ENVIRONMENTAL RESEARCH
HEALTH

PAPER

Early-life famine exposure may modify the association between long-term temperature variability and cardio-cerebrovascular diseases: a nationwide study

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Keywords: famine, temperature variability, cardio-cerebrovascular disease

Supplementary material for this article is available online

OPEN ACCESS

RECEIVED
22 December 2023

REVISED
21 June 2024

ACCEPTED FOR PUBLICATION
8 July 2024

PUBLISHED
27 January 2025

Abstract

We aimed to evaluate whether the association between long-term temperature variability (TV) and cardio-cerebrovascular diseases (CCVDs) was affected by famine exposure in different age stages. We used data from the fourth national urban and rural elderly population survey (2015). Participants were categorized into six groups based on their age at famine exposure (famine exposure under age 5, between ages 5 and 18, and during adulthood) and the severity (severely affected areas versus mildly affected areas) of the Great Chinese Famine (1959–1961) in their province of residence. Mixed-effects logistic regression model was used to quantify the association between long-term TV and the prevalence of CCVDs across six famine-exposed groups. A total of 222 179 participants were included. In severely affected areas, the odds ratio (OR) of CCVDs associated with per 1 °C increase in 5 year average TV were 1.07 (95% confidence interval [CI]: 1.02, 1.13) for those exposed to famine during adulthood, 1.28 (95% CI: 1.17, 1.40) under the age of 5 years. Urban residence, higher education, increased household income, and more frequent physical activity could mitigate the association between TV and CCVDs, particularly among those exposed to severe famine before the age of 5. Individuals exposed to famine before the age of 5 are more susceptible to TV-related CCVDs compared to those exposed during adulthood. Our findings highlight the importance of early-life nutrition in lowering susceptibility to CCVDs later in life.

1. Introduction

In the context of climate change, unstable weather is likely to increase in frequency and severity. (Watts *et al* 2019) Several studies have explored the association between long-term temperature variability (TV)—defined as the standard deviation of daily minimum and maximum temperature over months or

years—and the risk of cardio-cerebrovascular diseases (CCVDs), revealing considerable disease burden in China. (Zanobetti *et al* 2012, Shi *et al* 2015, Zhu *et al* 2020, Kang *et al* 2021)

Undernutrition is a major global health challenge, particularly in low- and middle- income countries. (Xu *et al* 2019) It is estimated that undernutrition causes 3.1 million deaths annually among children under five and affects over 150 million children with stunting. (Bhutta *et al* 2013, Popkin *et al* 2020) early-life undernutrition could have adverse impacts on health status in later life. (Li and Lumey 2017) The Great Chinese Famine in 1959–61 serves as a natural experiment to study the long-term impacts of famine exposure in early life. (Lumey *et al* 2011) Previous studies have linked the Great Chinese Famine exposure to an increased risk of CCVDs. (Du *et al* 2020, Meng *et al* 2020) In addition, early-life famine exposure has been associated with increased levels of DNA methylation, which may lead to a rising vulnerability to environmental factors in adulthood. (Wang *et al* 2020)

While both TV exposure and early-life famine exposure are established determinants of CCVDs, it remains unclear whether early-life exposure to famine increases adulthood vulnerability to TV, finally leading to increased morbidity or mortality. This warrants further investigation, especially for developing countries, which are more vulnerable to food scarcity and climate change impacts. Understanding the interplay between TV-related CCVD risk and early-life famine exposure is vital for developing targeted interventions and mitigation strategies. (Islam and Winkel 2017, Balasubramanian 2018)

This study utilizes a nationally representative sample of approximately 0.2 million Chinese older adults to investigate whether the risk of TV-related CCVDs varies based on the severity of famine exposure and whether those who experienced severe famine during childhood are at higher risk. Additionally, the study explores potential sources of differential susceptibility to CCVD risks attributed to TV for each type of famine exposure.

2. Methods

2.1. Study setting

Our study used data from the fourth urban and rural elderly population (UREP) study in 2015 led by the China National Committee on Aging (CNCA). (Su *et al* 2023, Wen *et al* 2023a) This nationally representative survey targeted elderly individuals aged 60 and above. A three-stage stratified cluster sampling method with probability proportional to size sampling was used to randomly recruit subjects. First, cities or counties (primary sampling units) were randomly selected. Within these primary units, streets or towns (secondary sampling units) and then communities or villages (tertiary sampling units) were chosen. Finally, a total of 1860 communities located in 30 provinces available of meteorological data were included. Locations of the 1860 communities are shown in figure 1, representing their geographical distribution across China. The CNCA approved the study and granted permission for secondary analysis of the data. The survey received approval from the Ethics Committee of the Chinese National Bureau of Statistics. Oral informed consent was obtained from all participants before the interview. Individual consent was exempted due to the use of anonymized data.

2.2. Data sources

2.2.1. Famine group definition

The Great Chinese Famine, the most serious famine event, was recorded in China between 1959 and 1961. All our participants were born before 1955 and thus were all exposed to the famine. Participants were categorized into three different famine-exposed groups based on age at exposure: under-5-exposed group (famine exposure under age 5), 5–18-exposed group (famine exposure between ages 5 and 18), and adult-exposed group (famine exposure during adulthood). (Wang *et al* 2016) Further, participants were grouped based on the severity of the Great Chinese Famine in their province of residence. Famine severity, reflecting factors like population density, food security coping strategies, and natural disaster severity, varied across regions. (Luo *et al* 2010) Consistent with previous studies, severity was determined by excess mortality burden, with provinces having an excess death rate above 50% classified as severely affected areas, and those below 50% as mildly affected (figure S1). (Luo *et al* 2010, Wang *et al* 2016). Excess death rate was calculated as the percentage change in mortality rate from the highest value during 1959–61 compared to the mean level during 1956–58. (Wang *et al* 2016) This classification resulted in six famine-exposed groups: mild: under-5-exposed, mild: 5–18-exposed, mild: adult-exposed, severe: under-5-exposed, severe: 5–18-exposed, and severe: adult-exposed. These groups allowed us to investigate the hypothesis that exposure to severe famine during childhood and adolescence could increase the association between TV and CCVDs.

2.2.2. Environmental exposure

We obtained data on daily minimum temperature, maximum temperature, and relative humidity from the ECMWF Reanalysis 5th Generation (ERA5) land dataset at 0.25° × 0.25° spatial resolution (https://cds.climate.copernicus.eu/cdsapp#!/home). The data were linked to the centroid of each community based on latitude and longitude. We obtained the fine particulate matter ($PM_{2.5}$) data from the Tracking Air Pollution database (TAP, http://tapdata.org.cn/) at a 10 km spatial resolution (Zanobetti *et al* 2012, Geng *et al* 2021, Xiao *et al* 2021a, 2021b). The daily $PM_{2.5}$ concentrations were linked to the centroid of each community based on latitude and longitude and we then calculated the yearly average concentration for each community.

2.2.3. Exposure definition

Long-term TV was calculated from the standard deviation (SD) of daily minimum (T_{min}) and maximum temperature (T_{min}) over varying periods (2010–14, 2011–14, 2012–14, 2013–14, and 2014) before the calendar year of the survey (2015). For example, TV for 2010–14 (TV 2010–14) was calculated as SD of daily T_{min} and T_{max} across all days from 2010 to 2014 (a total of 1826 d). Similarly, TV for 2014 (TV 2014) was calculated using the SD of daily T_{min} and T_{max} for all days in 2014 (365 d). Additionally, we calculated warm season (four consecutive warmest months) and cold season (four consecutive coldest months) TV as the SD of daily T_{min} and T_{max} for all days during these respective seasons.

2.2.4. Outcome and covariates

Participant data were collected through face-to-face interviews conducted by uniformly trained staff. Self-reported data on CCVDs (ICD 10: I00–I99) were obtained by asking 'Have you ever been diagnosed with cardiovascular and cerebrovascular diseases'. Additionally, demographic and socioeconomic characteristics were gathered, including gender (male and female), urbanity (urban and rural), education level, marital status (single and married), frequency of physical activity, and annual household income. Education levels were categorized as illiteracy/primary school and high school or higher. Physical activity was classified into three groups: never, exercising 1–5 times per week, and exercising over 6 times per week. Annual household income was divided into three categories based on terciles and the 2015 exchange rate between the US Dollar and Chinese Yuan: T1 (<$2388.54 per year), T2 ($2388.54–$6369.43 per year), and T3 (>$6369.43 per year).

2.3. Statistical analysis

We assessed the association between long-term TV and the prevalence of CCVDs using mixed-effects logistic regression models. The analyses were performed respectively in six famine-exposed groups. In each model, we controlled several covariates, including age, gender, urbanity, education attainment, marital status, frequency of physical activity, annual household income, and province (random effects term). In the regression model, a linear function was applied to TV to assess the association between TV and the prevalence CCVDs as our preliminary analysis and prior studies indicated an approximately linear effect of TV (figure S2). (Zhao *et al* 2018, Wu *et al* 2022) Different TV exposures were put into the model separately. Nonlinear associations with annual mean temperature and mean relative humidity were controlled using a natural cubic spline with three degrees of freedom (df), as several studies identified them as potential confounders. (Zhao *et al* 2018, Wu *et al* 2022) Besides, we controlled the $PM_{2.5}$ in the model. The association between TV and the prevalence of CCVDs was presented as the odds ratio (OR) with a 95% confidence interval (CI) associated with per 1 °C increase in TV.

We conducted stratified analyses using TV 2010–14 exposure, stratifying data by sex, urbanity, education level, physical activity, household income, and marital status. In each subgroup, we examined the associations between TV and CCVDs across six famine-exposed groups. Random-effect meta-regression fitted by maximum likelihood was used to assess the statistical significance of differences between ORs estimated for each famine group. (Xu *et al* 2019)

2.4. Sensitivity analysis

Sensitivity analyses were performed to examine the robustness of our results. First, we used the pre-famine based cohort size shrinkage index (p-CSSI) as an alternative measure of famine severity, as CSSI is derived from population census data, which can sometimes be more reliable than mortality statistics. (Liu *et al* 2021) For provinces or municipalities where CCSI could not be calculated due to different population policies and active immigration, the excess death rate was used to determine the severity. Also, we varied the df (from 3 to 6) for the nonlinear function of annual mean temperature and relative humidity or replaced the nonlinear function with the linear function. The statistical significance of differences between ORs estimated from

sensitivity analyses and our primary models were assessed using the fixed effect meta-regression model with no statistical adjustment. (Xu *et al* 2019)

R software (version 3.6.2) was used to perform all analyses. A two-sided P-value < 0.05 was declared as statistically significant.

3. Results

The distribution of survey sites and TV is shown in figure 1. Regional variation of TV was observed across China, with higher levels in the northern regions compared to the southern regions. Figure 2 shows the scatter plot of the relationship between TV 2010–14 and the prevalence of CCVDs in China. Scatter plots indicate a continuous increase in CCVD prevalence with rising TV levels ($P < 0.001$). The association between TV and CCVDs prevalence was stronger in severely affected areas compared to mildly affected areas.

The basic characteristics of the study population are shown in table 1. A total of 222 179 participants were included in our study. Characterizing by the severity of the Chinese Great Famine, 62.58% (139 035) of participants were severely exposed to famine. Among all the subjects, 7.07% (15 703) and 4.46% (9,917) suffered from severe and mild famine under the age of 5, respectively. The proportions of males and rural residents were slightly lower than those of females and urban residents. Most participants were illiterate or had only primary school education, particularly in adult-exposed groups in both severely affected areas (82.16%) and mildly affected areas (78.16%). Compared with adult-exposed groups, the 5–18 and under-5 exposed groups had higher proportions of married individuals. In addition, under-5-exposed groups were more likely to have higher household income and engage in more physical activity.

Table 2 shows the distribution of meteorological variables during the study period across six famine groups. Among 1860 communities, the mean TV ranged from 10.00 °C in the severe-affected adult-exposed group to 10.99 °C in the mildly-affected under-5-exposed group in 2010–14. The p-CCSI (an index of famine severity) was negatively correlated with TV but positively correlated with mean temperature and relative humidity (table S1).

Figure 3 shows the ORs for the prevalence of CCVDs associated with TV among the elderly. Overall, there were positive associations between TV and the prevalence of CCVDs at the national level. These associations were stronger in the severely affected groups compared to the mildly affected groups, particularly for those exposed to famine under the age of 5. For example, the ORs for TV 2010–14 were 1.13 (95% CI: 1.08, 1.19) for the mildly affected under-5-exposed groups and 1.28 (95% CI: 1.17–1.40) for the severely affected under-5-exposed groups. The magnitude of these associations decreased with older age at famine exposure. Compared to the adult-exposed groups, significantly stronger associations for under-5-exposed groups were identified in severely affected areas (table S2). These findings were consistent across different exposure periods, with higher associations observed for summer TV compared to winter TV (figures 3 and S3).

Figure 4 shows the ORs for CCVDs associated with every 1 °C increase in TV during 2010 and 2014, stratified by sex, urbanity, frequency of physical activity, marital status, education attainment, and annual household income. The results indicate higher associations for the under-5-exposed groups compared to the 5–18 and adult-exposed groups across most subgroups. Significant differences in risk between under-5-exposed groups and adult-exposed groups were observed among females, rural residents, individuals with lower education levels, those with lower annual family incomes, and participants engaging in physical activity less than six times per week, in severely affected areas (table S3).

Results from sensitivity analyses are shown in table S4 and figure S4. Using alternative method parameters and p-CCSI for famine severity produced almost identical results.

4. Discussion

To the best of our knowledge, this is the first and largest study investigating the impact of famine exposure on the association between long-term TV and the prevalence of CCVDs among the elderly. We found that participants exposed to famine under the age of 5 had a significantly stronger association between TV and CCVDs compared to those exposed during adulthood, particularly in regions severely affected by the Great Chinese Famine. Our findings also indicate that certain demographic and socioeconomic factors can mitigate the association between TV and CCVDs in individuals exposed to severe famine at an early age.

In this study, we found that long-term TV exposure was associated with an increased prevalence of CCVDs. As evidenced before, both short-term and long-term exposure to TV are significantly associated with the prevalence of CCVDs in the elderly. (Tian *et al* 2019, Kang *et al* 2021) It has been reported that each 1 °C increase in annual TV is associated with a 6% increase in CCVD risk, and a 1 °C increase in summer TV is associated with a 3.8% increase in myocardial infarction mortality. (Zanobetti *et al* 2012, Kang *et al* 2021) The biological mechanisms linking long-term TV exposure to CCVDs are not well understood, though

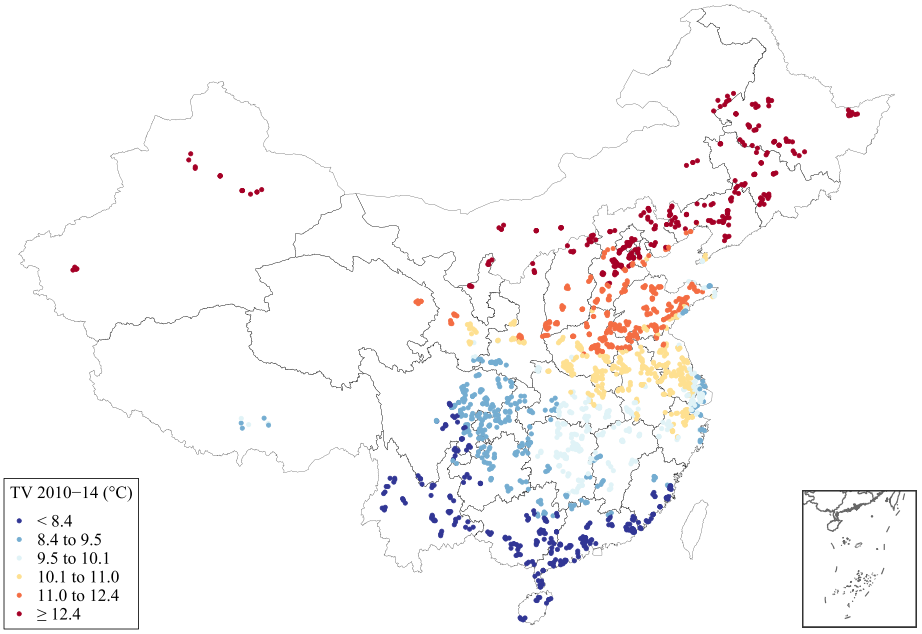

Figure 1. Location of 1860 communities included in this study and distribution of temperature variability (TV) in 2010–14 in China.

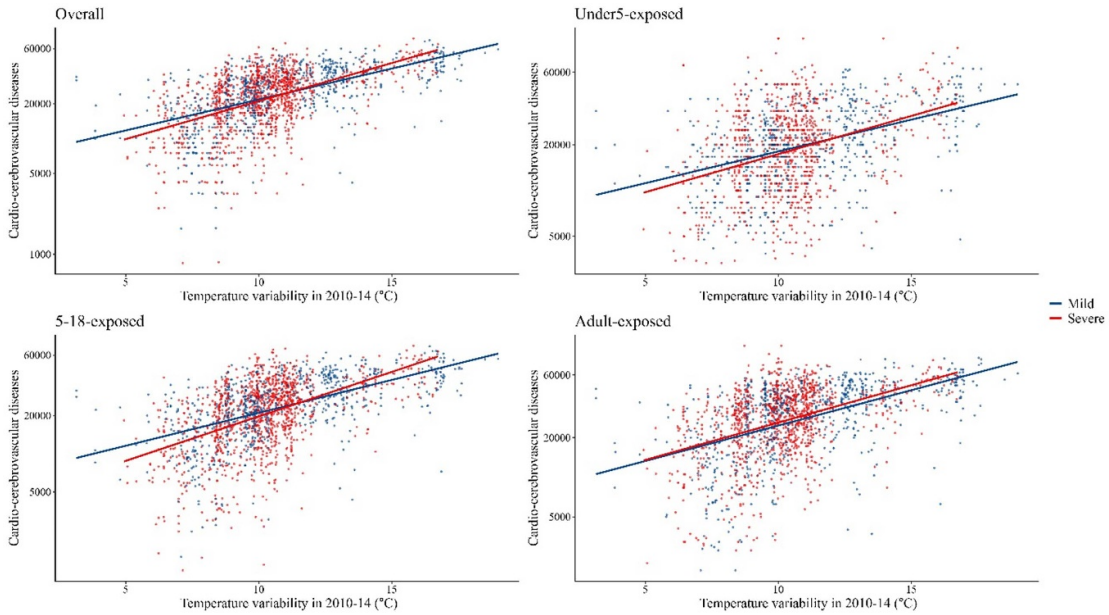

Figure 2. Scatter plots of the relationship between temperature variability (TV) in 2010–14 and the prevalence of cardio-cerebrovascular diseases (CCVDs) in 1860 communities in China.

plausible explanations exist. First, ambient temperature variation may disturb normal physiological thermoregulation, triggering autonomic nervous system activity and leading to adverse effects. (Lim *et al* 2013, Kang *et al* 2021) The elderly, who may have reduced thermoregulatory capabilities, are particularly at risk. (Ding *et al* 2016) Second, exposure to TV may affect heart rate and blood pressure, alter the plasma fibrinogen concentrations, and increase inflammatory markers. (Yang *et al* 2018, Tian *et al* 2019) Additionally, dramatic temperature changes can impede adaptation to local climate patterns, exacerbating the adverse impacts of TV. (Sun *et al* 2018, Zhao *et al* 2018)

Our study newly identifies early-life famine exposure as a significant modifier of the association between long-term TV and CCVDs. We found that individuals who experienced famine under the age of 5 had a more pronounced association between TV and CCVDs, especially in severely affected areas, implying the modification effect of early-life famine exposure. Although significant associations between prenatal

Table 1. Basic characteristics of the study population.

Variables	Mildly–affected areas			Severely–affected areas			*P* value
	Under-5-exposed	5–18-exposed	Adult-exposed	Under-5-exposed	5–18-exposed	Adult-exposed	
Total population	9917	50 211	23 016	15 703	84 463	38 869	
Gender, Male (%)	4780 (48.20)	24 507 (48.81)	10 509 (45.66)	7695 (49.00)	41 483 (49.11)	17 167 (44.17)	<0.001
Age (mean (SD))	60.42 (0.49)	66.62 (3.71)	80.27 (4.61)	60.41 (0.49)	66.64 (3.72)	80.37 (4.66)	<0.001
Rural (%)	4707 (47.46)	24 097 (47.99)	10 040 (43.62)	7500 (47.76)	42 057 (49.79)	18 118 (46.61)	<0.001
Education attainment (%)							<0.001
Illiteracy and primary	5539 (55.85)	33 023 (65.77)	17 989 (78.16)	9103 (57.97)	59 482 (70.42)	31 933 (82.16)	
High school and above	4355 (43.91)	17 045 (33.95)	4949 (21.50)	6538 (41.64)	24 686 (29.23)	6803 (17.50)	
Missing values	23 (0.23)	143 (0.28)	78 (0.34)	62 (0.39)	295 (0.35)	133 (0.34)	
Marital status (%)							<0.001
Single	1136 (11.46)	10 008 (19.93)	11 588 (50.35)	1637 (10.42)	16 598 (19.65)	20 095 (51.70)	
Married	8658 (87.30)	39 493 (78.65)	11 151 (48.45)	13 828 (88.06)	66 371 (78.58)	18 209 (46.85)	
Missing values	123 (1.24)	710 (1.41)	277 (1.20)	238 (1.52)	1494 (1.77)	565 (1.45)	
Frequency of physical activity (%)							<0.001
Never	4780 (48.20)	24 355 (48.51)	13 022 (56.58)	8006 (50.98)	44 446 (52.62)	24 273 (62.45)	
1–5 times/week	2494 (25.15)	12 383 (24.66)	4861 (21.12)	4321 (27.52)	21 977 (26.02)	8134 (20.93)	
>6 times/week	2592 (26.14)	13 193 (26.28)	5036 (21.88)	3285 (20.92)	17 528 (20.75)	6217 (15.99)	
Missing values	51 (0.51)	280 (0.56)	97 (0.42)	91 (0.58)	512 (0.61)	245 (0.63)	
Annual household income (%)							<0.001
T1 (<2316.78 US$ per year)	2597 (26.19)	16 021 (31.91)	7434 (32.30)	4425 (28.18)	32 085 (37.99)	16 572 (42.64)	
T2 (2316.78–6178.08 US$ per year)	3423 (34.52)	16 431 (32.72)	7181 (31.20)	5960 (37.95)	27 705 (32.80)	10 869 (27.96)	
T3 (>6178.08 US$ per year)	3806 (38.38)	17 159 (34.17)	8054 (34.99)	5233 (33.32)	24 008 (28.42)	10 988 (28.27)	
Missing values	91 (0.92)	600 (1.19)	347 (1.51)	85 (0.54)	665 (0.79)	440 (1.13)	
CCVDs (%)							<0.001
Yes	7807 (78.72)	36 402 (72.50)	15 455 (67.15)	12 349 (78.64)	61 228 (72.49)	25 900 (66.63)	
No	2068 (20.85)	13 565 (27.02)	7471 (32.46)	2611 (16.63)	19 146 (22.67)	11 056 (28.44)	
Missing values	42 (0.42)	244 (0.49)	90 (0.39)	743 (4.73)	4089 (4.84)	1913 (4.92)	

Definition of abbreviations: CCVDs, cardio-cerebrovascular diseases.

Table 2. Distribution of meteorological variables in 1860 communities during the study period (2010–2014).

Exposure	Mildly-affected areas			Severely–affected areas			P value
	Under-5-exposed	5–18-exposed	Adult-exposed	Under-5-exposed	5–18-exposed	Adult-exposed	
TV 2010–14 (°C)	10.99 (2.82)	10.88 (2.84)	10.67 (2.80)	10.23 (2.05)	10.15 (1.95)	10.00 (1.94)	<0.001
TV 2011–14 (°C)	10.99 (2.76)	10.89 (2.78)	10.68 (2.75)	10.25 (2.02)	10.18 (1.92)	10.03 (1.92)	<0.001
TV 2012–14 (°C)	10.94 (2.81)	10.83 (2.82)	10.62 (2.79)	10.21 (2.07)	10.13 (1.97)	9.98 (1.96)	<0.001
TV 2013–14 (°C)	10.81 (2.72)	10.70 (2.73)	10.49 (2.69)	10.08 (2.02)	10.00 (1.92)	9.85 (1.92)	<0.001
TV 2014 (°C)	10.52 (2.74)	10.43 (2.74)	10.24 (2.70)	9.71 (1.89)	9.62 (1.81)	9.48 (1.77)	<0.001
T_{mean} 2010–14 (°C)	13.96 (5.28)	14.23 (5.33)	14.72 (5.18)	15.50 (4.01)	15.59 (3.87)	15.94 (3.90)	<0.001
T_{mean} 2011–14 (°C)	13.98 (5.24)	14.25 (5.30)	14.74 (5.14)	15.53 (3.98)	15.61 (3.85)	15.96 (3.87)	<0.001
T_{mean} 2012–14 (°C)	14.06 (5.28)	14.33 (5.33)	14.82 (5.17)	15.63 (3.98)	15.72 (3.85)	16.06 (3.88)	<0.001
T_{mean} 2013–14 (°C)	14.30 (5.25)	14.57 (5.30)	15.05 (5.13)	15.87 (3.92)	15.96 (3.80)	16.29 (3.82)	<0.001
T_{mean} 2014 (°C)	14.34 (5.08)	14.60 (5.13)	15.07 (4.99)	15.85 (3.77)	15.90 (3.65)	16.24 (3.69)	<0.001
RH 2010–14 (%)	64.36 (10.90)	64.55 (11.20)	65.20 (11.01)	68.63 (6.75)	68.85 (6.67)	69.31 (6.58)	<0.001
RH 2011–14 (%)	64.27 (10.90)	64.45 (11.22)	65.09 (11.06)	68.50 (6.74)	68.73 (6.66)	69.19 (6.57)	<0.001
RH 2012–14 (%)	64.60 (11.18)	64.82 (11.52)	65.45 (11.39)	69.11 (6.95)	69.34 (6.88)	69.83 (6.79)	<0.001
RH 2013–14 (%)	64.57 (10.95)	64.77 (11.28)	65.36 (11.16)	68.98 (6.83)	69.20 (6.75)	69.66 (6.64)	<0.001
RH 2014 (%)	65.07 (11.82)	65.24 (12.19)	65.91 (12.02)	69.73 (7.79)	70.14 (7.68)	70.60 (7.50)	<0.001

Definition of abbreviations: TV, temperature variability; T_{mean}, mean temperature; and RH, mean relative humidity.

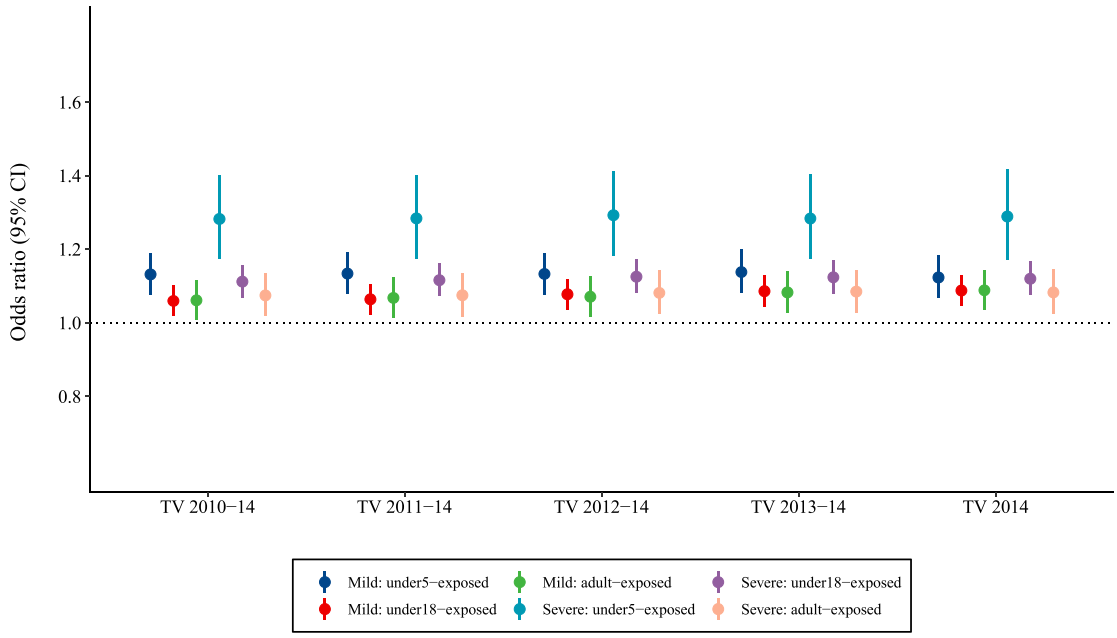

Figure 3. Odds ratios (ORs) for cardio-cerebrovascular diseases (CCVDs) associated with every 1 °C increase in temperature variability (TV) during different periods. Definition of abbreviations: TV, temperature variability.

exposure to famine and increased CCVDs risk were observed in previous studies, (Du *et al* 2020, Meng *et al* 2020) to our knowledge, none have examined the modification effects of early-life famine exposure on TV-related CCVDs. Our findings contribute to the understanding of the adverse impacts of childhood undernutrition. (van Abeelen *et al* 2012, Horenblas *et al* 2017) It has been proposed that early-life undernutrition may cause epigenetic changes via DNA methylation, leading to alterations in the structure of the cardiovascular system. (Heijmans *et al* 2008, Du *et al* 2020) Besides, rapid weight gain following early-life famine exposure, known as catch-up growth, is associated with later body fatness, increased blood pressure, and heightened cardiometabolic risk. (Baird *et al* 2005, Tarry-Adkins and Ozanne 2017, Arisaka *et al* 2020, Grey *et al* 2021) Compared with younger adults, children and adolescents may be more sensitive to the stress conditions of famine, which is a known risk factor for CCVDs. (Portrait *et al* 2011) These mechanisms suggest that individuals who experienced undernutrition early in life may be more vulnerable to temperature changes and have a higher risk of CCVDs.

Specific demographic and socioeconomic characteristics were identified as mitigating factors in the association between long-term TV and CCVDs in the under-5-exposed group. These factors include being male, living in urban areas, having a higher education level and household income, and exercising at least six times per week. Consistent with our finding in mildly affected areas, a cohort study in China found rural

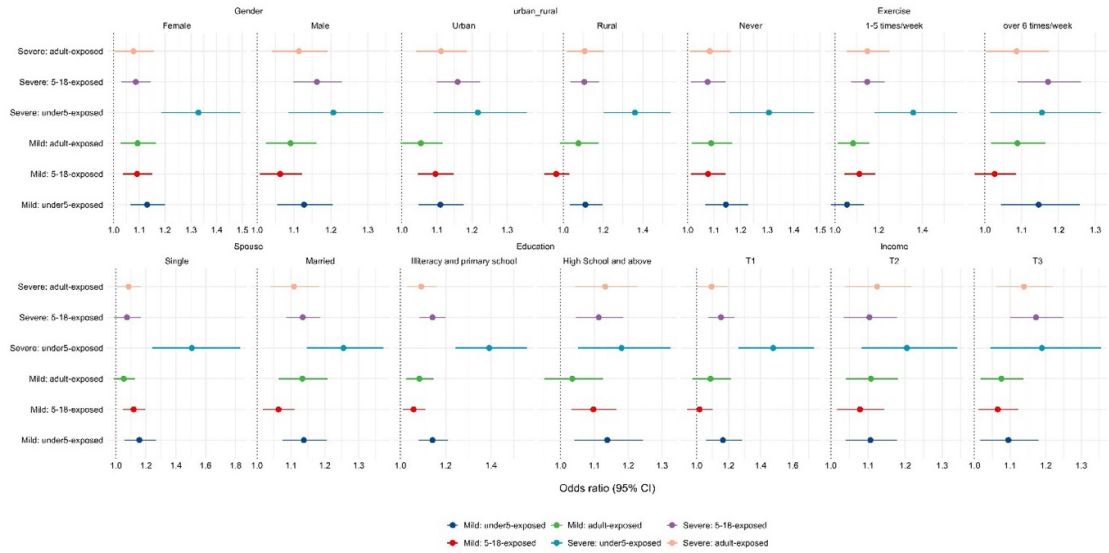

Figure 4. Odds ratios (ORs) for cardio-cerebrovascular diseases (CCVDs) associated with every 1 °C increase in temperature variability (TV) during 2010 and 2014, stratified by sex, urbanity, frequency of physical activity, marital status, education attainment, and annual household income. Definition of abbreviations: TV, temperature variability.

populations had a smaller significant effect of TV on cardiovascular disease incidence than urban populations, possibly due to greater green space. (Kang *et al* 2021) Nevertheless, our study showed that exposure to severe famine under the age of 5 might significantly increase the association between TV and CCVDs in rural areas, despite the mitigating effect of greenness. Individuals in urban areas and those with higher family income are more likely to have high socioeconomic status (SES), which our findings suggest as a potential mitigator of TV-related CCVDs for those exposed to severe famine under the age of 5. For education attainment, increased survival time related to TV exposure was associated with a higher proportion of the population aged over 25 years who completed college in the United States; another study in Hongkong observed those with lower education attainment had a greater risk for respiratory diseases when exposed to TV, which was consistent with our finding. (Zanobetti *et al* 2012, Sun *et al* 2018) The potential explanation for these findings remains unknown and further research is needed.

Moreover, the most striking result of the analysis is that participants in the under-5-exposed group who exercised over 6 times per week had a reduced risk for CCVDs when exposed to long-term TV. Unlike SES, sex, and urbanization, which are not easily changeable, physical inactivity is a modifiable risk factor. Regular physical activity is well-documented to benefit the cardiovascular system, suggesting it could mitigate the adverse effects of early-life famine exposure. (Green 2009, Wahid *et al* 2016, Lu *et al* 2020, Meng *et al* 2020) Previous studies have shown that physical activity significantly influences DNA methylation, potentially modifying the epigenetic effects of famine exposure. (Voisin *et al* 2015) According to the Global Action Plan on Physical Activity 2018–2030, over 80% of the adolescent population worldwide is insufficiently active, and a quarter of adults do not meet the recommended levels of physical activity. It is crucial for policymakers to implement strategies to promote physical activity, particularly in regions severely affected by famine, to reduce the long-term health impacts of early-life undernutrition.

Climate change and undernutrition are among the critical global issues of our time. The health impacts of TV have been widely documented, with climate change increasing the frequency and intensity of extreme temperature. (Wu *et al* 2021, Wen *et al* 2023b, 2024) Under the high greenhouse gas emission scenario, the average diurnal temperature range is projected to increase in most regions, leading to an increase in excess deaths. (Lee *et al* 2020) More often, public emergencies such as famine and the pandemic pose serious threats to human beings. Since the COVID-19 outbreak in 2019, a clear warning of vulnerability, there has been an elevated burden of mortality and undernutrition. (Osendarp *et al* 2021) After overcoming COVID-19, efforts must focus on mitigating its long-lasting effects. Our study demonstrated the long-term effect of extreme famine events but identified physical activity as a potential means to mitigate the adverse impact of early-life famine exposure. Immediate steps shoud be taken to protect human beings.

The study had some limitations. In this study, famine groups were classified based on age at the time of famine exposure, resulting in age variations among the groups (the adult-exposed group was older than the under-5-exposed group). Although our estimates for each group are unlikely to be significantly biased, differences in TV-related CCVDs between these groups can be attributed to both age at famine exposure and

age differences. Additionally, age variations can result in differences among other socio-demographic factors, such as education level and household income. Similarly, our mild-exposed and severe-exposed groups might also be subject to these issues due to socio-demographic differences across provinces. However, our adjustments for education level and household income can largely control their effects.

A self-reported measure of CCVDs was used in this study, which could lead to the underestimation of the association between TV and CCVDs, considering the lower prevalence of self-reported CCVDs compared with the real prevalence. (Ning *et al* 2016) The degree of underestimation might vary across different famine groups due to age differences among the under-5 exposed group, 5–18 exposed group, and adult exposed group. (Liu *et al* 2024) In addition, attenuation bias from false-negative reporting could be associated with lower education level and poverty, however, both the education level and the income were adjusted in our analyses, partially controlling for the effect of the self-reported outcome on the association between TV and CCVDs. (Onur and Velamuri 2018) Besides, misclassification may exist as we defined famine exposure based on the current province of residence, potentially overlooking migration. However, the Household Registration System (also known as hukou) in China has historically restricted population movement, particularly among the elderly. (Tong and Piotrowski 2012) Moreover, it has been demonstrated that most migrants tend to stay within the same province, (Hu *et al* 2011) suggesting that migration would not significantly affect our findings.

5. Conclusion

In conclusion, our study showed that severe famine exposure in early life was significantly associated with a higher risk of CCVDs attributable to TV. Our findings highlight the critical role of childhood food security in lowering susceptibility to chronic illnesses later in life, especially in developing nations. Additionally, strategies and policies that encourage physical activity are essential to mitigate the adverse effects of early-life famine exposure.

Data availability statement

The data cannot be made publicly available upon publication because they are owned by a third party and the terms of use prevent public distribution. The data that support the findings of this study are available upon reasonable request from the authors.

Authors' contributions

Y W and B W performed the main analysis and wrote the original draft. B S, Y W, B W, J X, and X W prepared the data. Y D contributed to the conception of the study. J X, B S, X W, M F, Y D, Y S, and J M revised the manuscript. All authors critically reviewed and accepted the final version of the manuscript. We thanked the China National Committee on Aging for supporting the survey and providing the data.

Sources of Funding

This study was funded in part by the sub-project of the National Key Research and Development Program of the Ministry of Science and Technology (2018YFC2000303).

Conflict of interest

Y W and B W were supported by China Scholarship Council (Grant Numbers 202006010044, 202006010043) (www.csc.edu.cn/chuguo/s/1844). The funding bodies did not play any role in the study design, data collection, data analyses, results interpretation, and writing of this manuscript.

Ethics approval

The Urban and Rural Elderly Population survey was approved by the Ethics Committee of the Chinese National Bureau of Statistics, and oral informed consent was obtained from all participants before the interview. The China National Committee on Aging approved this analysis, and informed consent was not required.

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