Research Square

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Residential altitude and incident gastrointestinal disease in middle-aged and older adults: a nationwide cohort study

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Research Article

Keywords: Residential altitude, Gastrointestinal disease, Propensity score matching, Environmental factor, CHARLS

Posted Date: November 6th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11378195/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Acute exposure to high altitude has been associated with gastrointestinal symptoms. However, whether long-term residential altitude influences the risk of incident gastrointestinal disease (GID) remains unclear.

Methods

This study utilized nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS) from 2011 to 2020. Residential altitude was estimated according to the elevation of participants' county-level residential administrative units and categorized into lower-altitude (< 1,000 m) and middle-altitude (≥ 1,000 m) groups. Propensity score matching (PSM) with a 1:4 ratio was performed to balance baseline characteristics. Cox proportional hazards models were applied to estimate the association between altitude and incident GID. Restricted cubic spline (RCS) regression was applied to assess potential nonlinear associations. Subgroup analyses and sensitivity analyses using inverse probability of treatment weighting (IPTW) and the full cohort (n = 10,345) were conducted to evaluate robustness of the primary findings.

Results

Among 6,099 participants in the matched cohort, 850 (13.9%) developed incident GID during the follow-up period. Compared with residents in low-altitude regions, participants living in middle-altitude areas exhibited an elevated risk of incident GID (HR = 1.24, 95% CI: 1.06–1.45, *P* = 0.008). There was a significant dose-response association between altitude and GID risk (*P* for trend < 0.001), and RCS analysis further confirmed a significant nonlinear relationship (*P* for nonlinear = 0.042), whereby GID risk reached a plateau at altitudes above 1,000 m. Subgroup analyses revealed a significant effect modification by educational attainment. Sensitivity analyses based on the full cohort and IPTW yielded consistent results.

Conclusions

Higher residential altitude was associated with an increased risk of incident GID among middle-aged and older adults in China, with a nonlinear exposure-response pattern. These findings suggest that residential altitude may represent a potential environmental factor of gastrointestinal health in aging populations.

1. Introduction

Gastrointestinal disease (GID) represents a major public health problem affecting the health and quality of life of middle-aged and older adults worldwide [1, 2]. The Global Burden of Disease Study showed that in 2019, there were 2.86 billion cases of digestive diseases globally, resulting in 8 million deaths and 277 million disability-adjusted life years (DALYs) [1]. A study in Hong Kong, China, further reported that the hospitalization rate for GID increased from 4,713 to 5,241 per 100,000 population in recent years [3]. With aging, the physiological functions of the gastrointestinal tract, including motility, secretion of digestive enzymes and hormones, and nutrient absorption, gradually decline, making middle-aged and older adults a high-risk population for GID [4]. In addition to established risk factors, such as diet, lifestyle behaviors, and chronic underlying diseases, increasing attention has been directed toward the potential role of environmental exposures in the development and progression of GID in recent years.

The high-altitude environment, characterized by low temperature, hypoxia, low atmospheric pressure, and intense ultraviolet radiation, has been increasingly recognized as a potential contributor to gastrointestinal dysfunction [5]. A prospective study of military personnel who rapidly ascended to an altitude of 4,500 m reported that the incidence of diarrhea, bloating, and constipation increased significantly following high-altitude exposure, with some symptoms persisting for up to 6 months [6]. In addition, studies have found that residents in high-altitude areas have a higher rate of Helicobacter pylori infection and greater

severity of gastric disease [7]. Globally, approximately 503 million people live at altitudes of 1,500 m and above, including 81.6 million living above 2,500 m and 14.4 million above 3,500 m. China has the largest population residing above 3,500 m, predominantly on the Tibetan Plateau [8, 9]. However, existing studies have primarily focused on the acute physiological responses of individuals undergoing rapid ascent to high altitude or have relied on animal models. In contrast, populations residing long-term at high altitude are chronically exposed to multiple environmental stressors, including hypoxia, low temperature, and intense ultraviolet radiation, which may increase their susceptibility to GID. Nevertheless, large-scale longitudinal evidence regarding the association between long-term high-altitude residence and the risk of developing GID remains limited.

To address this knowledge gap, we used large-scale longitudinal cohort data from the China Health and Retirement Longitudinal Study (CHARLS) collected between 2011 and 2020 to investigate the association between residential altitude and the risk of incident GID among middle-aged and older adults in China, and to further examine the potential dose-response association between altitude and GID risk. Our findings may provide epidemiological evidence to inform the prevention and health management of GID, as well as the development of public health interventions for middle-aged and older populations residing in high-altitude regions.

2. Materials and methods

2.1. Data and sample

This study used follow-up data from CHARLS, a nationwide survey that collects high-quality data through structured one-on-one interviews. CHARLS is based on a nationally representative sample of Chinese individuals selected through multistage probability sampling across 28 provinces, covering 150 counties/districts and 450 villages/urban communities [10]. Further information about the CHARLS database is available on the official website (https://charls.charlsdata.com/). Informed written consent was obtained from all participants before the survey, and the study received ethical approval (approval number: IRB00001052-11015).

In this study, we excluded participants who were aged < 45 years in 2011, had cancer, had extreme body mass index (BMI) values (< 10 kg/m^2 or > 50 kg/m^2), lacked health information such as baseline GID, lacked residential address information, had prevalent GID in 2011, or were lost to follow-up in all four subsequent surveys. A total of 10,345 eligible participants were initially included. After 1:4 propensity score matching (PSM), 6,099 eligible participants were ultimately included in this study. The detailed inclusion and exclusion flowchart is presented in Fig. 1.

2.2. Assessment of GID

GID status was defined based on participants' responses to the Health Status and Functioning questionnaire in CHARLS. All data were collected by trained interviewers using standardized questionnaires consistent with international standards for aging research. Participants were asked: "Have you ever been diagnosed by a doctor with stomach or other digestive diseases (excluding tumors or cancer)?" Participants who answered "Yes" were classified as having GID. A binary variable (GID: yes vs. no) was used in the analyses.

2.3. Assessment of altitude

To protect participants' privacy, CHARLS did not provide detailed address information for each participant. Only the name of the administrative district (county) in which each participant resided was publicly available. The participants' place of residence was determined by their community ID. We used the elevation of the centroid coordinates of each participant's administrative district (county) to represent their altitude. Altitude data were obtained from the global geographical database GeoNames (https://www.geonames.org/). This database provided mean elevation data with an accuracy of 30 m, derived from the National Aeronautics and Space Administration (NASA) Digital Elevation Model (DEM). Consistent with prior published work [11], altitude was operationalized as a binary variable: participants residing at < 1,000 m were categorized into the low-altitude group, and those living at ≥ 1,000 m were assigned to the middle-altitude group.

2.4. Covariates

We selected the following potential confounders associated with GID: age (45–59 or ≥ 60 years), gender (male or female), marital status (married/cohabiting or others), residence (urban or rural), education level (illiterate, primary school, middle school, or high school or above), smoking status (no or yes), drinking status (no or yes), BMI groups (underweight, normal weight, overweight, or obesity), sleep duration (< 6 h, 6–8 h, or ≥ 8 h), and chronic comorbidities (0, 1, and ≥ 2). BMI was calculated as weight in kilograms divided by height in meters squared. Underweight was defined as BMI < 18.5 kg/m^2, normal weight as 18.5 ≤ BMI < 24.0 kg/m^2, overweight as 24.0 ≤ BMI < 28.0 kg/m^2, and obesity as BMI ≥ 28.0 kg/m^2. Chronic comorbidities were defined as the total number of chronic diseases other than GID, including hypertension, dyslipidemia, diabetes, chronic lung diseases, liver disease, heart attack, stroke, kidney disease, emotional or psychiatric problems, memory-related disease, arthritis or rheumatism, and asthma.

2.5. Statistical analysis

In the present study, categorical variables were presented as numbers (percentages). Differences in characteristics between groups were compared using the chi-square test. PSM was used to balance differences between the low-altitude and middle-altitude groups. Age, gender, marital status, residence, education level, smoking status, drinking status, BMI groups, sleep duration, and chronic comorbidities were included as covariates in the PSM analysis. Nearest-neighbor matching was performed with a matching ratio of 1:4 and a caliper value set at 0.1. After matching, standardized mean difference (SMD) was used to assess the balance of baseline characteristics before and after matching. Love plot was used to evaluate the degree of imbalance between the two groups before and after matching.

We calculated the incidence rate of GID per 1,000 person-years. Cox proportional hazards regression models were used to examine the longitudinal association between altitude and incident GID from 2011 to 2020, with results presented as hazard ratios (HRs) along with 95% confidence intervals (CIs). In the CHARLS survey, participants were asked about the specific time of disease onset. The endpoint was defined as the occurrence of GID, and the underlying time scale ranged from 0 to 9 years. The log-rank test was used to examine differences in survival curves between the two groups. We further explored the effects of altitude quartiles (with altitude treated as a continuous variable) on GID incidence and calculated the *P* for trend. Three models were constructed to control for potential confounders: Model 1 adjusted for age, gender, marital status, residence, and education level; Model 2 additionally adjusted for smoking status, drinking status, BMI groups, and sleep duration based on Model 1; and Model 3 further adjusted for chronic comorbidities based on Model 2. Moreover, restricted cubic spline (RCS) regression was employed to explore the nonlinear associations between altitude and the risk of incident GID.

To test the robustness of our results, we performed the following analyses: (1) we conducted subgroup analyses stratified by all influencing factors to compare the associations across different subgroups; (2) we examined the main outcomes among all participants without PSM matching (n = 10,345); and (3) we used inverse probability of treatment weighting (IPTW) derived from propensity scores to assess the consistency between the results after IPTW and those of the main outcomes. All statistical analyses were performed using R version 4.5.3, with a two-tailed *P* value < 0.05 indicating statistical significance.

3. Results

3.1 Basic characteristics of the selected participants

After excluding ineligible participants, 10,345 middle-aged and older adults aged 45 years and older were included, of whom 9,094 (87.9%) resided in low altitude areas and 1,251 (12.1%) in middle altitude areas. Participants residing at different altitudes showed statistically significant differences in marital status, residence, education level, drinking status, BMI group, and sleep duration (all *P* < 0.05). To reduce these baseline imbalances, we performed 1: 4 PSM using these sociodemographic characteristics and health-related variables as matching variables. After matching, 4,810 participants were ultimately included, of whom 3,831 (79.6%) resided in low altitude areas and 979 (20.4%) in middle altitude areas. Except for BMI groups (*P* < 0.001), the two groups showed no statistically significant differences in sociodemographic characteristics or health-related variables (all *P* > 0.05) (Table 1). The love plot showing the absolute SMDs of all covariates indicated that all covariates achieved

adequate balance after matching, with post-matching SMDs < 0.1 (Fig. 2A). The density plots of the propensity score distribution before and after PSM matching also demonstrated satisfactory matching performance (Fig. 2B).

Table 1
Baseline characteristics of enrolled participants before and after PSM.

Characteristics	Before PSM					After PSM				
	Overall (n = 10345)	Low altitude (n = 9094)	Middle altitude (n = 1251)	SMD	*P* value	Overall (n = 6099)	Low altitude (n = 4854)	Middle altitude (n = 1245)	SMD	*P* value
Age, n (%)				0.006	0.871				0.008	0.832
45–59	5903 (57.1)	5186 (57.0)	717 (57.3)			3484 (57.1)	2769 (57.0)	715 (57.4)		
≥ 60	4442 (42.9)	3908 (43.0)	534 (42.7)			2615 (42.9)	2085 (43.0)	530 (42.6)		
Gender, n (%)				0.021	0.513				0.028	0.399
Male	5149 (49.8)	4515 (49.6)	634 (50.7)			3009 (49.3)	2381 (49.1)	628 (50.4)		
Female	5196 (50.2)	4579 (50.4)	617 (49.3)			3090 (50.7)	2473 (50.9)	617 (49.6)		
Marital status, n (%)				0.151	< 0.001				0.019	0.573
Married/Cohabited	9078 (87.8)	8038 (88.4)	1040 (83.1)			5129 (84.1)	4089 (84.2)	1040 (83.5)		
Others	1267 (12.2)	1056 (11.6)	211 (16.9)			970 (15.9)	765 (15.8)	205 (16.5)		
Residence, n (%)				0.112	< 0.001				0.016	0.629
Urban	3895 (37.7)	3483 (38.3)	412 (32.9)			2056 (33.7)	1644 (33.9)	412 (33.1)		
Rural	6450 (62.3)	5611 (61.7)	839 (67.1)			4043 (66.3)	3210 (66.1)	833 (66.9)		
Education level, n (%)				0.289	< 0.001				0.035	0.750
Illiterate	2769 (26.8)	2322 (25.5)	447 (35.7)			2099 (34.4)	1658 (34.2)	441 (35.4)		
Primary school	4066 (39.3)	3557 (39.1)	509 (40.7)			2514 (41.2)	2005 (41.3)	509 (40.9)		
Middle school	2271 (22.0)	2075 (22.8)	196 (15.7)			1011 (16.6)	815 (16.8)	196 (15.7)		
High school or above	1239 (12.0)	1140 (12.5)	99 (7.9)			475 (7.8)	376 (7.7)	99 (8.0)		
Smoking status, n (%)				0.034	0.264				0.009	0.797
No	6970 (67.4)	6145 (67.6)	825 (65.9)			4048 (66.4)	3226 (66.5)	822 (66.0)		
Yes	3375 (32.6)	2949 (32.4)	426 (34.1)			2051 (33.6)	1628 (33.5)	423 (34.0)		

Abbreviations: BMI, body mass index; PSM, propensity score matching; SMD, standardized mean difference.

Characteristics	Before PSM					After PSM				
	Overall (n = 10345)	Low altitude (n = 9094)	Middle altitude (n = 1251)	SMD	*P* value	Overall (n = 6099)	Low altitude (n = 4854)	Middle altitude (n = 1245)	SMD	*P* value
Drinking status, n (%)				0.112	< 0.001				0.010	0.769
No	6777 (65.5)	5900 (64.9)	877 (70.1)			4290 (70.3)	3419 (70.4)	871 (70.0)		
Yes	3568 (34.5)	3194 (35.1)	374 (29.9)			1809 (29.7)	1435 (29.6)	374 (30.0)		
BMI groups, n (%)				0.238	< 0.001				0.167	< 0.001
Underweight	499 (4.8)	399 (4.4)	100 (8.0)			337 (5.5)	237 (4.9)	100 (8.0)		
Normal weight	4373 (42.3)	3782 (41.6)	591 (47.2)			2881 (47.2)	2296 (47.3)	585 (47.0)		
Overweight	2425 (23.4)	2213 (24.3)	212 (16.9)			1264 (20.7)	1052 (21.7)	212 (17.0)		
Obesity	3048 (29.5)	2700 (29.7)	348 (27.8)			1617 (26.5)	1269 (26.1)	348 (28.0)		
Sleep duration, n (%)				0.228	< 0.001				0.028	0.677
< 6 h	2535 (24.5)	2219 (24.4)	316 (25.3)			1554 (25.5)	1239 (25.5)	315 (25.3)		
6–8 h	4708 (45.5)	4251 (46.7)	457 (36.5)			2291 (37.6)	1834 (37.8)	457 (36.7)		
≥ 8 h	3102 (30.0)	2624 (28.9)	478 (38.2)			2254 (37.0)	1781 (36.7)	473 (38.0)		
Chronic comorbidities, n (%)				0.055	0.194				0.014	0.907
0	4493 (43.4)	3977 (43.7)	516 (41.2)			2543 (41.7)	2028 (41.8)	515 (41.4)		
1	3208 (31.0)	2814 (30.9)	394 (31.5)			1935 (31.7)	1542 (31.8)	393 (31.6)		
≥ 2	2644 (25.6)	2303 (25.3)	341 (27.3)			1621 (26.6)	1284 (26.5)	337 (27.1)		

Abbreviations: BMI, body mass index; PSM, propensity score matching; SMD, standardized mean difference.

3.2 Association between altitude and incident GID

A total of 850 (13.9%) participants developed incident GID. Individuals with incident GID tended to be female, less educated, and have more chronic diseases (Supplementary Table S1). In the middle-altitude group, the incidence rate per 1,000 person-years was 21.20, which was 1.26 times that of the low-altitude group. After adjustment for all covariates, the final model (Model 3) showed that the risk of incident GID among those residing at middle altitude was 24% higher than that among those at low altitude (HR = 1.24, 95% CI: 1.06-1.45, *P* = 0.008) (Table 2, Supplementary Figure S1). The Q4 group (> 632.05 m) had a rate 1.39 times that of the Q1 group (< 43.50 m) (20.46 vs. 14.73 per 1,000 person-years). Model 3 showed that the risk of incident GID in the Q3 group (156.47-632.04 m) was 28% higher than that in the Q1 group (HR = 1.28, 95% CI: 1.05-1.56, *P* = 0.015), and those in

the Q4 group presented a 37% higher risk (HR = 1.37, 95% CI: 1.13-1.67, *P* = 0.002). A significant increasing trend in GID risk was observed across ascending altitude quartiles (*P* for trend < 0.001) (Table 2).

Table 2
Incidence rates and hazard ratios of incident GID across altitude groups after PSM.

Exposure	N	Number of events	Incidence rate per 1000 person-years	HR (95% CI)		
				Model 1	Model 2	Model 3
Altitude groups						
Low altitude	4854	646	16.84	Reference	Reference	Reference
Middle altitude	1245	204	21.20	1.26 (1.08–1.48)**	1.25 (1.04–1.46)**	1.24 (1.06–1.45)**
Altitude (m)						
Q1 (< 43.50)	1525	181	14.73	Reference	Reference	Reference
Q2 (43.50-156.46)	1525	193	16.05	1.16 (0.94–1.42)	1.16 (0.94–1.42)	1.13 (0.92–1.38)
Q3 (156.47-632.04)	1525	237	19.75	1.39 (1.14–1.70)***	1.36 (1.11–1.65)**	1.28 (1.05–1.56)*
Q4 (≥ 632.05)	1524	239	20.46	1.44 (1.18–1.75)***	1.43 (1.17–1.74)***	1.37 (1.13–1.67)**
P for trend				< 0.001	< 0.001	< 0.001

* *P* < 0.05; ** *P* < 0.01; *** *P* < 0.001

Model 1: adjusted for age, gender, marital status, residence, and education level; Model 2: additionally adjusted for smoking status, drinking status, BMI groups, and sleep duration based on Model 1; and Model 3: further adjusted for chronic comorbidities based on Model 2. Abbreviations: HR, hazard ratio; CI, confidence interval.

3.3 Survival probability and RCS analyses

Over the nine-year follow-up period, the middle-altitude group exhibited lower survival probability, and the log-rank test showed a statistically significant difference between the two groups (*P* = 0.005) (Figure 2C). RCS analysis showed the overall association between residential altitude and incident GID was statistically significant (*P* for overall < 0.001), and a significant nonlinear relationship was observed (*P* for nonlinear = 0.042). When altitude exceeded 1,000 m, the risk gradually stabilized and reached a plateau, although the wide 95% CI suggested greater uncertainty in effect estimates at higher altitudes (Figure 2D).

3.4 Subgroup and sensitivity analyses

The results of the subgroup analyses showed that the increased risk associated with middle-altitude residence was generally consistent across most subgroups (all *P* for interaction > 0.05). Notably, a significant effect modification was observed for education level (*P* for interaction = 0.008), with the strongest association found among participants with middle school education (HR = 2.31, 95% CI: 1.55-3.44, *P* < 0.001) (Figure 3). We further performed analyses in the full population to examine the robustness of the main findings. Among all participants (n = 10,345), a total of 1,387 (13.4%) middle-aged and older adults developed incident GID during 81,655 person-years of follow-up. The association between altitude and incident GID was consistent before and after PSM (Supplementary Table S2). To reduce confounding by observed covariates, IPTW was used to construct a weighted pseudo-population (Supplementary Table S3). Both the SMDs and the density plots of the propensity score distribution indicated that covariate balance was well achieved after weighting (Supplementary Figure S2, Supplementary Figure S3). The association between altitude and incident GID after IPTW was consistent with the results of the main outcomes (Supplementary Table S4).

4. Discussion

Based on the nationally representative CHARLS cohort of middle-aged and older adults from 2011 to 2020, this study revealed that residence at middle altitude (≥ 1,000 m) was significantly associated with an increased risk of incident GID, with an approximately 24% increase in risk and a nonlinear dose-response relationship, in which the incidence risk plateaued after altitude exceeded 1,000 m. Sensitivity analyses consistently supported the robustness of our main outcomes. These findings suggest that long-term residence in middle and high altitudes may be an important environmental risk factor for incident GID, and this study provides novel epidemiological evidence for this association based on a large-scale longitudinal cohort.

Previous studies on altitude and digestive system health have mostly focused on acute mountain sickness and small sample populations with short-term rapid ascent to high altitude [12-15], whereas evidence from long-term community-dwelling middle-aged and older adults remains limited. The present study found that the risk of incident GID was significantly higher among residents of middle-altitude areas than among those of low-altitude areas, and this result was generally consistent with previous findings on the effects of altitude on the association between altitude and other health outcomes. A study based on the West China Natural Population Cohort Study (WCNPCS) and the West China Health and Aging Trend (WCHAT) study found that individuals chronically exposed to high-altitude environments had a biological age significantly higher than their chronological age, and their psychological and social adaptation may also be affected by high-altitude environments [16]. Wu et al. [17] found that long-term residence at high altitude was positively associated with the risk of multimorbidity of chronic diseases. Populations in high-altitude regions of China, such as Tibet and Qinghai, tend to consume a traditional Tibetan diet characterized by high salt, high fat, and high animal protein, with a large intake of energy-dense foods such as beef, mutton, butter tea, and tsampa, and a very low frequency of fresh vegetable and fruit consumption [18]. This traditional Tibetan “three-high” dietary pattern aggravates the risk of multiple chronic disease multimorbidity [19]. In contrast, populations in low-altitude areas have more diverse food sources and greater availability of fresh vegetables and fruits, which may partly explain their relatively lower risk of incident GID. Interventions such as dietary modification and probiotic supplementation are promising strategies for the prevention and treatment of high-altitude-related intestinal diseases [20], and may improve health outcomes among high-altitude residents.

Notably, the RCS analysis indicated that the risk of incident GID did not increase monotonically with altitude, but instead plateaued after 1,000 m. This pattern differs from the continuously increasing disease risk reported in previous studies of populations with short-term rapid ascent to high altitude [6, 21]. We propose the following explanations for this discrepancy. First, the participants in this study were middle-aged and older permanent residents who had resided long-term at their respective altitudes, rather than individuals with short-term high-altitude exposure. Populations residing at high altitude may develop compensatory physiological changes through long-term acclimatization [22, 23]. Second, survivor bias and environmental selection effects may also contribute to the observed associations. Indigenous high-altitude populations may establish stable adaptive mechanisms via pathways including EPAS1 gene variants, nitric oxide-mediated regulation of vasodilatory function, and improved oxygen utilization efficiency [24, 25]. Moreover, adaptive remodeling of the gut microbiota may be an important factor. After Han Chinese individuals from low-altitude areas migrate to high altitude, their gut microbiota composition gradually resembles that of indigenous Tibetan high-altitude populations, and this microbial alteration appears to be environmentally reversible [26]. Following prolonged high-altitude residence, initial acute gastrointestinal stress gradually subsides, accompanied by a continuous shift in gut microbiota toward the microbial profile characteristic of indigenous high-altitude populations [27-29]. However, the number of high-altitude residents included in this study was relatively small, and the confidence intervals of the RCS curve were wide at high altitudes. Therefore, the precise location and shape of the plateau require further validation in future studies that include larger samples of permanent high-altitude residents.

In terms of potential mechanisms, high-altitude hypoxia can stabilize hypoxia-inducible factor-1α (HIF-1α), leading to microcirculatory disturbances in the gastrointestinal mucosa, reduced mucosal blood flow, and disrupted energy metabolism [30]. Hypoxia can also decrease splanchnic perfusion, induce inflammatory responses and oxidative stress, and impair the intestinal barrier [31, 32]. Meanwhile, it disrupts the structure of the gut microbiota and reduces protective metabolites such as short-chain fatty acids, thereby increasing the risk of GID [20, 33, 34]. Animal experiments have further confirmed that hypoxia can aggravate gastric mucosal injury caused by Helicobacter pylori infection and inhibit the Nrf2

antioxidant pathway [35]. In addition, high-altitude residents exhibit distinct dietary patterns and disparities in healthcare accessibility and medication utilization [19], which may act synergistically with hypoxia to modulate gastrointestinal health risk.

Subgroup analyses revealed significant effect modification by education level in the association between altitude and incident GID (*P* for interaction = 0.008), with the greatest increase in risk observed among participants with a middle school education (HR = 2.31). This finding may reflect differences in disease awareness and healthcare utilization across education levels. Previous studies have shown that lower educational attainment is closely associated with lower health literacy [36], and older adults in China with lower socioeconomic status may experience more pronounced underdiagnosis of chronic diseases [37]. In this study, no significant association was observed among participants with primary school education or below, which may partly arise from fewer opportunities for medical consultation and disease diagnosis. In addition, education level may also reflect different occupational and lifestyle characteristics. Individuals with middle school education may experience higher levels of physical labor or irregular lifestyles. A study of railway construction workers on the Qinghai-Tibet Plateau in China found that the incidence of gastrointestinal bleeding increased with altitude, with observed lesions including hemorrhagic gastritis, gastric and duodenal ulcers, and gastric mucosal erosion [38]. Therefore, occupational or lifestyle-related exposures may act additively with high-altitude hypoxia.

To our knowledge, this study is the first to examine the association between altitude and the risk of incident GID among long-term middle-aged and older residents based on a large-scale population and longitudinal database. However, this study has several limitations. First, because CHARLS does not provide detailed geographic location data, we used the altitude of the administrative district (county) of residence as a proxy for individual altitude exposure, which may not accurately capture participants' individual exposure histories. Second, CHARLS did not collect detailed information on specific GID subtypes, preventing stratified analyses by specific disease subtypes. Finally, although we included as many confounding factors as possible, residual confounding could not be completely excluded. Owing to the limitations of CHARLS, we did not include the potential confounding effects of factors such as dietary patterns and medications. Future larger-scale, targeted cohort studies of long-term residents in high-altitude areas should incorporate more specific GID subtypes and biomarkers such as gut microbiota to further elucidate the association between altitude and incident GID in this population.

5. Conclusion

In summary, our findings suggest that residential altitude is associated with a higher risk of incident GID among middle-aged and older adults. Compared with residents of low-altitude areas, residents of middle-altitude areas had an approximately 24% higher risk of incident GID, with a nonlinear dose-response relationship that appeared to plateau beyond 1,000 m. This study provides an important reference for future public health policy and program development. Interventions targeting modifiable factors, such as improving dietary structure, protecting gut microecology, and promoting early screening and chronic disease management for GID, may help reduce the GID burden in this population. Looking ahead, conducting research aimed at formulating evidence-based health policy recommendations for higher-altitude areas and promoting intervention studies on hypoxia-related gastrointestinal injury will be crucial for reducing the health risks associated with high-altitude residence.

Abbreviations

CHARLS
China Health and Retirement Longitudinal Study
CI
confidence interval
GID
gastrointestinal disease
HR
hazard ratio
IPTW

inverse probability of treatment weighting
PSM
Propensity score matching
RCS
Restricted cubic spline
SMD
standardized mean difference

Declarations

Acknowledgments

We sincerely acknowledge all participants of the China Health and Retirement Longitudinal Study (CHARLS) for their valuable contributions and thank the CHARLS research team for their dedication to data collection, management, and dissemination of this high-quality longitudinal cohort dataset.

Funding

No funding has been received for the study.

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SS: Conceptualization, Software, Formal analysis, Writing–review & editing. YZ: Methodology, Writing–review & editing. DM: Data curation, Writing–review & editing. LZ, XW: Writing–review & editing. ST: Conceptualization, Supervision, Writing–review & editing. All authors approved the final version.

Data Availability

The datasets supporting the findings of this study are publicly available from the China Health and Retirement Longitudinal Study (CHARLS) repository: [http://charls.pku.edu.cn/en].

Ethics Approval and Consent to Participate

This study was approved by the Biomedical Ethics Review Committee of Peking University (approval number: IRB00001052-11015) and adhered to the ethical guidelines of the Declaration of Helsinki. All participants provided written informed consent.

Consent for Publication

Not applicable

Competing interests

The authors declare no competing interests.

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Figures

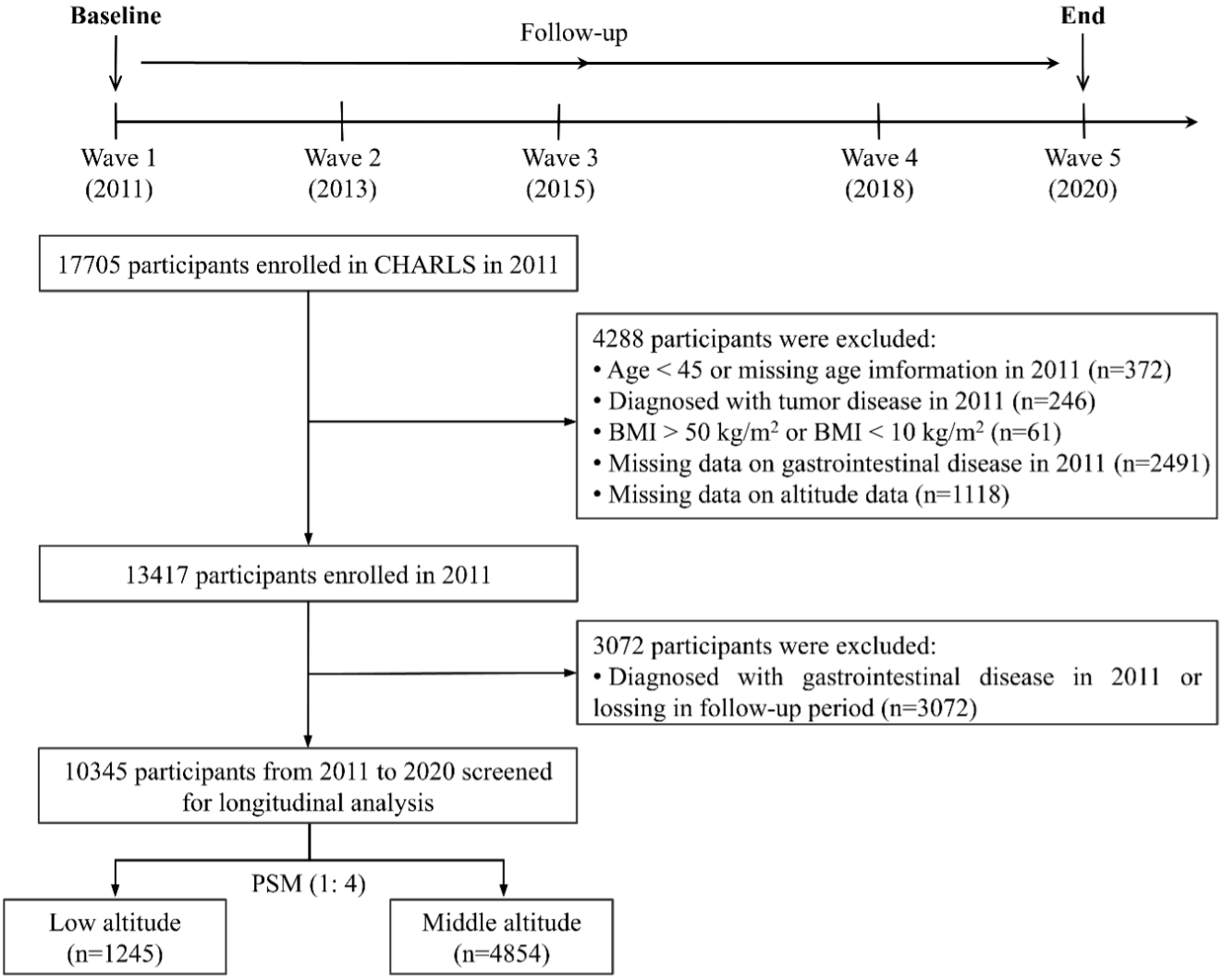


Figure 1

Flowchart of samples screened in the study.

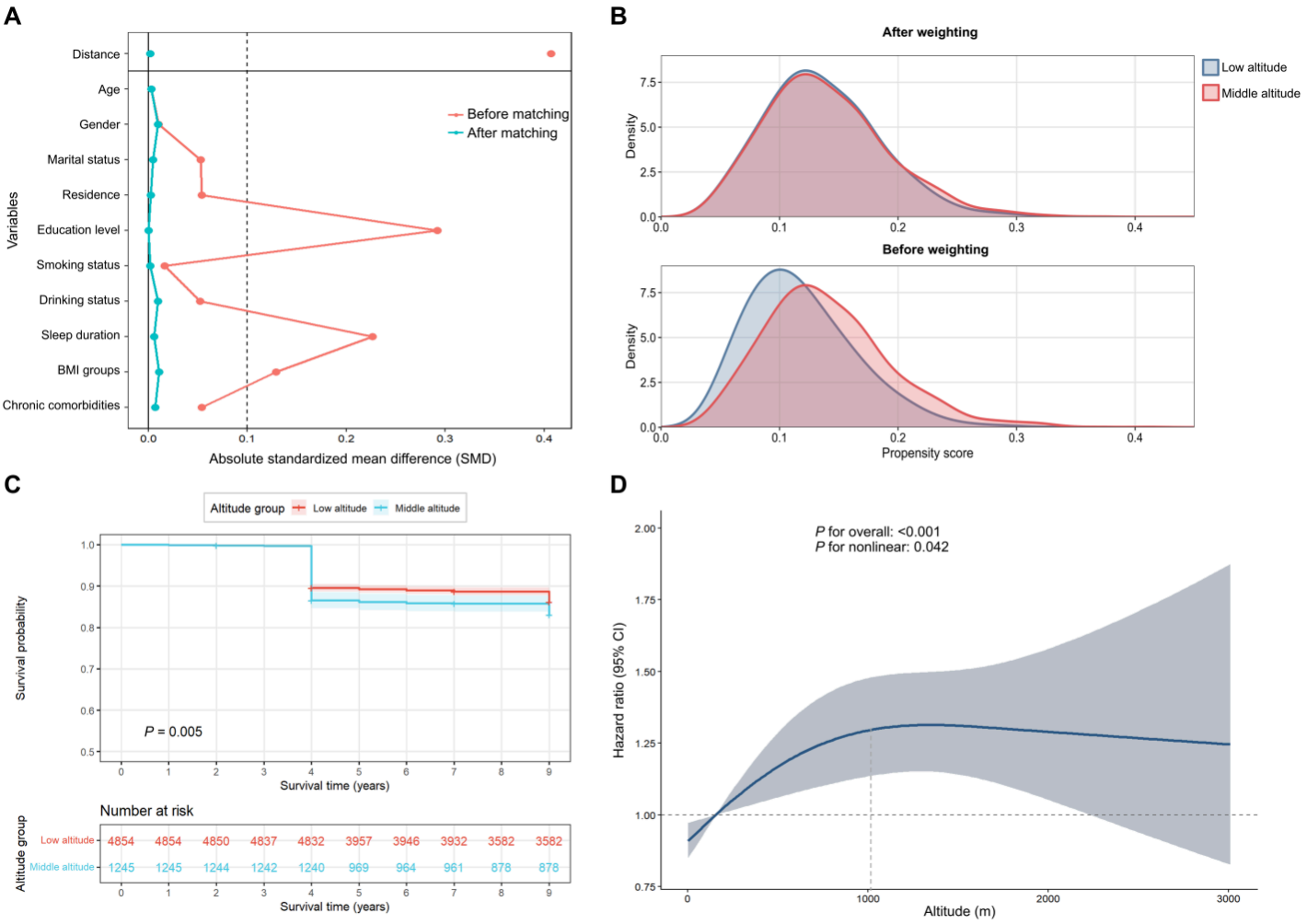


Figure 2

Association between altitude and the incidence of GID after PSM. (A)Absolute SMDs of covariates before and after PSM. The vertical dashed line indicates the SMD threshold of 0.1. (B) Propensity score distribution density before and after matching. (C) Kaplan-Meier survival curves according to altitude groups, with numbers at risk shown below. (D) RCS plot showing the dose-response relationship between altitude and the hazard ratio for GID, all covariates were adjusted.

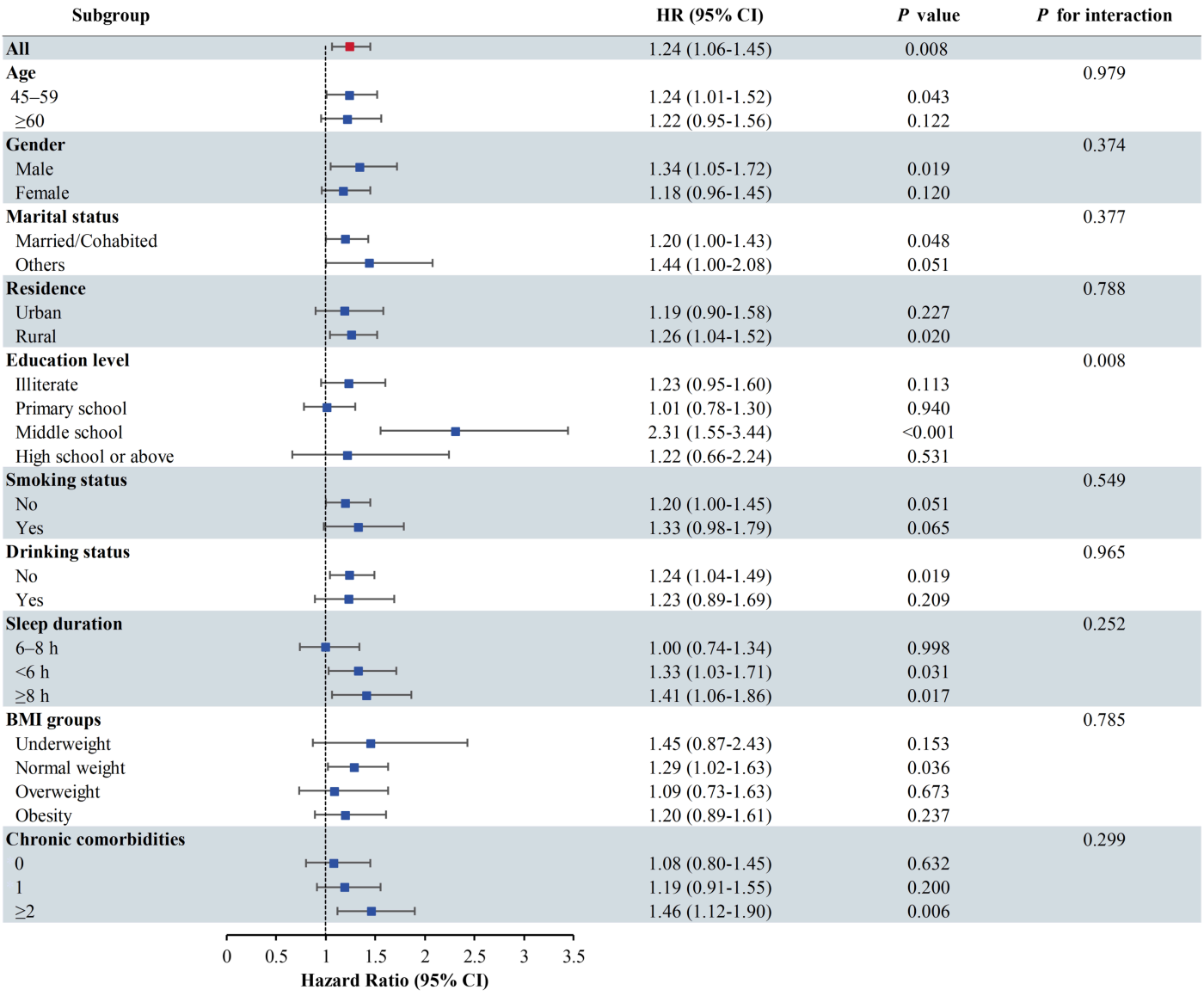


Figure 3

Forest plots of subgroup analyses.

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