Depression at High Altitude: The Relationship Between Altitude and Depression Risk

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Abstract

To investigate the relationship between altitude and depression in populations, this study utilized data from the 2016-2020 China Family Panel Studies, the 2015 China Health and Retirement Longitudinal Study, the 2016 Adult Physical and Mental Health Survey in Yushu, Qinghai, and the China City Statistical Yearbook, among others, and employed multilevel linear models, mediation models, and epidemiological case-control methods for data analysis. The results indicate that: after controlling for individual- and regional-level factors, there exists a positive correlation between altitude and depression; per capita GDP and C-reactive protein exert a mediating effect between altitude and depression; populations living at altitudes of 500-1,000, 1,000-2,000, and 4,000-6,000 meters have depression risks that are 1.53-1.79 times, 1.67-2.25 times, and approximately 9 times higher, respectively, compared to those living below 500 meters; in areas at 500-2,000 meters altitude, middle-aged and older adults have higher depression risk than young adults, while in high-altitude regions of 4,000-6,000 meters, young adults have higher depression risk than middle-aged and older adults. In summary, the study suggests that altitude is a risk factor for depression, and that depression prevention efforts among different age groups in different altitude regions warrant heightened attention.

Full Text

Melancholy Above the Plateau: The Relationship Between Altitude and Depression Risk

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Abstract

To elucidate the relationship between altitude and depression in human populations, this study analyzed data from the 2016–2020 China Family Panel Studies, the 2015 China Health and Retirement Longitudinal Study, the 2016 Yushu Adult Physical and Mental Health Survey in Qinghai, and the *China City Statistical Yearbook*. Multilevel linear modeling, mediation analysis, and epidemiological case-control methods were employed. The results demonstrate a positive association between altitude and depression after controlling for individual- and regional-level factors. Per capita GDP and C-reactive protein serve as mediators in the altitude-depression relationship. Compared to individuals living below 500 meters, those residing at 500–1,000 meters, 1,000–2,000 meters, and 4,000–6,000 meters face 1.53–1.79 times, 1.67–2.25 times, and approximately 9 times higher depression risk, respectively. Middle-aged and elderly individuals in 500–2,000 meter zones exhibit higher depression risk than younger populations, whereas young people in 4,000–6,000 meter zones show higher risk than middle-aged and elderly residents. These findings indicate that altitude constitutes a risk factor for depression, necessitating heightened prevention efforts tailored to different altitude zones and age groups.

Keywords: depression risk, plateau, altitude, age difference

Depression represents one of the most prevalent psychiatric disorders globally (Wang et al., 2014), attracting widespread concern and emerging as a critical public health issue (Liu et al., 2020). Global burden of disease data indicate that approximately 330 million people suffered from depression worldwide in 2021, yielding a prevalence rate of 4.4% (Institute of Health Metrics and Evaluation, 2021). In China, the lifetime prevalence of depressive disorders among adults reaches 6.8%, with a 12-month prevalence of 3.6%, underscoring the urgent need to address mental health among Chinese residents (Lu et al., 2021). Multiple studies confirm that depression inflicts substantial health losses on individuals, with depressed patients exhibiting heightened vulnerability to cardiovascular diseases (Freedland et al., 2021), elevated hospitalization risks, and increased mortality (Correll et al., 2015). Moreover, individuals with depression may suffer recurrent episodes throughout their lives (Monroe, 2022), making further research on depression critically important.

Existing research has identified numerous depression risk factors, including biological genetics, inflammation, and socioeconomic environments (Otte et al., 2016; Malhi & Mann, 2018; Kwong et al., 2019). Clinical studies suggest that inflammation and vascular dysfunction contribute to depression onset (Dudek et al., 2020). Depression development closely relates to central neurotransmitters such as serotonin, dopamine, norepinephrine, and epinephrine (Mulinari, 2012), with interleukin levels and peripheral blood tryptophan concentrations also correlating with depression severity (Maes et al., 1997). Additionally, factors including age, gender, marital status, ethnicity, education level, and socioeconomic status have demonstrated associations with depression (Cao et al., 2021; Zhang et al., 2022; Shi & Yang, 2020).

Bronfenbrenner's ecological systems theory, a foundational framework in developmental psychology, posits that individuals' ecological environments comprise microsystems, mesosystems, exosystems, macrosystems, and chronosystems, all of which interact with developing individuals and shape psychological development (Bronfenbrenner, 1979). Under this theoretical influence, the importance of natural environmental factors in psychological development has gained increasing recognition, with growing attention to how air quality and other natural environmental factors affect mental health (Ascone et al., 2024). Such research is viewed as a valuable complement to micro-level, individual-centered perspectives (Zhao et al., 2024). However, despite altitude being a crucial geographical environmental characteristic in human ecosystems, research examining its relationship with depression remains limited. Nelson (1982) assessed 20 American mountaineers during a 35-day expedition, administering depression tests at 3,810 meters and 5,000 meters, finding that depression scores increased with altitude. DelMastro et al. (2011) analyzed U.S. health survey data, revealing a correlation between state-level depression prevalence and average altitude. Similarly, Zaeh et al. (2016) compared residents of Peru living at 3,825 meters versus below 200 meters, finding major depression rates approximately six times higher in high-altitude regions. Kious et al. (2019) used 900 meters as a cutoff to classify high- and low-altitude groups, finding that U.S. medical students migrating from low to high altitude exhibited increased depression scores. Beyond these studies, evidence on the altitude-depression relationship remains scarce, and current findings derive primarily from U.S. and Peruvian populations. For China, with its vast plateau regions, research on this relationship is extremely limited, with existing studies focusing mainly on altitude's impact on social adaptation or physical health (Gao et al., 2023). Therefore, this study's first objective is:

Research Objective 1: To analyze the relationship between altitude and depression among Chinese residents, providing additional evidence from Chinese populations.

Mechanism analysis facilitates deeper understanding of causal relationships between factors, enabling more accurate prediction and interpretation of systemic or phenomenological logic. Following examination of the altitude-depression relationship, further investigation of underlying mechanisms is warranted. As psychiatric research advances, evidence suggests that many mental disorders, including depression, result from gene-environment interactions (Matosin et al., 2018). The diathesis-stress model, which emphasizes interactions between environment and individual vulnerability, has become an important theoretical framework for explaining depression onset and progression (Finkel et al., 2022). This model posits that dynamic interactions between stressful environments and individual characteristics constitute key factors in depression development (Monroe & Simons, 1991), with stressful environments potentially amplifying vulnerability factors (such as genetic makeup and early adverse experiences) and increasing depression susceptibility (Colodro-Conde et al., 2018). Guided by this model, researchers have found that environmental factors can alter biological characteristics like genes and proteins, with these changes associating with depressive symptoms (Nielsen et al., 2020). In high-altitude regions, hypobaric hypoxia and cold, dry stress environments can induce oxidative stress, which interacts with neuroinflammation and related genes to trigger depression (Ng et al., 2008; Salim, 2014). Additionally, research indicates that hypoxic environments at high altitude cause cellular hypoxia, increasing inflammatory risk and elevating inflammatory markers such as C-reactive protein (Hu et al., 2016). Inflammation plays a crucial role in depression etiology (Barnes et al., 2017), with depressive symptoms correlating with C-reactive protein concentrations (Frank et al., 2021; Ma et al., 2024), and depressed patients typically showing higher C-reactive protein levels than healthy individuals (Jorgensen, 2018). Thus, examining C-reactive protein's mediating role in the altitude-depression relationship is essential when considering gene-environment interactions.

Furthermore, the diathesis-stress model identifies stressful life events and high-risk living environments as depression risk factors (Ringwald et al., 2022), with stressful environments amplifying individual vulnerability and increasing mental illness risk (Arnau-Soler et al., 2019; Wang et al., 2023). Socioeconomic environments, as important components of living conditions, have attracted increasing attention regarding their relationship with depression. Research indicates that income and financial stress strongly correlate with depression (Dijkstra-Kersten et al., 2015), with poorer economic conditions increasing population depression incidence (Dunn et al., 2011; Jin et al., 2020). Studies also show that socioeconomic development level constitutes an important factor explaining regional differences in depression prevalence (Li et al., 2021), with lower economic development potentially increasing residents' depression risk (Domènech-Abella et al., 2018). Residents in poor socioeconomic environments face substantially increased poverty risk, with poverty-related worries, uncertainty, and lower social status representing important mental illness risk factors (Ridley et al., 2020). In China, high-altitude regions' geographical and climatic constraints typically result in slower economic development than low-altitude areas, with altitude's negative impact on regional economy empirically confirmed (Zhai & Sun, 2012). Regional per capita GDP serves as a crucial indicator of socioeconomic environment, necessitating investigation of its mediating mechanism between altitude and depression from an economic perspective. Therefore, this study's second objective is:

Research Objective 2: To analyze the mediating roles of C-reactive protein and regional per capita GDP in the relationship between altitude and depression.

Age constitutes a disease risk factor, with health and disease patterns varying across age groups. On one hand, different age groups face distinct psychological developmental tasks and challenges: adolescents confront academic pressure and identity formation, middle-aged individuals face occupational, familial, and midlife crisis pressures, while elderly adults deal with physical decline. These differences may produce varying psychological states and depression risks across age groups. On the other hand, long-term high-altitude residents develop physiological adaptations to environmental conditions that enhance tolerance to high-altitude natural environments and reduce health risks (Julian & Moore, 2019). Research shows that Tibetan Plateau residents exhibit distinct genetic differences in erythropoiesis-promoting and hypoxia pathway genes compared to lowland populations (Huerta-Sánchez, 2014; Semenza, 2023), facilitating better adaptation to hypobaric hypoxia. Thus, middle-aged and elderly individuals with decades of high-altitude residence may have better biological adaptation, whereas younger populations may still be adapting. These differential adaptation processes may produce age-related variations in biological markers and consequent depression risk differences. Therefore, this study's third objective is:

Research Objective 3: To analyze age-related heterogeneity in depression risk among multi-age residents living at different altitudes.

Study 1: Altitude and Depression Among Chinese Residents

2.1 Data Sources and Sample Selection Study 1 utilized data from the fifth wave of the China Family Panel Studies (CFPS2020). Implemented by the Institute of Social Science Survey at Peking University, CFPS is a national, comprehensive longitudinal social survey conducted biennially to track changes in Chinese society, economy, and health. In 2010, CFPS launched its baseline survey across 162 districts/counties in 25 provinces, covering 649 villages/residential communities, ultimately completing interviews with 14,960 households, 33,600 adults, and 8,990 children, achieving an individual-level response rate of 84.14%. CFPS employs a multistage, stratified, probability-proportional-to-size systematic sampling method, yielding a representative sample. CFPS2020, completed in December 2020, distributed 19,000 household samples through face-to-face and telephone interviews, collecting 33,888 individual questionnaires. Based on analytical objectives and regression model requirements, this study selected CFPS2020 respondents aged $ 18whocompleteddepressionassessmentsandresidedinregionswith > 30samplecases.Thefinalanalyticalsamplecomprised18, 208individuals(9, 072males[49.82±1.04, averageeduc

Regional macro-level indicators from the 2020 *China City Statistical Yearbook* (Department of Urban Society and Economic Statistics, National Bureau of Statistics of China, 2020) and *China Statistical Yearbook* (National Bureau of Statistics of China, 2020) were matched with CFPS2020 data to construct an analytical database incorporating individual- and regional-level variables. These yearbooks, compiled by the National Bureau of Statistics, systematically collect annual statistical data on population, resources, environment, economic development, and public services across Chinese provinces and cities, providing comprehensive documentation of regional economic and social conditions. Drawing on previous research regarding natural environments and depression (Thompson et al., 2018; Lawrance et al., 2022), this study selected regional indicators including mean temperature, rainfall, PM2.5 concentration, and per capita GDP as control variables. Altitude data for sample regions were obtained from the *China Atlas* (Du & Tang, 2012), a provincial and municipal atlas published by SinoMaps Press containing terrain, climate, and land cover information. After matching regional macro-indicators with CFPS2020 data, sample regions showed a mean altitude of 0.46$±0.58*kilometers*, 52.90±11.87*hospitalbedsper*10, 000*people*, *percapitaGDPof*62, 300±38, 100*yuan*, *mean*

2.2 Measures and Analytical Methods CFPS2020 employed the 8-item Center for Epidemiological Studies Depression Scale (CES-D 8) to measure depression scores. Developed by Radloff (1977) as a brief version of the full CES-D, this scale's strong reliability and validity across age groups have made it one of the most widely used depression measures. All items use a 4-point Likert scale ranging from "0=never" to "3=most of the time," with total scores ranging from 0–24. The scale's Cronbach's alpha was 0.77, indicating good reliability. Given the nested structure of altitude's effect on depression across individuals and regions, traditional ordinary least squares models face non-independence issues. Hierarchical Linear Modeling (HLM) accounts for random errors and variable information from different levels, providing more accurate standard error estimates, more effective confidence intervals, and hypothesis testing, thus appropriately handling such non-independence. Therefore, this study used R 4.3.2 software to construct multilevel linear models analyzing the relationship between regional altitude and population depression.

2.3 Results and Discussion First, a null model containing only the dependent variable was run to calculate the intra-class correlation coefficient (ICC). Results showed individual-level error variance of 11.25 and regional-level error variance of 0.87, yielding an ICC of 0.067, which exceeds the critical reference value of 0.059. This indicates that regional-level variables explain 6.7% of variance in individual depression levels, necessitating multilevel modeling. Second, a random intercept model was run, assuming different initial depression levels across altitude regions but identical annual growth rates. Results (see) showed a positive association between altitude and depression scores after controlling for individual- and regional-level variables (β=0.46, SE=0.13, 95% CI [0.14,0.78], p=0.005). Third, a random slope model was run, assuming identical initial depression levels but different growth rates across altitude regions. Results (see) maintained a positive altitude-depression relationship (β=0.68, SE=0.20, 95% CI [0.29, 1.08], p=0.001). Finally, a mixed random slope and random intercept model was run, assuming both initial levels and growth rates differ across altitude regions, specified as: $y = \alpha[\,] + \beta[\,]x + \gamma X +$, where i and j index individuals and regions, $\alpha[\,]$ represents initial depression scores, $\beta[\,]$ represents annual growth rates, γX represents combined individual- and regional-level control variables, and represents error terms. Results (see) showed altitude remained positively associated with depression scores after controlling for individual- and regional-level factors (β=0.49, SE=0.18, 95% CI [0.13, 0.85], p=0.008).

In summary, Study 1 results demonstrate a significant positive relationship between altitude and adult residents' depression scores across different assumptions, suggesting altitude may be a depression risk factor where higher altitude increases depression risk. These findings align with international altitude-depression research (DelMastro et al., 2011) and support ecological systems theory. First, low atmospheric pressure and hypoxia at high altitude may alter depression-related biological factors in residents. Research indicates that hypobaric, oxygen-scarce environments adversely affect human inflammatory and hormonal mechanisms (Hüfner et al., 2019), reduce brain serotonin levels, trigger migraines, impair cognitive function and attention (Lieberman et al., 1994; Bailey et al., 2019; Aboouf et al., 2023), and disrupt normal neuronal regulation of stress and depression (Ray et al., 2011; Bian et al., 2019), thereby facilitating depression onset and progression. Second, hypobaric hypoxia reduces mental control and emotional regulation capacity (Lemos et al., 2012), increasing difficulty in managing anxiety, unease, and anger, consequently elevating depression risk. Additionally, high-altitude low pressure and hypoxia significantly impair sleep quality (Risal et al., 2016; Sun et al., 2021), and poor sleep constitutes an important depression risk factor. Finally, high-altitude natural environmental systems may increase depression risk. According to ecological systems theory, individuals' ecological environments comprise interdependent, mutually influencing subsystems including family, community, and natural environment, which jointly shape cognitive and psychological development. High-altitude regions feature cold temperatures, strong winds, and intense solar radiation, exacerbated by climate change-induced decreasing precipitation and increasing aridification in China's plateau areas (Zhang et al., 2023). Research suggests climate change may induce confusion, anxiety, and disappointment (Berry et al., 2010), ultimately negatively impacting population mental health.

Study 2: Mediating Mechanisms of Per Capita GDP and C-Reactive Protein

3.1 Data Sources and Sample Selection Study 2 used CFPS2016 and CFPS2018 data to examine per capita GDP's mediating role between altitude and depression. CFPS2016 (completed November 2016) included 14,763 household samples and 45,319 individual samples with an 82% individual tracking rate; CFPS2018 (completed March 2019) included 15,000 household samples and 44,000 individual samples with an 80.8% tracking rate. Based on research objectives and causal inference reliability, this study selected tracked samples aged $ 18 *whocompleteddepressionassessmentsinbothwaves*, *yielding*13, 857*cases*(6, 800*males*[49.07±0.98, *average*

However, since 98% of CFPS samples concentrate in low- and medium-altitude areas below 2,000 meters, lacking samples from the Qinghai-Tibet Plateau and other high-altitude regions, this limitation affects the accuracy of per capita GDP mediation analysis. To address this, propensity score matching (PSM) was used to match CFPS2016 data with the 2016 Yushu Adult Physical and

Mental Health Survey ("Yushu Survey"), creating a database encompassing both low-medium and high-altitude plateau samples to further test per capita GDP's mediating effect. The Yushu Survey, jointly conducted by the Institute of Psychology, Chinese Academy of Sciences and the National Health Commission's Institute of Science and Technology in 2016, targeted Yushu Prefecture in the Qinghai-Tibet Plateau interior (mean altitude 4,200 meters). Using cluster sampling of permanent residents, the survey covered basic demographics and depression, with assistance from county maternal and child health hospitals and township health center staff. The survey distributed 30,000 questionnaires and recovered 28,288. After PSM matching, 7,636 respondents aged $ 18whocompleteddepressionassessmentswereobtained(4,042males[52.93±5.31years,meanageof44.06±15.05

Finally, Study 2 used the third wave of the China Health and Retirement Longitudinal Study (CHARLS2015) to examine C-reactive protein's mediating role between altitude and depression. Implemented by the China Center for Economic Research at Peking University's National School of Development, CHARLS collects high-quality microdata representing Chinese households and individuals aged 45 and older. Using multistage sampling with probability-proportional-to-size methods at county and village levels, CHARLS covers 150 county-level units and 450 village-level units across 28 provinces, providing representative samples. The baseline survey in 2011 covered approximately 17,000 individuals from 10,000 households, with follow-ups every two to three years. In the 2015 follow-up, CHARLS collaborated with county-level CDCs to collect venous blood samples from 13,420 respondents. CDC staff collected three blood tubes per respondent (two 2-ml tubes and one 6-ml tube), which were transported to local hospitals or testing companies for analysis of glycated hemoglobin, C-reactive protein, uric acid, cystatin C, and other indicators. This study selected 13,420 respondents who completed both blood testing and depression assessment, including 6,174 males (46.00%) and 7,246 females (54.00%); 9,959 rural residents (74.21%) and 3,461 urban residents (25.79%); 11,683 married individuals (87.06%) and 1,737 unmarried/divorced/widowed individuals (12.84%); 8,232 individuals with chronic diseases (61.34%) and 5,188 without (38.66%); 5,729 with primary school education or less (42.69%) and 7,691 with more than primary school education (57.31%); 8,756 non-drinkers (65.25%) and 4,664 drinkers (34.75%); 8,681 non-smokers (64.69%) and 4,739 smokers (35.31%). The sample had a mean age of 59.93$±10.11years,meandepressionscoreof17.78±6.39,andmeanC − reactiveproteinlevelof2.73±5.95mg/l.Regionalcharacteristicsincludedmeanaltitudeof0.38±0.52kilometers,

3.2 Measures and Analytical Methods Consistent with Study 1, CFPS2016 and CFPS2018 primarily used CES-D 8 to measure depression scores, with Cronbach's alpha values of 0.78 and 0.77, respectively. CFPS2016 also administered the 10-item CES-D (CES-D 10) to approximately 20% of respondents. The CES-D 10, also derived from the full CES-D (Andresen et al., 1994), demonstrates high reliability and validity, using the same 4-point Likert scale (0–30 range). Its Cronbach's alpha in CFPS2016 was 0.78. CHARLS2015 and the 2016 Yushu Survey also used CES-D 10, with Cronbach's alpha values of 0.80 and 0.92, respectively. The SPSS PS Matching 3.04 plugin was used for caliper matching between CFPS2016 and the 2016 Yushu Survey databases. Based on variable characteristics and previous research recommendations (Austin, 2009), a caliper value of 0.02 was set, with matching variables including age, gender, education years, and marital status. Finally, AMOS 26.0 was used to construct mediation models, with bootstrap methods (5,000 iterations, 95% confidence level) testing mediation effects. Bootstrap resampling estimates mediation effects and confidence intervals from the given sample; confidence intervals excluding zero indicate significant mediation (Wen & Ye, 2014).

3.3 Results and Discussion To enhance causal inference reliability for the macro-level factor per capita GDP, both per capita GDP and depression scores were lagged by one period. After controlling for baseline depression scores, age, gender, education years, chronic disease status, employment, marital status, hospital beds per 10,000 people, mean annual temperature, and annual rainfall, mediation model results showed altitude had a direct positive effect on depression scores (β=0.02, SE=0.01, 95% CI [0.01, 0.04], p=0.005), a negative effect on per capita GDP (β=-0.41, SE=0.01, 95% CI [-0.42, -0.40], $p<0.001$), and per capita GDP negatively affected depression scores (β=-0.10, SE=0.01, 95% CI [-0.11, -0.08], $p<0.001$), suggesting per capita GDP may mediate the altitude-depression relationship. Bootstrap mediation tests (see) showed both the direct effect of altitude on depression and the indirect effect through per capita GDP had 95% confidence intervals excluding zero, confirming per capita GDP's mediating role. To address CFPS's lack of high-altitude samples, CFPS2016 and 2016 Yushu Survey matched data further tested this mediation. After controlling for individual- and regional-level variables, altitude positively correlated with depression scores (β=0.10, SE=0.01, 95% CI [0.08, 0.12], $p<0.001$), negatively correlated with per capita GDP (β=-0.58, SE=0.01, 95% CI [-0.59, -0.57], $p<0.001$), and per capita GDP negatively correlated with depression scores (β=-0.07, SE=0.01, 95% CI [-0.09, -0.05], $p<0.001$). Bootstrap results again confirmed per capita GDP's mediating role. Finally, C-reactive protein mediation analysis showed that after controlling for individual- and regional-level variables, altitude positively correlated with depression scores (β=0.12, SE=0.001, 95% CI [0.10, 0.14], $p<0.001$), positively correlated with C-reactive protein (β=0.02, SE=0.001, 95% CI [0.01, 0.04], p=0.004), and C-reactive protein positively correlated with depression scores (β=0.03, SE=0.001, 95% CI [0.01, 0.04], p=0.006). Bootstrap mediation tests confirmed both the direct effect of altitude on depression and C-reactive protein's mediating effect, with 95% confidence intervals excluding zero.

In summary, Study 2 demonstrates that per capita GDP and C-reactive protein mediate the altitude-depression relationship. As regional altitude increases, per capita GDP decreases and residents' blood C-reactive protein concentrations increase, indirectly elevating depression risk. First, high-altitude regions' complex geography increases infrastructure development difficulty, hindering population and industry agglomeration and resulting in slower economic development (Zhai & Sun, 2012) and lower per capita GDP than lowland areas. Per capita GDP reflects regional economic development; lower values may indicate relatively lower living standards, reduced access to high-quality healthcare, and greater income and employment uncertainty, thereby increasing depression risk (Ridley et al., 2020; Scott et al., 2016). Social causation theory posits that adverse economic conditions like poverty and low socioeconomic status increase mental illness risk over time through economic pressure, scarce social capital, poor living conditions, and social isolation (Wickham et al., 2017; Kim et al., 2022). Residents in economically underdeveloped regions possess fewer baseline assets, making them more vulnerable to external risk impacts (Lund & Cois, 2018; Aretz, 2022) and consequently increasing their depression risk. Second, these results align with previous C-reactive protein-depression research (Copeland et al., 2012). Chronic hypoxia at high altitude increases oxidative stress and inflammatory responses (Osimo et al., 2019; Baygutalp et al., 2021). C-reactive protein, a typical inflammatory marker (Tang et al., 2018), increases with altitude-induced stress and inflammation (Gleeson et al., 2011). As a pro-inflammatory cytokine, C-reactive protein may alter central neurotransmitter and stress-responsive neuroendocrine levels, leading to mental health problems like depression (Dantzer et al., 2008; Tabatabaeizadeh et al., 2018). Thus, regional GDP and C-reactive protein jointly influence the altitude-depression relationship, further confirming the diathesis-stress model's applicability in mental illness.

Study 3: Age Heterogeneity in Altitude-Related Depression Risk

4.1 Data Sources and Sample Selection Study 3 used CFPS2016, CFPS2018, and CFPS2020 data to analyze age differences in depression risk at low-to-medium altitudes. Based on analytical objectives, samples aged $ 18whocompleteddepressionassessmentswereselected : 31, 783CFPS2016cases(15, 888males[50.01±16.46years, meandepressionscore5.21±4.05; 28, 970CFPS2018c
Study 3 also used PSM-matched Yushu Survey and CFPS2016 data to analyze age differences in depression risk at high altitudes. With Yushu Prefecture's mean altitude of 4,200 meters representing a typical high-altitude region and CFPS2016 concentrating in low-medium altitude areas, the marked altitude difference between databases enabled comparative analysis. The matching method, post-matching sample size, and basic sample information were consistent with Study 2.

4.2 Measures and Analytical Methods The Yushu Survey used CES-D 10, while CFPS2018 and CFPS2020 used CES-D 8. CFPS2016 administered CES-D 10 to approximately 20% of respondents and CES-D 8 to the remainder. All scales showed Cronbach's alpha values consistent with Studies 1 and 2. Following Keyes (2013) and Briggs (2018), depression risk was defined as CES-D 8 $ $9 or CES-D 10 $ $14, while absence of risk was defined as CES-D 8 <3 or CES-D 10 <10. In epidemiological research, case-control studies commonly examine associations between predictors and disease risk, with odds ratios (OR) intuitively reflecting these relationships. OR values >1 indicate that risk factor A increases disease B's odds. Therefore, this study used OR analysis to examine altitude-depression risk associations. Altitude categories followed geographical conventions and data characteristics (Li et al., 2008): <500 meters (low altitude), 500–1,000 meters (low-medium altitude), 1,000–2,000 meters (medium altitude), 2,000–4,000 meters (sub-high altitude), and 4,000–6,000 meters (high altitude). No samples exceeded 6,000 meters.

4.3 Results and Discussion presents the relationship between 500–2,000 meter altitude exposure and depression risk across age groups. Using 10-year age intervals based on data characteristics and previous research (Lu et al., 2021), results show that individuals living at 500–1,000 meters face 1.53–1.79 times higher depression risk than those below 500 meters. Age heterogeneity analysis reveals that 41–50-year-old middle-aged individuals at 500–1,000 meters have the highest depression risk across all age groups, while those $ $60 years show higher risk than younger adults. Additionally, individuals at 1,000–2,000 meters face 1.67–2.25 times higher depression risk than those below 500 meters, with those $ $60 years showing markedly higher risk than other age groups. Similar to the 500–1,000 meter zone, elderly individuals at 1,000–2,000 meters show higher depression risk than younger adults.

presents the relationship between 4,000–6,000 meter altitude exposure and depression risk across age groups. Results indicate that individuals living at 4,000–6,000 meters face approximately 9 times higher depression risk than those below 500 meters. Age heterogeneity analysis shows that 18–40-year-old young adults at 4,000–6,000 meters face 28–54 times higher depression risk than their low-altitude counterparts—a pattern contrasting with low-medium altitude zones where young adults at 4,000–6,000 meters show higher depression risk than middle-aged and elderly residents.

These findings confirm the positive altitude-depression risk association, validating Study 1's conclusions. They also reveal that middle-aged and elderly individuals face higher depression risk at 500–2,000 meters, while young adults face higher risk at 4,000–6,000 meters, indicating a non-linear age relationship in altitude-depression associations. Several factors may explain these age heterogeneity patterns. Young people's higher neuroplasticity, combined with relatively mild hypoxia at 500–2,000 meters, may minimize altitude's impact on brain function, structure, and neurotransmitter synthesis/metabolism (Arregui et al., 1991), resulting in lower oxidative stress, inflammation, and depression risk. Conversely, middle-aged and elderly individuals' declining physiological function and nervous system integrity may increase vulnerability to hypoxia-induced oxidative stress and inflammation, inhibiting mood-regulating neurotransmitter synthesis and amplifying negative effects. Additionally, China's social transformations have shifted national mentality, with middle-aged and elderly individuals facing multiple pressures from family caregiving, income, and social expectations under traditional constraints, generating internalizing problems like depression and anxiety. Younger generations, pursuing self-actualization and freedom with fewer traditional constraints and more stress-release outlets, may experience lower depression risk at 500–2,000 meters.

Furthermore, long-term residents at 4,000–6,000 meters have developed physiological adaptations through natural selection, including greater lung capacity, blood oxygen saturation, gas exchange efficiency, and lower hemoglobin concentrations (Yi et al., 2010; Mairbäurl et al., 2020), enhancing hypoxia adaptation. Elderly individuals with decades of plateau residence thus possess greater environmental adaptability, while younger residents' shorter duration may limit comprehensive physiological adaptation, increasing altitude-related impacts and depression risk. Evolutionary theory suggests that middle-aged and elderly survivors at 4,000–6,000 meters represent long-term natural selection outcomes, having endured extreme environmental challenges and developed resilience. Additionally, lower economic development in high-altitude regions reduces young people's access to quality education, limiting labor market competitiveness and creating employment stress that generates depression and anxiety (Cheng & Zhao, 2019). Limited social capital, low income levels, and restricted social mobility in resource-scarce plateau environments further increase anxiety and mental health risks (Ma, 2011). Finally, strong religious culture and tight social networks in China's high-altitude regions may create age-related depression risk differences. The 4,000–6,000 meter samples from Yushu, Qinghai, include high proportions of ethnic Tibetans whose cultural traditions foster strong family and community bonds, with elderly residents more deeply integrated into these networks, potentially reducing depression risk. Moreover, elderly Tibetans' devout Buddhist beliefs in karma and reincarnation may enable positive coping with life hardships, suppressing depression risk (Ishikawa et al., 2019).

Conclusion and Limitations

This study yields three main findings: (1) Altitude positively associates with depression, with higher altitude increasing depression risk. This finding fills a research gap in China regarding altitude and depression, providing empirical evidence for this relationship and supporting ecological systems theory's hypothesis about natural environments' impact on psychological development. (2) Per capita GDP and C-reactive protein mediate the altitude-depression relationship. High-altitude hypobaric hypoxia may elevate C-reactive protein levels, indirectly increasing depression risk, while simultaneously reducing per capita GDP relative to lowland areas, further indirectly increasing depression risk. This finding validates the diathesis-stress model's applicability in mental illness, deepening understanding of health-disease relationships and offering broader perspectives for future mental health research. (3) Age heterogeneity exists in the altitude-depression relationship, with middle-aged and elderly individuals at 500–2,000 meters and young adults at 4,000–6,000 meters facing higher depression risk. This non-linear age relationship challenges linear perspectives on age and mental health, indicating that targeted mental health interventions must consider both individual and environmental characteristics.

Several limitations warrant acknowledgment. First, while PSM was used to address CFPS's lack of plateau samples and control confounding factors, improving statistical reliability, the data remain imperfect and may introduce bias. The Yushu Survey's limited indicators restrict control variable selection, potentially leaving some confounders uncontrolled. Additionally, the lack of plateau samples in existing databases necessitates reliance on this single source, which may introduce selection bias. Second, when examining altitude's depression mechanisms, the absence of blood indicators in the Yushu Survey precluded C-reactive protein mediation analysis for 4,000–6,000 meter samples, potentially compromising causal inference accuracy and mechanism analysis. Finally, while this study applied ecological systems theory and the diathesis-stress model to validate their applicability in mental health, further theoretical exploration of environmental impacts on individual mental health is needed.

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