sources/       | 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                                      |                    |
| measurement         |        |                                                                                                                                                                                                              |                    |
| Bias                | 9      | Describe any efforts to address potential sources of bias                                                                                                                                                     | 8                  |
| Study size | 10 | Explain how the study size was arrived at | 5 |
|-----------|----|------------------------------------------|---|
| 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, including those used to control for confounding | 8-9 |
| | | (b) Describe any methods used to examine subgroups and interactions | 9 |
| | | (c) Explain how missing data were addressed | 6 |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy | 5-6 |
| | | (e) Describe any sensitivity analyses | |
| Results | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | |
| | | (b) Give reasons for non-participation at each stage | |
| | | (c) Consider use of a flow diagram | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | |
| | | (b) Indicate number of participants with missing data for each variable of interest | |
| Outcome data | 15* | Report numbers of outcome events or summary measures | |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 9-14 |
| | | (b) Report category boundaries when continuous variables were categorized | 10-14 |
|   |   | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
|---|---|---|
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| Discussion |   |   |
| Key results | 18 | Summarise key results with reference to study objectives |
| 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 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results |
| 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 |

*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.
Heat maps of cardiovascular disease risk factor clustering among community-dwelling older people in Xinjiang: a cross-sectional study

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| Keywords:         | CARDIOLOGY, EPIDEMIOLOGY, GERIATRIC MEDICINE |
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Heat maps of cardiovascular disease risk factor clustering among community-dwelling older people in Xinjiang: a cross-sectional study

Wenwen Xiao, Aishanjiang Wumaer, Zhuoya Maimaitiwusiman, Jinling Liu, Saiyare Xuekelati, Hongmei Wang

Second Department of Cadre Health Care Center of People’s Hospital of Xinjiang Uygur Autonomous Region, Urumqi, China

Correspondence to: Dr Hongmei Wang; whmdoctor@163.com
ABSTRACT

Objective: The clustering of multiple cardiovascular disease risk factors (CRFs) increases the risk of cardiovascular disease (CVD) prevalence and mortality. Little is known about CRF clustering among community-dwelling older people in Xinjiang. The objective of this study was to explore the prevalence of CRF clustering in this population.

Design: Cross-sectional study.

Setting: Xinjiang, China.

Participants: Multi-level random sampling was used to survey individuals aged ≥60 in six regions of Xinjiang. In total, 87,000 participants volunteered, with a response rate of 96.67%; 702 participants with incomplete data were excluded and data from 86,298 participants were analyzed.

Outcome measures: The prevalence of smoking, hypertension, diabetes, dyslipidemia and overweight/obesity was 9.4%, 52.1%, 16.8%, 28.6%, and 62.7%, respectively. The prevalence of CRF clusters among people of different ages, regions, and ethnic groups differed significantly. The 85.7% of the participants presented at least one CRFs and 55.9% of the participants presented clustering of CRFs. The proportion of CRF clusters tended to be higher in men, 60–69 year old group, northern Xinjiang, and the Kazakh population. After adjusting for age and sex, logistic regression analysis revealed that men, 60–69 year old group, northern Xinjiang, and the Kazakh population were more likely to have clustering of CRFs, compared with their counterparts.

Conclusions: The prevalence of CRFs in the older Xinjiang population is high and their clustering differs by sex, age, region, and ethnicity. CRF prevention and management should be active in this population, and strategies to reduce CVD risk based on sex, age, ethnic group, and region are warranted.
Strengths and limitations of this study

- The study is the first epidemiological investigation of CRF clustering in the older population of Xinjiang.

- Strengths included the use of multi-level random sampling, representative samples, a large sample size, strict pre-survey staff training, and standard protocols and instruments to ensure the reliability of the data.

- Cross-sectional studies cannot quantify the importance, nor can they determine the causality and temporality, of the relationship between CRF clustering and the morbidity of CVD.

- The study did not conduct an oral glucose tolerance test, which may underestimate the morbidity of diabetes.
INTRODUCTION

Cardiovascular disease (CVD) remains the primary burden of global population health due to its high morbidity and mortality rate. Studies suggest that the prevalence of CVD is increasing in developing countries compared with developed countries, more than 80% of CVD deaths occur in low-income and middle-income countries (LMICs). The Report on Cardiovascular Health and Diseases Burden in China: an Updated Summary of 2020 showed that due to widespread cardiovascular disease risk factors (CRFs) exposure, the prevalence of CVD in China is continuously on the rise, with an estimated 330 million CVD patients in 2020. A rapid aging process will further increase the prevalence and mortality rate of CVD in China. The CVD mortality rate ranks first among urban and rural residents, and the total cost of hospitalization due to CVD increases annually, further highlighting the urgency of CVD prevention and control.

CVD are caused by quite a few factors. Some of them are invariable (gender, age, genetic heritage), others are variable (cigarette smoking, dyslipidemia, diabetes, elevated blood pressure, obesity, physical inactivity, excessive alcohol consumption, low intake of fruits and vegetables, psychosocial stress). Variable risk factors can be influenced by changing bad habits. Framingham Heart Study has reported that CRFs are closely related to the incidence and prevalence of CVD. For example, each increment of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure doubles the risk of CVD at 40 to 70 years of age. Diabetes is associated with a 2- to 3-fold increase in the likelihood of developing CVD. A 10% drop in serum cholesterol reduces the risk of coronary heart disease by 50% at age 40. In most people, CVD is the product of several risk factors. Clustering of multiple CRFs has been found to increase the risk of CVD occurrence and death. Individuals with more than one CRF have a greater risk of CVD than those with a single CRF. Additionally, studies have found that the prevalence of clustered CRFs in different countries, populations, regions and ethnic groups is not uniform. These variations may be related to differences in national income, urbanization, industrialization, environmental exposures, socio-economic status, diets, cultural habits, and lifestyle behaviors.
Therefore, understanding these differences may assist with CVD prevention and control through the targeting of CRFs unique to different regions and ethnic groups.

Xinjiang is located in northwestern China, Eurasia hinterland. Since ancient times, Xinjiang has been a multi-ethnic, multi-cultural, and multi-religious place. Xinjiang spans a large latitude and longitude and has large differences in altitude, temperature (in southern and northern Xinjiang), and residents' genetic background, cultural customs, and eating habits. Uyghur, Han, Kazakh, and Hui people accounted for 97.32% of the total population at this time. Population of Xinjiang aged ≥65 years in 2015 accounted for 7.21% of the total population, the growth rate of which is much faster than that of Xinjiang's total population, highlighting this aging population. At present, there have been no large-scale surveys or analyses of the prevalence and clustering of CRFs in the older population of Xinjiang.

It is also well known that findings from the younger population may not be applicable to the older. Therefore, our research aims to provide the latest prevalence of CRFs and their clusters in the older population of Xinjiang. By understanding the differences in CRFs and their clusters among different sexes, ages, regions, and ethnic groups, we can formulate specific intervention measures against CRFs to prevent, manage, and reduce the mortality of CVD and the economic burden of medical insurance.

MATERIALS AND METHODS

Study population

The study was approved by the Ethics Committee of People's Hospital of Xinjiang Uygur Autonomous Region (Xinjiang, China). Written informed consent was obtained from all participants before data collection and measurement.

This study was a cross-sectional epidemiological survey of the older population of Xinjiang. According to natural settings and climate patterns, Xinjiang is divided into three distinct subregions (north, south, and east). A multi-stage random sampling
method was used between January and December 2019 to administer surveys in this population. In the first stage, two prefectures were randomly selected from southern, northern, and eastern Xinjiang (Altai and Tacheng in northern Xinjiang, Kashgar and Hotan in southern Xinjiang, and Hami and Turpan in East Xinjiang). In the second stage, one city was randomly selected from each prefecture. In the third stage, two counties were randomly selected from each city. In the fourth stage, 7,500 people aged ≥60 were randomly selected from each county. From this pool, a total of 90,000 participants were randomly selected. All participants met the inclusion criteria of this survey: participants were aged ≥60 with independent consciousness, who were able to understand and cooperate with investigations and sign an informed consent form. Ultimately, 87,000 participants accepted the survey, with a response rate of 96.67%; 702 participants with incomplete data were excluded and data from 86,298 people were analyzed (figure 1).

Research methods

Questionnaire

A set of standardized questionnaires was completed under physician guidance. The questionnaire collected information such as age, sex, ethnic group, education, occupation, disease history, medication history, family history, drinking history, smoking history, eating habits, and other details.

Physical examination

A detailed physical examination was carried out on each subject by a physician and blood pressure, weight, and height, were measured by qualified professionals according to standard methods.

Blood pressure measurement: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the method recommended by the American Heart Federation. All participants were prohibited from smoking and drinking alcohol, tea, coffee, and other such caffeinated drinks 30 minutes before. Participants were seated and the blood pressure of their right upper arm was measured after a 10-minute rest. A specialist doctor used a desktop mercury sphygmomanometer to measure blood
pressure every two minutes for three consecutive measurements, with room temperature kept above 18°C.

Weight measurement: The participants were required to have an empty stomach, take off their shoes, and wear only light clothes. A calibrated medical scale was used for weighing. The participants were relaxed and stood upright in the middle of the scale’s chassis, with the reading being accurate to 0.1 kg.

Height measurement: A measuring ruler with a minimum scale of 1 mm was fixed vertically to the ground. The participants stood upright with both heels together and their body, hips, and shoulders close to the ruler. The examiner put a square ruler on the top of the participants' head, with one side of the right angle being near to the measuring ruler and the other side to the participants' scalp. The reading on the measuring ruler was accurate to 1 mm.

Calculation of BMI = weight (kg) / height (m)².

Collection of blood samples and laboratory testing

Disposable blood collection equipment was used to draw 10 ml of fasting peripheral venous blood from all participants in the morning (participants’ stomachs should have been empty for a minimum of 10 hours). Plasma (serum) was centrifugally separated from blood cells immediately and both components were stored at -80°C. Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum creatinine (sCr), serum urea nitrogen (SUN), and other biochemical indicators were examined within one month, using a Hitachi 7600 automatic biochemical analyzer at the clinical Laboratory Center of People's Hospital of Xinjiang Uyghur Autonomous Region (a Third-Grade Class A hospital).

Assessment criteria

Hypertension: SBP ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, or a previous diagnosis of hypertension with the use of antihypertensive medication.
Diabetes: Fasting plasma glucose (FPG) concentration \( \geq 7.0 \) mmol/L or a previous diagnosis of diabetes with use of hypoglycemic agents.

Overweight/obesity: According to criteria listed in the Guidelines for Prevention and Control of Overweight and Obesity in Chinese Adults, a BMI of 18.5–24 kg/m\(^2\) was considered as normal weight, 24.0–28.0 kg/m\(^2\) as overweight, and \( \geq 28.0 \) kg/m\(^2\) as obese.

Dyslipidemia: According to criteria from the Guidelines for Prevention and Control of Dyslipidemia in Chinese Adults (2016 Revised Edition), dyslipidemia was defined as the presence of at least one of the following: TC \( \geq 6.2 \) mmol/L, TG \( \geq 2.3 \) mmol/L, HDL-C <1.0 mmol/L, and LDL-C \( \geq 4.1 \) mmol/L.

Smoking: According to World Health Organization standards, participants were defined as smokers if they smoked continuously or smoked for a cumulative period of at least 6 months.

The clustering of CRFs: Smoking, hypertension, diabetes, dyslipidemia, and overweight/obesity were the CRFs included in this study. Clustering referred to the same individual exposed to at least two of the above CRFs.

**Quality control**

Standard methods and unified, standardized instruments (checked and corrected by professionals) were used to collect the relevant data. In order to control observer error to the greatest extent, investigators were rigorously trained and assessed to administer the questionnaire (the questionnaire administrator was a specialist doctor), and to perform physical examination, blood sample collection, transportation, separation, preservation, marking, recording, questionnaire review, data entry, etc. Only trained and qualified individuals could administer the survey. Double blind data entry was used in which two professionals entered data in parallel and performed statistical analysis after verification.

**Statistical analysis**

Data analyses were performed using SPSS for Windows (version 19.0; SPSS Inc.,
Chicago, IL, USA). Values were expressed as the mean ± standard deviation (SD). Count data was shown as the number of total cases (n) or percentages (%). Comparisons of clinical phenotypic measurement data between two groups were performed using a Student’s t-test, and categorical data were analyzed using a chi-squared test. Logistic regression analysis was used to analyze the influence of differences in sex, age, region, and ethnicity on the clustering of CRFs after adjusting for age and sex. P < 0.05 indicated that the difference was statistically significant.

Patient and public involvement

Participants and the public were not involved in the design, implementation or analysis of this study.

RESULTS

Demographic and physiological characteristics of participants

As shown in table 1, a total of 86,298 participants aged ≥60 years were involved in this study, including 41,087 (47.6%) males and 45,211 (52.4%) females. Moreover, 33.5%, 6.1%, 57.3%, and 3.1% of participants were of Han, Kazakh, Uyghur, and Hui ethnicities, respectively. The DBP value of men was higher than that of women (P < 0.05); smoking rate in men was also significantly higher than in women (P < 0.001). The BMI, SBP, TC, TG, LDL-C, HDL-C, and FPG values of women were all higher than those of men (P < 0.001). The prevalence of smoking, hypertension, diabetes, dyslipidemia, and overweight/obesity among the older population of Xinjiang was 9.4%, 52.1%, 16.8%, 28.6%, and 62.7%. Men were more likely than women to have a bad health-related behavior of smoking. The prevalence of hypertension, diabetes, dyslipidemia, and overweight/obesity were higher in women than in men (P < 0.001).

| Table 1 | Demographic and physiological characteristics of participants in Xinjiang, China |
|---------|----------------------------------------------------------------------------------|

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
| Characteristic          | Total (n=86298) | Men (n=41087) | Women (n=45211) | t/χ² value | P value |
|-------------------------|----------------|--------------|----------------|------------|---------|
| Age*, years             | 73.5±6.0       | 73.6±6.1     | 73.3±5.9       | 6.46       | <0.001  |
| Ethnic group, n (%)     |                |              |                | 262.14     | <0.001  |
| Han                     | 28129(33.5)    | 12447(31.1)  | 15682(35.7)    |            |         |
| Kazakh                  | 5132(6.1)      | 2263(5.7)    | 2869(6.5)      |            |         |
| Uyghur                  | 48088(57.3)    | 24035(60.1)  | 24053(54.8)    |            |         |
| Hui                     | 2547(3.1)      | 1239(3.1)    | 1308(3.0)      |            |         |
| BMI*, kg/m²             | 25.7±4.4       | 25.3±4.0     | 26.1±4.7       | -28.64     | <0.001  |
| SBP*, mmHg              | 135.4±20.4     | 134.2±20.1   | 136.5±20.6     | -16.44     | <0.001  |
| DBP*, mmHg              | 77.1±12.3      | 77.2±12.3    | 76.9±12.3      | 2.85       | 0.004   |
| TC*, mmol/L             | 4.8±1.2        | 4.6±1.1      | 4.9±1.2        | -47.01     | <0.001  |
| TG*, mmol/L             | 1.5±1.0        | 1.4±0.9      | 1.6±1.0        | -29.68     | <0.001  |
| LDL-C*, mmol/L          | 2.6±0.9        | 2.5±0.9      | 2.7±0.9        | -22.21     | <0.001  |
| HDL-C*, mmol/L          | 1.4±0.4        | 1.3±0.4      | 1.4±0.4        | -39.07     | <0.001  |
| FBG*, mmol/L            | 6.0±2.1        | 5.9±2.1      | 6.0±2.2        | -10.57     | <0.001  |
| Smoking, n (%)          | 7832(9.4)      | 7646(18.9)   | 186(0.4)       | 8371.27    | <0.001  |
| Hypertension, n (%)     | 44595(52.1)    | 20084(49.2)  | 24511(54.6)    | 248.96     | <0.001  |
| Diabetes, n (%)         | 14175(16.8)    | 6227(15.5)   | 7948(18)       | 90.61      | <0.001  |
| Dyslipidemia, n (%)     | 24130(28.6)    | 10787(26.8)  | 13343(30.2)    | 117.85     | <0.001  |
| Overweight/Obesity, n (%)| 53294(62.7)    | 24308(60.2)  | 28986(65.1)    | 214.98     | <0.001  |

*Mean±SD.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, serum total cholesterol; TG, triglyceride; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.

The prevalence of CRFs among different ages, regions, and ethnic groups in the older population of Xinjiang, China

Participants were divided into five groups by age (60–69 years old, 70–79 years old,
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80–89 years old, 90–99 years old, ≥100 years old). Differences in the prevalence of smoking, hypertension, diabetes, dyslipidemia, and overweight/obesity across age groups were statistically significant (P <0.05). Prevalence rates of smoking, dyslipidemia and overweight/obesity were highest in the 60–69 year old group; diabetes prevalence was highest in the 70–79 year old group; and hypertension was highest in the 80–89 year old group, thereafter showing a downward trend with age (table 2).

| Category                  | Smoking   | Hypertension | Diabetes | Dyslipidemia | Overweight/Obesity |
|---------------------------|-----------|--------------|----------|--------------|-------------------|
| Age group, n (%)          |           |              |          |              |                   |
| 60-69                     | 2977(11.7)| 12770(48.7)  | 4144(16.0)| 7491(28.8)  | 17515(67.3)       |
| 70-79                     | 3809(8.7) | 24105(53.5)  | 7748(17.4)| 12784(28.7) | 28021(62.6)       |
| 80-89                     | 996(7.8)  | 7139(54.6)   | 2153(16.9)| 3546(27.9)  | 7210(55.7)        |
| 90-99                     | 50(4.3)   | 560(46.7)    | 126(10.8) | 292(25.2)   | 522(43.9)         |
| ≥100                      | 0(0.0)    | 21(33.3)     | 4(6.3)   | 17(27.0)    | 29(46.0)          |
| χ² value                  | 265.31    | <0.001       | <0.001   | <0.001      | <0.001            |
| P value                   | <0.001    | <0.001       | <0.001   | <0.001      | <0.001            |
| Geographic region, n (%)  |           |              |          |              |                   |
| Northern Xinjiang         | 2833(11.3)| 15419(61.4)  | 5009(20.2)| 7003(28.1)  | 17317(69.2)       |
| Eastern Xinjiang          | 1978(9.6) | 12503(54.7)  | 3558(16.2)| 6010(27.3)  | 13456(60.2)       |
| Southern Xinjiang         | 3021(8.0)| 16673(44.3)  | 5608(15.0)| 11117(29.6)| 22524(59.9)       |
| χ² value                  | 195.52    | 1847.79      | 281.77   | 40.63       | 634.09            |
| P value                   | <0.001    | <0.001       | <0.001   | <0.001      | <0.001            |
| Ethnic group, n (%)       |           |              |          |              |                   |
| Han                       | 3172(11.5)| 15438(55.2)  | 5974(21.9)| 8266(30.2)  | 17840(64.8)       |
| Kazakh                    | 428(8.4)  | 3400(66.3)   | 490(9.7) | 1413(27.9)  | 3827(75.0)        |
| Uyghur                    | 3742(8.1) | 22877(48.0)  | 6754(14.3)| 13005(27.5)| 28206(59.5)       |
| Hui                       | 177(7.6)  | 1494(59.0)   | 569(22.9)| 680(28.3)   | 1775(70.3)        |
| χ² value                  | 244.43    | 879.85       | 961.01   | 58.93       | 645.23            |
| P value                   | <0.001    | <0.001       | <0.001   | <0.001      | <0.001            |

There were statistically significant differences in the prevalence of all five CRFs between northern, eastern, and southern Xinjiang (P <0.05). The prevalence of smoking, hypertension, diabetes and overweight/obesity was highest in northern Xinjiang, followed by eastern and southern Xinjiang. The prevalence of dyslipidemia was highest
in southern Xinjiang, followed by northern and eastern Xinjiang (table 2).

Statistically significant differences in the prevalence of the five CRFs were also found between ethnic groups (P <0.05). Kazakh individuals had the highest prevalence of hypertension and overweight/obesity, followed by Hui and Han; Uyghurs had the lowest. However, nearly half or more than half of all participants suffered from hypertension and overweight/obesity. The prevalence of smoking and dyslipidemia in Han individuals were higher than in other ethnic groups. The prevalence of diabetes was the highest in Hui individuals (table 2).

Heat maps of CRF clustering among the older population of Xinjiang, China

In Xinjiang, only 14.3% of the older population did not have any CRFs. People with 1, 2 or ≥3 CRFs accounted for 29.8%, 33.3% and 22.6% of those sampled, while those with ≥1, ≥2, ≥3 or ≥4 CRFs accounted for 85.7%, 55.9% and 22.6%, respectively (table 3).

| Category                        | None (0) | Clustering(≥1) | Clustering(≥2) | Clustering(≥3) | χ² value | P value |
|---------------------------------|----------|----------------|----------------|----------------|----------|---------|
| Gender                          |          |                |                |                | 48.55    | <0.001  |
| Men                             | 5788(14.8)| 33229(85.2)    | 21776(55.8)    | 9201(23.6)     |          |         |
| Women                           | 5718(13.8)| 35824(86.2)    | 23235(55.9)    | 8992(21.6)     |          |         |
| Age group, n (%)                |          |                |                |                | 202.30   | <0.001  |
| 60-69                           | 3336(13.4)| 21489(86.6)    | 14096(56.8)    | 5717(23.0)     |          |         |
| 70-79                           | 6039(14.2)| 36474(85.8)    | 24011(56.5)    | 9799(23.0)     |          |         |
| 80-89                           | 1879(15.6)| 10186(84.4)    | 6439(53.4)     | 2550(21.1)     |          |         |
| 90-99                           | 240(21.8)  | 859(78.2)      | 447(40.7)      | 124(11.3)      |          |         |
| ≥100                            | 12(21.1)   | 45(78.9)       | 18(31.6)       | 3(5.3)         |          |         |
| Geographic region, n (%)        |          |                |                |                | 1215.68  | <0.001  |
| Northern Xinjiang               | 2452(9.9) | 22295(90.1)    | 15952(64.5)    | 7058(28.5)     |          |         |
| Eastern Xinjiang                | 2773(14.8)| 15974(85.2)    | 10168(54.2)    | 4094(21.8)     |          |         |
| Southern Xinjiang               | 6281(16.9)| 30784(83.1)    | 18891(51.0)    | 7041(19.0)     |          |         |
| Ethnic group, n (%)             |          |                |                |                | 1266.81  | <0.001  |
| Han                             | 3057(11.6)| 23398(88.4)    | 16230(61.3)    | 7309(27.6)     |          |         |
| Kazakh                          | 392(7.9)  | 4587(92.1)     | 3302(66.3)     | 1232(24.7)     |          |         |
| Uyghur                          | 7580(17.0)| 37030(83.0)    | 22611(50.7)    | 8379(18.8)     |          |         |
Differences in the prevalence of CRFs clustering differed by sex, age, region, and ethnic group (P <0.05). Men had more CRF clusters than women. Furthermore, CRF clustering decreased gradually with age (Figure 5). People in northern Xinjiang with \( \geq 1, \geq 2 \) or \( \geq 3 \) clustered CRFs had the highest morbidity. Moreover, 90.1% of people were exposed to at least one CRF. After eastern Xinjiang, people in southern Xinjiang had the lowest morbidity. By ethnic group: Kazakhs with \( \geq 1 \) or \( \geq 2 \) clustered CRFs had the highest morbidity; Hui with \( \geq 3 \) clustered CRFs had the highest morbidity; and Uyghurs with \( \geq 1, \geq 2 \) or \( \geq 3 \) clustered CRFs had the lowest morbidity (table 3).

**Logistic regression analysis of \( \geq 1, \geq 2 \) and \( \geq 3 \) clustered CRFs among different sexes, ages, regions, and ethnic groups in the older population of Xinjiang**

After adjusting for age and sex, the logistic regression analysis revealed that the risk of illness (OR (95%CI) in women with \( \geq 1, \geq 2 \) and \( \geq 3 \) clustered CRFs was 1.087 (1.045 to 1.131), 1.002 (0.974 to 1.030) and 0.893 (0.864 to 0.923) times that of a man, respectively. Compared with people aged 60 to 69 years old, the odds ratios of CRFs clustering decreased gradually with age. Northern Xinjiang, and the Kazakh population were more likely to have clustering of CRFs (Table 4).

**Table 4** Adjusted odds ratios (95% confidence intervals) of having \( \geq 1, \geq 2, \geq 3 \) Vs. none CRFs associated with different groups

| Category | \( \geq 1 \) risk factors | \( \geq 2 \) risk factors | \( \geq 3 \) risk factors |
|----------|---------------------------|---------------------------|---------------------------|
| Gender*  |                           |                           |                           |
| Men      | Reference                 | Reference                 | Reference                 |
| Women    | 1.087 (1.045 to 1.131)     | 1.002 (0.974 to 1.030)     | 0.893 (0.864 to 0.923)     |
| Age group** | Reference | Reference | Reference |
| 60-69    |                           |                           |                           |
| 70-79    | 0.937 (0.896 to 0.981)     | 0.988 (0.957 to 1.019)     | 1.002 (0.965 to 1.040)     |
| 80-89    | 0.844 (0.794 to 0.898)     | 0.871 (0.834 to 0.910)     | 0.892 (0.846 to 0.940)     |
| 90-99    | 0.558 (0.482 to 0.647)     | 0.522 (0.461 to 0.590)     | 0.422 (0.349 to 0.510)     |
A logistic regression model was used to estimate ORs with 95% CIs.

*The odds ratios for gender groups were adjusted for age.

**The odds ratios for age groups were adjusted for gender.

***The odds ratios for region groups were adjusted for age and gender.

****The odds ratios for ethnic groups were adjusted for age and gender.

## DISCUSSION

In this study, we investigated the epidemic characteristics of CRFs clustering among a large representative sample in the older Xinjiang population. The results show that the prevalence of CRFs was very high, and over 85% of participants had one CRF at least. Half of the older adults had two or more CRFs. After adjusting the confounding factors, the clustering of CRFs differs by sex, age, region, and ethnicity.

This study found a high morbidity of clustered CRFs in Xinjiang; only 14.3% of the older population was not affected by any CRFs. The most common CRFs in our study were overweight/obesity (62.7%) and hypertension (52.1%). The prevalence of overweight/obesity, hypertension and diabetes (16.8%) were higher than the national level (28.2%, 26.1%, 5.2%, data collected in 2005 by InterAsia), while the morbidities of smoking (9.4%) and dyslipidemia (28.6%) were lower (34.4%, 53.6%); these findings are consistent with that of previous research. Additionally, the morbidity of the participants with ≥2 and ≥3 clustered CRFs (55.9%, 22.6%) was higher than the
national level (45.9%, 17.2%), and that of northeastern China (32.7%, 10.0%), suburban areas of Beijing (47.2%, 17.5%), Qamdo (47.1%, 20.9%), Nanjing (35.2%, none), Malaysia (33.0%, 14.0%), and southwest Nigeria (47.0%, 23.9%). In contrast, the morbidity of the participants with ≥2 and ≥3 clustered CRFs was lower than that reported in the USA (73.0%, 35.9%), India (78.6%, none), Nepal (86.0%, 63.4%), rural areas of Yunnan (66.2%, 34.8%). Potential reasons for these differences may include differences in social economy, environmental exposures, cultural customs and diets. Moreover, the differences across different studies could be attributed to differences in participants’ age range, the sample size, definitions, and diagnostic criteria used in those studies. Our study shows that the older population in Xinjiang is more likely to have clustered CRFs; thus, active public health measures should be taken to prevent and control these factors.

In this study, the prevalence of smoking was significantly higher in males (18.9%) than in females (0.4%). Conversely, the prevalence of the other four CRFs in males were lower than in females. This study also found that women had a higher risk than men of having at least one clustered CRF, while men had a higher risk than women of having ≥3 clustered CRFs. This is in line with the study results of Zhao et al. and Wang, who found that CRF clustering occurs easily in men. A study showed that the morbidity of CVD in women was further increased in participants aged 51 years (the average menopausal age of Asian women) or older. Like in whites, the onset of menopause may further increase the risk of CVD. Compared with pre-menopausal women, post-menopausal women have higher levels of CRF indicators (hypertension, diabetes, dyslipidemia) related to metabolism. Considering the decline of hormone levels in post-menopausal women, the protective effect is reduced for metabolic CRFs. Meanwhile, lifestyle and eating habits are hard to change in a short time. Furthermore, we conjectured that smoking may be somehow increased the tendency of CRFs clustering in men, as smoking was more common among men than women.

The study also found that the highest CRF exposure was in those aged 60–69 years old, and that both CRF clustering and age- and sex-adjusted CRF clustering gradually
decreased with age. Numerous studies have shown that correlations between several traditional CRFs and cardiovascular events are reduced in the older adult. For individuals whose lifestyle risk factors remain the same throughout life, their lifetime risk of CVD is lower at 70 years old than at 50 years old. Similarly, a strong relationship has been found between hypertension and the hazard of death in the older at younger ages, while a weak relationship has been found at very older ages. The risk of hypertension does not continue to increase with age. This may be because people with a high risk of CVD are more likely to have early lifetime events, and multiple clustered CRFs and competition between diseases lead to a greater risk of death. Another possible reason may be that more older survivors with one CRF are less likely to have been adversely affected by other CRFs. People with longer lifespans may either have a genetic composition resistant to CVD or have a lower burden of CRFs, which in turn reduce their risk of CVD. Moreover, the physiological changes that occur during aging may change the effects of some CRFs. One study found that a minimum cholesterol level is necessary to maintain neuronal function; a very older individual with a heavy weight in the overweight range may reflect lower weakness and less loss of physiological reserve; the optimal BMI for an older individual is considered higher than that of one who is middle-aged. In this study, it was found that the morbidity of cardiovascular CRFs was relatively low among individuals aged 100 years old and above, which is consistent with the results of Zyczkowska et al. In this study, participants ≥100 years did not smoke, and had a healthier lifestyle with a low morbidity (33.3%, 6.3%, 27.0%, 46%) of hypertension, diabetes, dyslipidemia, and overweight/obesity. This explains to some extent why fewer than 3 CRFs were clustered in this age group.

Consistent with our results, one systematic review of 16 studies published in 2007 and another of 101 Canadian studies published in 2015 certified that there are striking differences in the morbidity of clustered CRFs across ethnic groups. After adjustment for age and sex, the odds ratios for the prevalence of ≥1, and ≥2 clustered CRFs were higher in the Kazakh population than in the Han; odds ratios in the Uyghur
population was lower than in the Han. The differences may be due to the striking
differences between ethnic groups about the prevalence of smoking, hypertension,
diabetes, dyslipidemia, and overweight/obesity. The morbidity of overweight/obesity
and hypertension in Kazakhs (75.0%, 66.3%) was higher than other ethnic groups. The
morbidity of smoking, and dyslipidemia in the Han population (11.5%, 30.2%) was
also higher than other ethnic groups. The prevalence of diabetes in the Hui population
(22.9%) was higher than in other ethnic groups. The mechanisms underlying these
phenomenons may be associated with environment of inhabited area, residents' genetic
background, cultural customs, and eating habits. The striking differences between
ethnic groups about the prevalence of CRFs suggests that it is necessary to develop the
ethnic-specific CVD prevention programs and health services.

This study also showed that among the clustered CRFs, the morbidity of smoking,
hypertension, diabetes, and overweight/obesity was higher in northern Xinjiang than in
eastern and southern Xinjiang. Hypertension, diabetes, obesity, and dyslipidemia are
multi-factor diseases affected by genetics and the environment. In northern Xinjiang,
the temperature is relatively low with an average annual temperature of -4–9 °C. It is
dominated by animal husbandry and 96.4% of the Kazakh in China live here. The
Kazakh population mainly follow a nomadic lifestyle. Men often drink hard liquor and
eat a simple diet of meat and salt to resist the cold, with fewer fruits and vegetables.
In contrast, southern Xinjiang is a typical comprehensive zone integrating three systems:
oasis, mountain, and desert. Belonging to an arid and warm temperate climate, it has
low rainfall. Light and heat are abundant. Most Uygurs live here. Residents mainly rely
on farming for their livelihood and they eat sufficient fruits and vegetables. Eastern
Xinjiang is a typical continental desert climate. It is arid and hot, with a large
temperature difference between day and night. The annual precipitation is low and
evaporation is large. Salinization and desertification are serious. The natural
environments, production, and lifestyles mentioned above may cause differences in the
morbidity and clustering of CRFs. This study suggests that the morbidity and clustering
of CRFs in northern, eastern, and southern Xinjiang are different, with the highest
clustering of CRFs in northern Xinjiang, and a relatively low risk of CRFs clustering in southern Xinjiang and eastern Xinjiang. Therefore, it is necessary to take region-oriented CRFs prevention and control measures.

The advantages of this study were distinct. First, the results were based on a community-dwelling population with a large sample size, which made our conclusions more convincible. Second, to the best of our current knowledge, this was the first epidemiological investigation of CRF clustering specifically for older people in Xinjiang. Third, the high-quality study design, high response rate, multi-level random sampling, representative samples, strict pre-survey staff training, and standard protocols and instruments were used to ensure the reliability of the data. Despite these strengths, our study also had several limitations. The cross-sectional studies cannot quantify the importance, nor can they determine the causality and temporality, of the relationship between CRF clustering and the prevalence of CVD. Therefore, further prospective studies should be conducted. Additionally, the study did not perform an oral glucose tolerance test or check 2-hour postprandial blood glucose, which may underestimate the morbidity of diabetes.

CONCLUSIONS

In summary, the morbidity risk of CVD in the older population of Xinjiang is high, and there are differences in CRFs based on sex, age, region, and ethnic group. Some studies have found that eliminating health-threatening behavior (such as smoking, sedentary lifestyle, unreasonable diet) through the evaluation and early screening of high-risk groups contributes to the prevention of at least 80% of CVD cases. Similarly, the "Million Hearts" plan in the USA has achieved good results after implementation. The results of this study suggest that in the older population in Xinjiang, it is necessary to actively carry out measures for the prevention and treatment of CRFs, and to formulate specific strategies based on sex, age, region, and ethnic group to reduce the risk of CVD. These strategies include promoting smoking cessation among men and Han population, encouraging women to exercise and lose weight, increasing fruit and vegetable consumption for population of Northern Xinjiang, and designing hypertension-,
diabetes- and dyslipidemia-prevention programs for Kazakh and Hui populations. These measures might help to reduce the prevalence of CRFs and the burden of CVD.
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Contributors

HW contributed to the study design, data collection, and provided critical manuscript revisions. WX analysed the data, interpreted the results, and wrote the article. AW, ZM, JL, and SX were involved in the data collection and analysis and also provided critical manuscript revisions. All authors read and approved the submitted manuscript.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

The studies involving human participants were reviewed and approved by Ethics Committee of People’s Hospital of Xinjiang Uygur Autonomous Region (reference number: NNSFC 2016011). The participants provided their written informed consent to participate in this study.

Data availability statement

The original contributions presented in the study are included in the article, further
inquiries can be directed to the corresponding author/s.
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FIGURE 1 Selection procedure of the study participants
From January to December 2019, surveys conducted among community-dwelling older people in Xinjiang, n=90,000

Inability to cooperate with the investigators, n=3,000

87,000 participants left eligible

Missing age data, n=12
Missing body mass index, n=429
Missing blood pressure, n=45
Missing ethnicity, n=216

Data analyzed for 86,298 participants

FIGURE 1 Selection procedure of the study participants

90x90mm (300 x 300 DPI)
### 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<br>(b) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-2                |
| **Introduction**               | 2      | Explain the scientific background and rationale for the investigation being reported | 4-5                |
| **Objectives**                 | 3      | State specific objectives, including any prespecified hypotheses                  | 5                  |
| **Methods**                    | 4      | Present key elements of study design early in the paper                           | 5                  |
| **Study design**               | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6                |
| **Setting**                    | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants | 5-6                |
| **Participants**               | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-8                |
| **Variables**                  | 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 | Not applicable     |
| **Data sources/measurement**   | 9      | Describe any efforts to address potential sources of bias                         | 8                  |
| **Bias**                       | 10     | Explain how the study size was arrived at                                         | 5                  |
| **Study size**                 | 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, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) If applicable, describe analytical methods taking account of sampling strategy<br>(e) Describe any sensitivity analyses | 8-9                |
| **Results**                    |        |                                                                                  |                    |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
|-------------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|             |     | (b) Give reasons for non-participation at each stage                                                                                                                                                          |
|             |     | (c) Consider use of a flow diagram                                                                                                                                                                          |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders                                                                         |
|             |     | (b) Indicate number of participants with missing data for each variable of interest                                                                                                                         |
| Outcome data | 15* | Report numbers of outcome events or summary measures                                                                                                                                                          |
| Main results | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
|             |     | (b) Report category boundaries when continuous variables were categorized                                                                                                                                   |
|             |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period                                                                                             |
| Other analyses | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                                                                                                                  |
| Discussion  |     |                                                                                                                                                                                                             |
| Key results  | 18  | Summarise key results with reference to study objectives                                                                                                                                                       |
| 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                                                                 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                                      |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results                                                                                                                                         |
| 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                                                                 |

*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.