



OPEN In utero and childhood exposure to the great Chinese famine and risk of aging in adulthood

Tao Ma^{1,2,3,4,8}, Xiao-Meng Hao^{1,2,3,4,8}, Xiaowei Zhang^{5,8}, Xin-Yu Liu^{1,2,3,4}, Yi-Ming Wang⁶, Qing-Song Zhang⁷ & Jin Zhang^{1,2,3,4}✉

Background Early-life exposure to famine may influence the occurrence of chronic diseases and aging in midlife among those exposed. This study aims to explore the relationship between exposure to the Chinese Great Famine and aging in middle-aged individuals. **Methods** Participants born in 1963–1965 (unexposed), 1959–1961 (in utero exposure), and 1955–1957 (childhood exposure) from the Kailuan Study were included. Their biological age at 2010, 2014, and 2018 was investigated, and age acceleration (biological age minus actual age) was calculated to assess aging. Logistic regression analysis was employed to describe the relationship between famine exposure and the aging risk. Subgroup and sensitivity analysis were conducted to explore differences and stability in this relationship among different groups. **Results** A total of 17,543 participants were included in this study. Among them, 12,762 (72.7%) were male, and 4,781 (27.3%) were female, with 2,543 participants experiencing aging events. Compared to unexposed participants, those exposed during childhood and in utero exhibited a 1.69-fold (OR = 1.69, 95%CI: 1.53–1.87) and 1.22-fold (OR = 1.22, 95%CI: 1.08–1.37) increased risk of aging. Subgroup analysis revealed an interaction with income (P for interaction = 0.008), and additional interaction analysis suggested that increasing income could partially mitigate the detrimental effects of early-life famine exposure. Furthermore, experiencing famine in severely affected regions exacerbated the risk of aging (OR = 1.41, 95%CI: 1.21–1.63). **Conclusion** Exposure to famine in utero or during childhood may elevate the risk of midlife aging among exposed individuals, and these relationships are influenced by the severity of famine exposure. Increasing income may also help mitigate these effects.

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Keywords Famine, Aging, Income, In utero, Childhood

Aging, a process that has garnered considerable research interest in recent years, is characterized by a decline in the body's immune function and an increased risk of complications [1]. A comprehensive understanding of the mechanisms and triggers that contribute to aging is pivotal for addressing the challenges posed by an aging population. Research has underscored the influence of nutritional status, physical activity, and external environmental factors on the initiation of aging [2]. Recent studies suggest that nutritional deficiencies during the intrauterine and childhood phases may precipitate an earlier onset and heightened risk of cerebral hemorrhage in individuals during middle age [3]. Furthermore, early-life adversities, such as natural disasters or conflicts, have been correlated with an increased prevalence of metabolic diseases and elevated systemic inflammation. Consequently, this research posits that events of early-life adversity may also have significant implications for the biological aging process.

¹The Third Department of Breast Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin 300060, China. ²Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Tianjin, China. ³Tianjin's Clinical Research Center for Cancer, Tianjin, China. ⁴Key Laboratory of Cancer Prevention and Therapy, Tianjin, China. ⁵Department of Gastrointestinal Surgery, Department of Clinical Nutrition, Beijing Shijitan Hospital, Capital Medical University, Beijing, China. ⁶Department of Hepatological Surgery, Kailuan General Hospital, Tangshan, China. ⁷Department of General Surgery, Kailuan General Hospital, Tangshan 063000, China. ⁸Tao Ma, Xiao-Meng Hao and Xiaowei Zhang contributed equally to this work. ✉email: evergreen176700@163.com

Between 1959 and 1961, China endured the most catastrophic famine since World War II, marking a period of extreme hardship and widespread malnutrition that led to millions of fatalities. This three-year calamity not only resulted in an unprecedented loss of life due to starvation but also perpetuated a legacy of malnutrition and heightened disease vulnerability among the survivors [4]. The famine, epitomized by acute food scarcity, had enduring implications for the health outcomes of the affected populations. Notably, Clair et al. were the first to identify a correlation between famine exposure and an elevated risk of schizophrenia, laying the groundwork for subsequent investigations into the famine's far-reaching health consequences [5]. In the aftermath, comprehensive studies have been rigorously conducted to elucidate the extensive impacts of this famine, contributing to a broader understanding of the interplay between early-life adversities and long-term health.

Based on this, we hypothesize that exposure to famine during the intrauterine and childhood periods may exacerbate the risk of aging in individuals during middle age. Despite the reduction in large-scale famines due to natural causes with socio-economic development, uneven distribution of nutritional resources persists, influenced by factors such as wars and public health events (e.g., COVID-19), leading to persistent malnutrition in early life [6, 7]. Therefore, this study aims to explore the relationship between famine exposure and the risk of aging in middle age through an extensive and large-scale prospective cohort study from northern China.

Methods

Study population

All participants in this study were derived from the Kailuan Study (registered at <https://www.chictr.org.cn/>, registration number: ChiCTR2000029767). Initiated in 2006, the Kailuan Study was originally launched by the Kailuan Group in Tangshan, with the aim of detecting and mitigating cardiovascular and cancer risks among the local population. The comprehensive research design has been delineated in preceding studies [8, 9]. Starting in 2006, the population in the region has been subjected to biennial health examinations. These examinations encompass general assessments, laboratory tests, imaging studies, and questionnaire surveys.

To ensure age homogeneity among the unexposed, in utero exposed, and childhood exposed groups (thereby mitigating the influence of age as a confounding factor), individuals born in the years 1963–1965, 1959–1961, and 1955–1957 were included, who participated in the health examinations conducted in 2010, 2014, and 2018. The initial cohort consisted of 21,183 participants. We excluded 1,843 individuals due to incomplete information regarding marital status, educational attainment, income level, smoking habits, and alcohol consumption. Furthermore, to accurately determine whether participants were born in regions severely affected by the famine, an additional 1,797 participants were excluded because of missing birthplace data (Fig. 1(A)). Additionally, imputation was performed for missing continuous variables, incorporating 823 participants with missing body mass index (BMI) data, 285 with missing waist circumference (WC) data, 47 with missing uric acid (UA) levels, and 96 with missing high-density lipoprotein cholesterol (HDL-C) values. All participants provided informed consent, and the study's methodology was in strict compliance with the principles of the Helsinki Declaration.

Famine and severity

Participants were stratified based on their birth years relative to the Chinese famine's timeframe (1959–1961), resulting in three distinct groups: the unexposed group (born in 1963–1965), the in utero exposed group (born in 1959–1961), and the childhood exposed group (born in 1955–1957) [10]. To mitigate the confounding effects of normal aging, follow-up was concluded at varying years for each cohort: 2018 for the unexposed group, 2014 for the in utero exposed group, and 2010 for the childhood exposed group. This strategy was employed to ensure that the age range of participants in each group was consistently controlled at 55–57 years. Figure 1 (B) provides detailed grouping methods for the study population in the current study.

While the initial study location of Tangshan did experience a significant famine, it is crucial to acknowledge that the extent of famine varied considerably across different regions in China. Drawing on methodologies outlined in prior research, we adopted a classification system for famine severity based on reported excess mortality rates across various provinces. Specifically, participants originating from provinces with an excess mortality rate below 50% were designated as experiencing non-severe famine exposure. In contrast, individuals born in provinces with a mortality rate exceeding 50% were identified as having been severely exposed. The provinces classified under the severely exposed category include Jilin, Guangdong, Jiangsu, Shandong, Fujian, Hubei, Liaoning, Guangxi, Hunan, Gansu, Henan, Sichuan, Qinghai, Guizhou, and Anhui [11]. However, it is important to note that even within these provinces, local variations in famine severity could exist.

Definition of outcome

The primary outcome of this study is aging, operationalized through the use of the Bioage package to construct a phenotypic age formula leveraging existing variables. Specifically, aging is defined by a phenoage advance greater than 0, where phenoage advance is calculated as the difference between Phenotypic age and chronological age: $\text{phenoage advance} = \text{Phenotypic age} - \text{chronological age}$. The calculation of phenoage and age acceleration involved several specific biomarkers and variables. The Phenotypic age itself is derived from a formula that integrates various biomarkers and chronological age, calculated as follows: First, a base value x_b is determined by the equation: $x_b = -12.579 - 0.0351 \times \text{albumin (Alb)} - 0.0091 \times \text{lymph} + 0.2931 \times \ln\text{CRP} + 0.0856 \times \text{glucose} + 0.0104 \times \text{creatinine} + 0.0743 \times \text{white blood cell count} + 0.0827 \times \text{chronological age}$. The specific biomarkers included in the formula were Alb, lymph, CRP, glucose, creatinine, and white blood cell count. Subsequently, Phenotypic age is computed using $141.8 + \ln[-0.00581 \times (-1.37211 \times \exp(x_b)) / 0.0071982] / 0.08742$. This comprehensive approach allows for a nuanced analysis of aging by comparing biological markers of aging with chronological age, thereby quantifying the extent of biological aging beyond what is expected by chronological age alone.

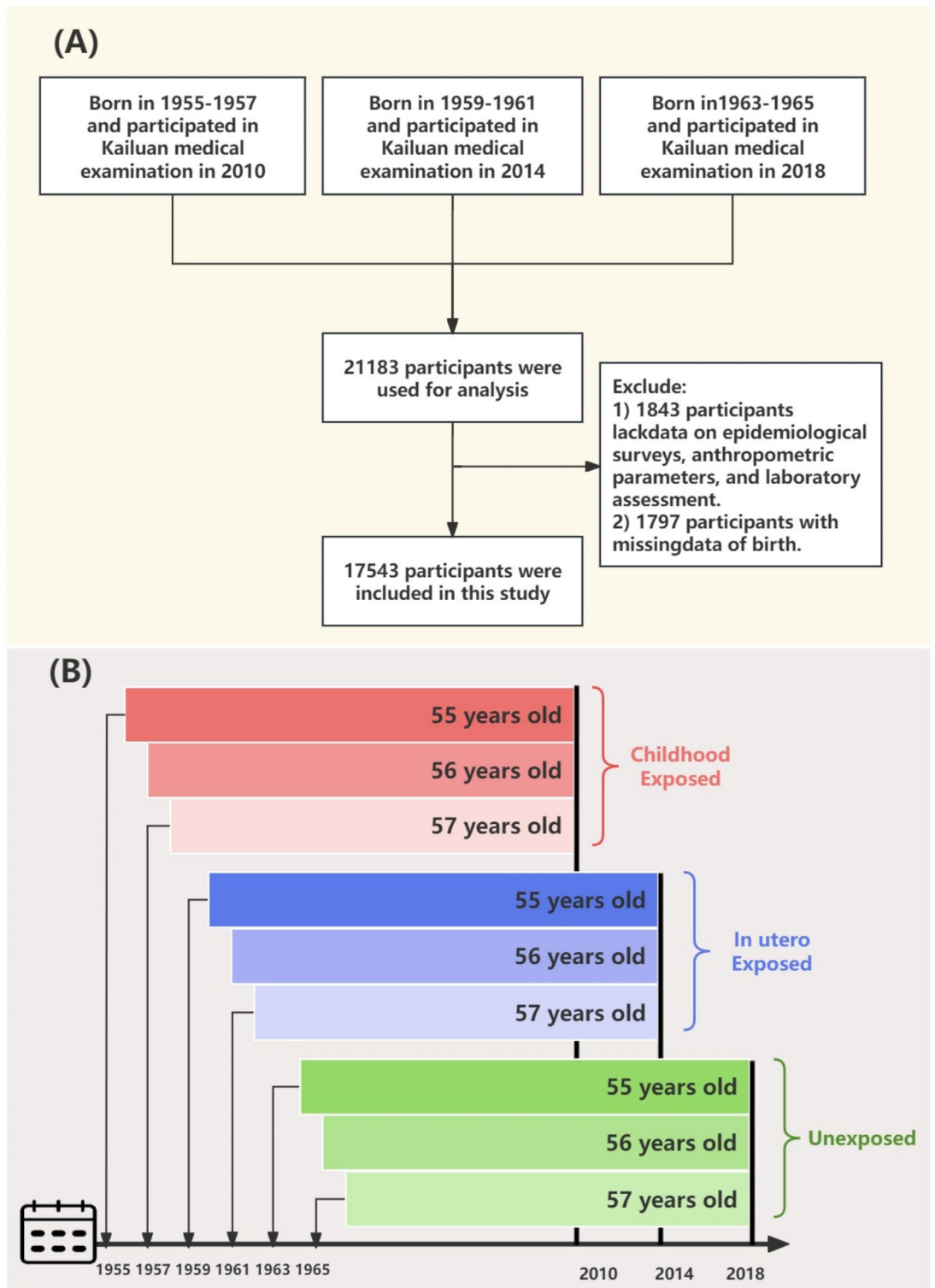


Fig. 1. (A) Flowchart depicting the study population in the Kailuan Study. (B) Detailed grouping methods for the study population in the current study.

Definition of the covariates

All participants in this study voluntarily agreed to have their laboratory data collected at Kailuan General Hospital. They visited the hospital after fasting for at least 8 h to undergo blood tests, including measurements of triglycerides (TG), HDL-C, fasting blood glucose (FBG), albumin (Alb), UA, hemoglobin (HB), and C-reactive protein (CRP). In conjunction with these tests, participants also completed routine questionnaire surveys, which captured information on age, sex, education level, type of employment, income, smoking status, alcohol

consumption, and regular physical activity. Regular physical exercise is defined as engaging in physical activity at least 3 times per week, with each session lasting 30 min or more. Body measurements taken included waist circumference (WC), height, and weight. A normal WC is defined as less than 90 cm for men and less than 80 cm for women. The BMI was calculated by dividing the weight in kilograms (kg) by the square of the height in meters (m²), with a BMI of 28 kg/m² or greater indicating obesity. Information on comorbidities, including hypertension, diabetes, and fatty liver, was also collected [12].

Statistical analysis

All statistical analyses were performed using SAS version 9.4 and R version 4.2.0. Two-sided P-values less than 0.05 were deemed statistically significant. Continuous variables were described as mean \pm standard deviation or median (IQR) based on the distribution's normality. Differences among groups were assessed using one-way Analysis of Variance (ANOVA) or non-parametric tests, contingent on the distribution normality of the data. Categorical variables were presented as numbers (percentages) and the differences between groups were evaluated using the chi-square test. The Bioage package facilitated the generation of the formula for calculating phenotypic age, thus determining the phenotypic age for each participant [13]. Logistic regression analysis was employed to elucidate the relationship between famine exposure and aging. Multivariate analysis adjusted for age, CRP, sex, type of employment, educational level, regular physical exercise, income, smoking, and alcohol consumption, hypertension, diabetes, WC, BMI, HDL-C, UA, Alb, and TG. Subgroup and interaction analyses were conducted to investigate the impact of famine exposure on aging across different population segments. Sensitivity analyses were carried out to ensure the robustness of the results, which included the exclusion of participants with significant nutritional variations, anemia, advanced age, and those diagnosed with cancer.

Results

Baseline characteristics of the study participants

A total of 17,543 participants were included from the Kailuan Study, with an average age of 54.60 \pm 1.08 years. The cohort comprised 12,762 men (72.7%) and 4,781 women (27.3%). Among these, 2,543 participants exhibited aging events. As delineated in Table 1, those exposed to the famine during childhood or in utero demonstrated a higher phenotypic age and a larger proportion of males compared to the unexposed group. Additionally, these individuals were more likely to be engaged in physical labor and had lower levels of education and income. Behavioral patterns revealed that famine-exposed participants were more inclined to smoke and consume alcohol. Physically, they exhibited lower waist circumference and BMI values. From a laboratory perspective, these participants also showed reduced levels of TG.

Relationship between famine and aging

The logistic regression outcomes presented in Table 2 reveal that, compared to participants unexposed to famine, those exposed during childhood (OR = 1.69, 95%CI: 1.53–1.87) and in utero (OR = 1.22, 95%CI: 1.08–1.37) exhibited significantly increased risks of aging in the crude models. Even after adjusting for potential risk factors, the heightened risk persisted among participants exposed during childhood (OR = 1.67, 95%CI: 1.51–2.22) and in utero (OR = 1.46, 95%CI: 1.12–1.92).

Groups	Unexposed	Childhood exposed	In utero exposed	P value
n	5723	7766	4054	
Age (mean (SD), years)	54.37(1.15)	54.53(0.94)	54.93(0.98)	<0.001
Phenoage (mean (SD), years)	48.38(6.78)	49.59(6.35)	49.61(6.25)	<0.001
Men (%)	3873(67.7)	6083(78.3)	2806(69.2)	<0.001
Work type (Physical labor, %)	1223(21.4)	6966(89.7)	3879(95.7)	<0.001
High school and above (%)	2064(36.1)	1239(16.0)	606(14.9)	<0.001
Regular physical exercise (%)	813(14.2)	982(12.6)	669(16.5)	<0.001
Income (> 3000 ¥, %)	3648(63.7)	4411(56.8)	2669(65.8)	<0.001
Current smoker (%)	1633(28.5)	3304(42.5)	1799(44.4)	<0.001
Current drinker (%)	1005(17.6)	1747(22.5)	803(19.8)	<0.001
Fatty liver (%)	2826(49.4)	3535(45.5)	1966(48.5)	<0.001
Hypertension (%)	2814(49.2)	3671(47.3)	1723(42.5)	<0.001
Diabetes (%)	882(15.4)	865(11.1)	668(16.5)	<0.001
WC (median [IQR], cm)	89.0[83.0,94.0]	88.0[82.0,95.0]	86.0[82.0,92.0]	<0.001
BMI (median [IQR], kg/m ²)	25.08[23.37,27.44]	24.90[22.86,27.06]	24.80[22.86,27.03]	<0.001
HDL-C (median [IQR], mmol/L)	1.44[1.23,1.67]	1.48[1.22,1.83]	1.31[1.09,1.51]	<0.001
TG (median [IQR], mmol/L)	1.42[1.00,2.12]	1.32[0.91,1.99]	1.33[0.90,2.03]	<0.001
Uric acid (median [IQR], μ mol/L)	319.3[266.0,379.0]	299.1[252.0,358.0]	325.0[274.8,389.0]	<0.001
Hb (median [IQR], g/L)	152.0[141.0,161.0]	149.0[140.0,158.0]	151.0[140.8,160.0]	<0.001

Table 1. Baseline characteristics. Note: WC: waist circumference; BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride; Hb: hemoglobin.

Groups	Events/Total	Crude		Adjusted	
		OR (95% CI)	P value	OR (95% CI)	P value
Unexposed	641/5723	Ref.		Ref.	
Childhood exposed	1363/7766	1.69(1.53,1.87)	<0.001	1.67(1.25,2.22)	<0.001
In utero exposed	539/4054	1.22(1.08,1.37)	0.002	1.46(1.12,1.92)	0.006

Table 2. The association between famine exposure and aging. Note: Adjusted models included age, CRP, sex, work type, educational level, regular physical exercise, income, smoke, drink, hypertension, diabetes, WC, BMI, HDL, uric acid, Alb and TG. CRP: C-reactive protein; WC: waist circumference; BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; Alb: albumin; TG: triglyceride.

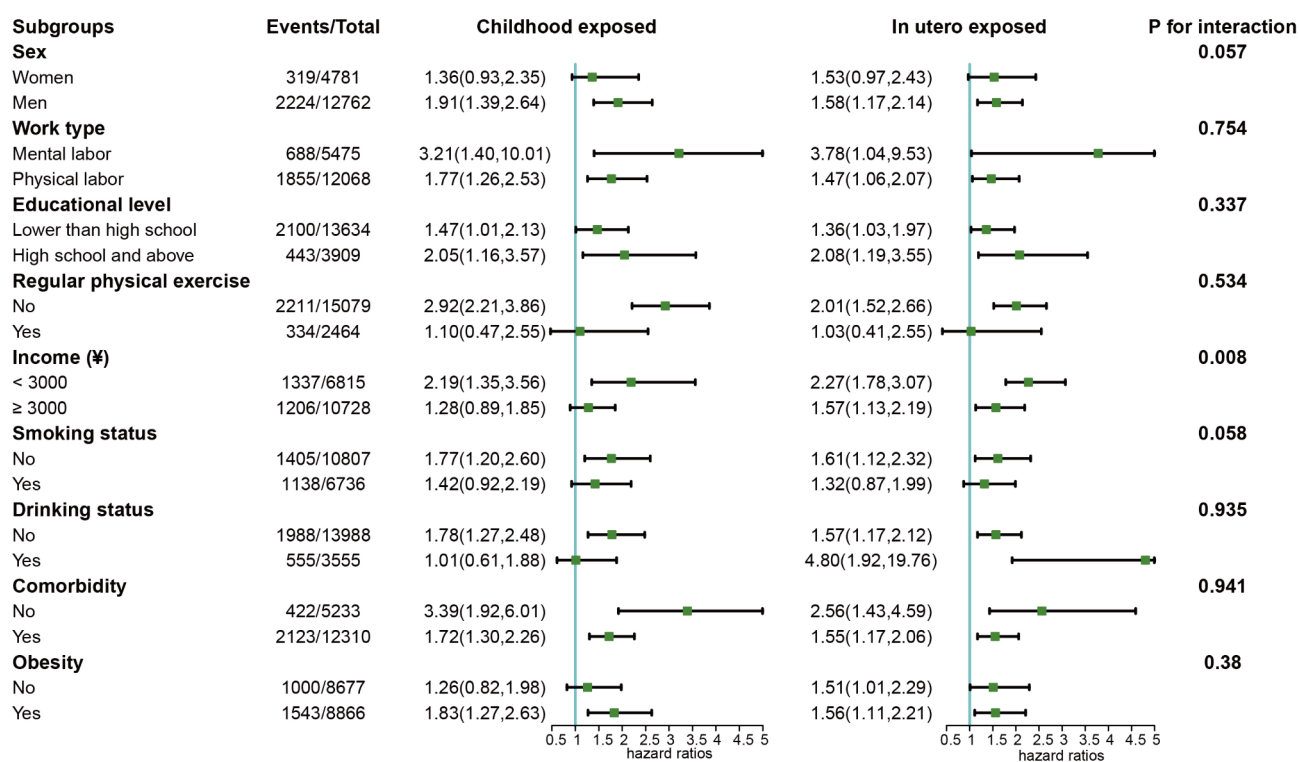


Fig. 2. Subgroup analysis of the association between famine exposure and aging. Note: The model was adjusted for age, CRP, sex, work type, educational level, regular physical exercise, income, smoke, drink, hypertension, diabetes, WC, BMI, HDL, uric acid, Alb and TG, except for the stratified factors. CRP: C-reactive protein; WC: waist circumference; BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; Alb: albumin; TG: triglyceride.

To delve deeper into the influence of famine exposure on aging across different demographics, subgroup analyses were conducted, considering variables such as gender, occupation, education level, regular physical exercise, income, smoking, drinking, comorbidities, waist circumference, and BMI (Fig. 2). These analyses revealed a consistent relationship across most subgroups, with income emerging as a significant modifier of the effect (p for interaction = 0.008). Specifically, among participants earning less than 3000 yuan, those exposed to famine during childhood (OR = 2.19, 95%CI: 1.35–3.56) and in utero (OR = 2.27, 95%CI: 1.78–3.07) faced an elevated risk of aging.

Further additive joint analyses (Figure S1) underscored that, relative to participants with concurrent low income and famine exposure, the risk of aging decreased for those with low income but without famine exposure (OR = 0.55, 95%CI: 0.34–0.87), those with high income and famine exposure (OR = 0.51, 95%CI: 0.37–0.69), and those with high income without famine exposure (OR = 0.36, 95%CI: 0.21–0.61).

Severity of famine and sensitivity analysis

The differential impact of famine severity on aging risk was substantiated, as evidenced in Table S1. Participants from areas severely affected by famine exhibited a significantly increased risk of aging in comparison to those from areas with less severe famine exposure (OR = 1.41, 95%CI: 1.21–1.63). Moreover, the population was stratified into five distinct groups for further analysis. Relative to participants with no famine exposure, those exposed during childhood to areas of low severity did not experience a statistically significant increase in aging

risk (OR = 1.36, 95%CI: 0.94–2.20). Conversely, individuals exposed during childhood to areas of high severity (OR = 1.58, 95%CI: 1.19–2.10), exposed in utero to low-severity (OR = 1.50, 95%CI: 1.15–1.97), and high-severity areas (OR = 2.92, 95%CI: 1.74–4.79) all demonstrated elevated risks of aging (Table 3).

Comprehensive sensitivity analyses were executed to ascertain the stability of these findings (Table S2). By excluding participants with significant nutritional variations, anemia, advanced age, and cancer diagnoses, the analyses affirmed the consistency of the primary outcomes. Both childhood and in utero exposures to famine conditions were linked with an augmented risk of aging in middle age, underscoring the lasting health implications of early-life famine exposure.

Discussion

This investigation leverages a prospective, repeated-measure cohort design, characterized by age homogeneity among participants but differing in terms of famine exposure. This study uniquely demonstrates that individuals exposed to famine during childhood or in utero exhibit a significantly elevated risk of aging in middle age, compared to those not exposed to famine. Notably, analyses stratified by income reveal that the adverse effects of famine exposure on aging are more pronounced in lower-income populations. This finding suggests that higher income levels may offer a protective buffer against the detrimental impacts of early-life famine exposure. Furthermore, the study elucidates that the severity of famine exposure is a critical factor, with more severe famine conditions correlating with an increased risk of aging. This research underscores the complex interplay between early-life environmental factors, socio-economic status, and long-term health outcomes, highlighting the importance of addressing social determinants of health in mitigating aging risks.

Recent research has illuminated the long-term health effects of famine exposure, and this study is one of the most comprehensive analyses on the relationship between exposure to the Chinese Great Famine and aging. Consistent with our prior findings, exposure during in utero (HR = 2.14, 95%CI: 1.78–2.56) and childhood (HR = 2.49, 95%CI: 2.16–2.88) is significantly associated with an increased risk of cancer and cancer-related mortality in adulthood [14]. We focused on middle-aged individuals (55–57 years old) to more accurately capture aging challenges [15, 16]. Comparing these outcomes globally, studies on the Leningrad Siege show persistent cardiovascular risks and aging effects [17]. Similarly, Cheng et al. found that Dutch Famine survivors experienced accelerated biological aging six decades later [18]. These findings underscore the universal and long-lasting impacts of early-life famine exposure on health, irrespective of geographical and cultural differences.

Beyond the scope of aging, studies have shown that early life famine exposure is linked to a higher prevalence of cardiovascular diseases in later life. Chen et al. highlighted the sex-specific effects of fetal exposure to the 1959–1961 Chinese famine, showing a significant association with an increased risk of adult hypertension, particularly in males [19]. Further supporting this, Meng et al. demonstrated that prenatal famine exposure is associated with specific adulthood obesity patterns and an increased risk of type 2 diabetes, further emphasizing the profound and lasting impact of early life nutritional deprivation on long-term health outcomes [20]. Research from the Netherlands indicates irreversible effects of prenatal famine exposure on cerebral blood perfusion, particularly in the prefrontal cortex of males, potentially mediated by metabolic parameters like mid-life blood glucose levels [21]. Furthermore, exposure during pregnancy is suggested to impact gland development significantly, affecting thyroid function and health by age 50 [22]. These findings underscore the heightened susceptibility to diseases in middle age among individuals exposed to famine during early life. A comprehensive review by Heike et al. reveals that such exposure induces DNA methylation changes in genes associated with neuronal, neuroendocrine, and immune functions, leading to genetic-level qualitative changes [23]. As individuals age, these methylation abnormalities grow exponentially, contributing to the deterioration in neurological and mental health, and ultimately accelerating aging across various bodily organs and systems [24].

The interaction analysis between famine exposure and income is noteworthy. Higher income levels may mitigate the adverse effects of early life famine exposure through several potential mechanisms. Improved nutrition and dietary diversity are likely significant factors, as higher income allows for better access to a variety of nutrient-rich foods, which is critical for long-term health and aging [25]. Access to quality healthcare also plays a crucial role; individuals with higher incomes can afford better healthcare services, enabling early detection and treatment of health issues, thereby reducing the risk of aging-related diseases [26]. Reduced stress is another important factor; financial stability associated with higher income reduces chronic stress, which is known to have a detrimental impact on health and accelerate aging [27]. Additionally, higher income may facilitate healthier living conditions and access to resources that promote overall well-being, further mitigating

Groups	Events/Total	OR (95% CI)	P value
Unexposed	641/5723	Ref.	
In childhood exposed and less severe region	1308/7476	1.36 (0.94, 2.20)	0.940
In childhood exposed and severe region	55/290	1.58 (1.19, 2.10)	0.001
In utero exposed and less severe region	501/3871	1.50 (1.15, 1.97)	0.003
In utero exposed and severe region	38/183	2.92 (1.74, 4.79)	<0.001

Table 3. Famine severity exposure and aging. Note: Models were adjusted for age, CRP, sex, work type, educational level, regular physical exercise, income, smoke, drink, hypertension, diabetes, WC, BMI, HDL, uric acid, Alb and TG. CRP: C-reactive protein; WC: waist circumference; BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; Alb: albumin; TG: triglyceride.

the impacts of early life adversity [28]. These findings align with previous studies that highlight the buffering effect of socio-economic status on health outcomes following early life adversities [29].

In essence, exposure to famine during childhood and in utero represents a critical phase of early-life malnutrition. Recent global survey research underscores that malnutrition is second only to congenital anomalies in contributing to the burden of non-fatal diseases among children, with a pronounced impact on infants and toddlers under the age of 5 [30]. The immediate repercussions of early malnutrition not only precipitate health issues in affected children but also levy an economic strain on their families. Preliminary research delineates a correlation between severe childhood malnutrition and liver dysfunction indicators, such as fatty degeneration and hypoalbuminemia. Early nutritional deficiencies are linked to significant impairments in hepatic peroxisomes and mitochondria, alongside compromised metabolic liver functions. Without timely intervention, these detriments exacerbate with age, fostering metabolic irregularities and precipitating premature aging [31].

These findings lend credence to the “catch-up growth” hypothesis posited by Barker et al., which intimates that early-life adversities imprint lasting vulnerabilities on infants. Fetal growth restrictions due to malnutrition may instigate catch-up growth in later stages, markedly elevating disease susceptibility in adulthood [32]. Intriguingly, interaction analysis reveals that the detrimental impacts of early famine exposure might be mitigated by subsequent increases in income, ostensibly linked to enhancements in life quality and dietary habits. This observation aligns with Meng et al.’s analysis of the Jia Dao Biobank data in China, which associates prenatal famine exposure with heightened cardiovascular disease risks, moderated by the participants’ subsequent urban or rural residencies (p for interaction < 0.001) [33].

This body of work underscores the pivotal role of nutritional catch-up and dietary quality improvement in diminishing disease risks among those who endured early famine exposure. Income fluctuations throughout life significantly influence malnutrition risk, with lower-income families experiencing more pronounced weight loss and nutritional deficiencies [34]. The China Health and Nutrition Survey further elucidates that higher income levels engender dietary diversity [35], highlighting the global challenge of nutritional intake inequality exacerbated by economic disparities. Consequently, even for individuals who experienced famine, enhancements in socioeconomic status may partially rectify the damage inflicted by early malnutrition [36].

This study offers valuable insights into the long-term effects of famine exposure, but several limitations must be acknowledged. First, the cohort is drawn from an industrial city in northern China, specifically Hebei, where famine conditions were relatively moderate. This regional specificity may limit the generalizability of our findings to areas with more extreme famine conditions. Second, the cohort predominantly comprises male participants, which may not fully reflect gender-specific responses to famine. Although no significant gender interaction was detected, this could be due to the study’s limited ability to capture gender differences, as prior research has suggested sex-based variations in metabolic responses to famine [37–40], particularly regarding biological aging [18]. To address this, we performed subgroup analyses by sex, finding that famine significantly accelerated biological aging in men but not in women. However, the interaction effect was not significant, possibly due to the smaller sample size of female participants. Additionally, the absence of detailed data on adult dietary habits limits our ability to explore how post-famine nutrition might influence long-term health outcomes. This gap complicates the interpretation of the nuanced relationship between early-life famine exposure and aging processes [41]. Lastly, while we utilized PhenoAge as our primary measure of biological aging [42], the study did not incorporate newer third-generation biomarkers like DunedinPace due to dataset limitations [43]. Future research should include these advanced biomarkers to enhance the reliability and comprehensiveness of findings across different biological aging measures.

Conclusion

In summary, this study highlights that early-life famine exposure, whether during in utero or childhood phases, is associated with an elevated risk of aging in midlife. These effects are influenced by factors such as income levels and famine severity. From a public health perspective, it is crucial for individuals with such exposures to maintain healthy dietary habits and lifestyle choices. Proactive management of these aspects can help mitigate age-related diseases. This underscores the need for targeted health interventions and policies to improve long-term health outcomes for populations with historical famine exposure.

Data availability

Data will be made available upon reasonable request (Jin Zhang; E-mail: evergreen176700@163.com:).

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Author contributions

Tao Ma: Methodology, Software, Writing- original draft; Xiao-Meng Hao: Writing- original draft; Xiao-Wei Zhang: Methodology, Software; Xin-Yu Liu: Supervision, Validation; Yi-Ming Wang: Validation, Resources, Visualization; Qing-Song Zhang: Validation, Supervision; Jin Zhang: Conceptualization, Supervision, Validation, Resources, Project administration.

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Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Kailuan General Hospital and Tianjin Medical University Cancer Institute and Hospital and adhered to the principles of the Declaration of Helsinki. Participants or their legal representatives provided written informed consent. The Kailuan Study was retrospectively registered in the Chinese Clinical Trial Register (ChiCTR) on 24 August, 2011 (ChiCTR-TNRC-11001489; <http://www.chictr.org.cn/showprojen.aspx?proj=8050>).

Competing interests

The authors declare no competing interests.

Transparency statement

The manuscript's guarantor affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Correspondence and requests for materials should be addressed to J.Z.

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