Preplanned Studies

# Differences in Major Causes of Death and Disease Burden Among Residents of Kashin-Beck Disease Endemic and Non-Endemic Areas — Heilongjiang Province, China, 2024

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**Summary**

**What is already known about this topic?**

Kashin-Beck disease (KBD) imposes a heavy burden on both patients and their families. However, there are no reports on the health disparities between residents with long-term exposure to KBD risk factors in endemic and non-endemic areas.

**What is added by this report?**

For ischemic heart diseases, the age-standardized mortality rates (ASMR) were significantly higher in endemic areas, particularly among males, residents aged ≥65 years, and residents in economically developed regions. For malignant neoplasms of the digestive organs, ASMR was higher in endemic areas, and a significant difference in ASMR between the two areas was observed in females. For cerebral infarction, the ASMR was significantly lower in endemic areas, particularly among residents in economically developed regions. The rate of life lost due to ischemic heart diseases and malignant neoplasms of digestive organs was relatively high in endemic areas, while the rate due to cerebral infarction was relatively high in non-endemic areas.

**What are the implications for public health practice?**

These findings provide scientific evidence for optimizing comprehensive prevention and control strategies for endemic diseases, and strengthening interventions for key diseases.

## ABSTRACT

**Introduction**: This study compared the major causes of death and disease burden in Kashin-Beck disease (KBD) endemic and non-endemic areas of Heilongjiang Province in 2024.

**Methods**: Data were obtained from the National Disease Surveillance Point system. Age-standardized mortality rates (ASMR), rate ratio, cause-eliminated life expectancy, potential gains in life expectancy, and the rate of life lost were calculated.

**Results**: The ASMR for ischemic heart disease was higher in endemic areas, whereas cerebral infarction showed a lower ASMR. For ischemic heart diseases, the ASMR was significantly higher in endemic areas, particularly among males [risk ratio (*RR*)=2.79, 95% confidence interval (*CI*): 1.77, 5.38], residents aged ≥ 65 years (*RR*=2.17, 95% *CI*: 1.52, 3.39) and residents in economically developed regions (*RR*=3.00, 95% *CI*: 1.90, 5.93). For malignant neoplasms of digestive organs, the ASMR was higher in endemic areas than that in non-endemic areas, and a significant difference in ASMR between the two areas was observed in females (*RR*=4.14, 95% *CI*: 1.63, 16.30). For cerebral infarction, the ASMR was significantly lower in endemic areas than that in non-endemic areas, particularly among residents in economically developed regions (*RR*=0.32, 95% *CI*: 0.20, 0.55). The rates of life lost due to ischemic heart disease, cerebral infarction, and malignant neoplasms of the digestive organs in endemic areas were 11.32%, 1.42%, and 1.84%, respectively, compared with 4.22%, 6.36%, and 1.41% in non-endemic areas, respectively.

**Conclusion**: These findings provide evidence for optimizing comprehensive prevention and control strategies for endemic diseases and strengthening interventions.

Kashin-Beck disease (KBD) is an endemic, disabling osteoarticular disorder of unknown etiology. Mild cases present with joint pain, swelling, deformity, and limited limb mobility, whereas severe cases manifest as brachydactyly and dwarfism, leading to a loss of labor capacity (*1*). This disease imposes a heavy burden on patients and their families (*2*).

Heilongjiang Province, China, is heavily affected by KBD. Environmental risk factors (ERFs) such as selenium deficiency and T-2 toxin are primary contributors to KBD (*3*–*4*). However, there are no reports on health disparities between residents with long-term exposure in endemic areas and those in non-endemic areas.

All administrative villages in Heilongjiang Province were classified according to KBD endemic areas criteria, defined as follows: 1) KBD endemic areas (hereafter termed endemic areas): Residents of clinical I degrees or higher prevalence exceeding 5%, and children aged 7–12 exhibiting multiple, symmetrical epiphyseal changes on hand radiographs. Endemic areas were further classified as: mild endemic areas (prevalence of the local residents of clinical I degrees and above or X-ray detection rate ≤10% in 7–12-year-old children), moderate endemic areas (prevalence of the local residents of clinical I degrees and above or X-ray detection rate >10% and ≤20% in 7–12-year-old children), and severe endemic areas (prevalence of the local residents of clinical I degrees and above or X-ray detection rate >20% in 7–12-year-old children); 2) Non-endemic areas: Administrative villages not meeting the criteria for endemic areas. Heilongjiang Province had 9,073 administrative villages, including 7,199 non-endemic areas, 1,405 mild endemic areas, 148 moderate endemic areas, and 321 severe endemic areas in 2024.

Stratified random sampling was employed to select 165 administrative villages, including 47 mild endemic areas, 42 moderate endemic areas, 45 severe endemic areas, and 31 non-endemic areas. The administrative villages were classified into economically developed and underdeveloped regions based on the regional gross domestic product (GDP). Causes of death were obtained from the National Disease Surveillance Point (DSP) System. In April 2004, Heilongjiang Province officially launched online direct reporting of individual death case information across the province, relying on the Disease Surveillance Information Report Management System (Major Epidemic Online Direct Reporting System). By 2007, this system was connected to the National Cause of Death Registration Reporting Information System, thereby achieving full online direct reporting of individual death cases in all counties and districts across the province. All causes of death were identified and classified according to the International Classification of Diseases ICD-10 standard. Information on the 2024 permanent population (defined as individuals who had lived in the sampled administrative villages for more than six months) was collected through a complete census. The census covered all types of residential premises within the jurisdiction. Duplicate registrations and erroneous information were eliminated using multiple verification methods, including logical verification and cross-departmental data comparison.

Age-standardized mortality rates (ASMRs) were calculated based on 2020 Chinese National Census data. The Poisson parametric bootstrap method was used to compare rate ratios (*RR*s), 95% confidence intervals (*CI*s), and *P*. The unit of analysis was the administrative village included in the study. Point estimates of *RR* were derived directly by calculating the ratio of ASMRs between the compared areas, whereas group-specific resampling with replacement (sample size matching the original) was performed to estimate the 95% *CI*s and *P*. Poisson regression analyses were performed for the composite major causes of death, the three major causes of death, and their main subtypes to verify the robustness of the results. The false discovery rate (FDR) method was used to adjust the *P* across all tables. Cause-eliminated life expectancy (CELE) was calculated using the life table method. This reflects the potential increase in a population's average life expectancy if a specific cause of death is eliminated. Potential gains in life expectancy (PGLEs) represented the increase in life expectancy following the elimination of a specific cause of death (PGLEs = CELE – life expectancy) and served as an indicator of population life expectancy gains. The rate of life lost refers to the proportion of the total life expectancy lost due to a specific cause of death [rate of life loss = (potential additional years of life expectancy) × 100%]. CELE was truncated at age 95.

The baseline characteristics of the participants were reported descriptively, with frequencies (percentages) for binary variables and medians (interquartile range) for continuous variables. Intergroup comparisons were performed using the Mann-Whitney U, Kruskal-Wallis, $\chi^2$ tests, or Fisher's exact tests. All analyses were conducted using the R software (version 4.4.3; R Foundation for Statistical Computing, Vienna, Austria). A two-sided $P<0.05$ was considered statistically significant.

The primary causes of death in the general population were heart diseases (31.94%), malignant neoplasms (25.71%), and cerebrovascular diseases (24.98%), which were the major causes of mortality (Table 1).

The ASMR for the composite major causes of death

TABLE 1. General characteristics of decedents by area in Heilongjiang Province, 2024.

| Variables | Total (*n*=1,365) | Endemic areas (*n*=1,128) | Non-endemic areas (*n*=237) | $P_{\text{Endemic areas vs. Non-endemic areas}}$ | Mild endemic areas (*n*=388) | Moderate endemic areas (*n*=487) | Severe endemic areas (*n*=253) | $P_{\text{Mild endemic areas vs. Moderate endemic areas vs. Severe endemic areas}}$* |
|---|---|---|---|---|---|---|---|---|
| Age (years) | 73 (65–80) | 73 (65–80) | 72 (62–79) | 0.261 | 72 (66–79) | 74 (65–81) | 73 (62–79) | 0.334 |
| Sex (*n*, %) | | | | 0.334 | | | | 0.880 |
| Male | 815 (59.71) | 681 (60.37) | 134 (56.54) | | 236 (60.82) | 290 (59.55) | 155 (61.26) | |
| Female | 550 (40.29) | 447 (39.63) | 103 (43.46) | | 152 (39.18) | 197 (40.45) | 98 (38.74) | |
| Economic conditions (*n*, %) | | | | <0.001 | | | | <0.001 |
| Developed regions | 795 (58.24) | 690 (61.17) | 105 (43.30) | | 196 (50.52) | 335 (68.79) | 159 (62.85) | |
| Underdeveloped regions | 570 (41.76) | 438 (38.83) | 132 (55.70) | | 192 (49.48) | 152 (31.21) | 94 (37.15) | |
| Causes of death (*n*, %) | | | | <0.001 | | | | <0.001 |
| Heart diseases | 436 (31.94) | 380 (33.69) | 56 (23.63) | | 114 (29.38) | 162 (33.26) | 104 (41.11) | |
| Malignant neoplasms | 351 (25.71) | 298 (26.42) | 53 (22.63) | | 94 (24.23) | 137 (28.13) | 67 (26.48) | |
| Cerebrovascular diseases | 341 (24.98) | 259 (22.96) | 82 (34.60) | | 93 (23.97) | 114 (23.41) | 52 (20.55) | |
| Diseases of the respiratory system | 81 (5.93) | 67 (5.94) | 14 (5.91) | | 34 (8.76) | 28 (5.75) | 5 (1.98) | |
| External causes of mortality | 36 (2.64) | 29 (2.57) | 7 (2.95) | | 12 (3.09) | 9 (1.85) | 8 (3.16) | |
| Diseases of the digestive system | 29 (2.12) | 24 (2.13) | 5 (2.11) | | 6 (1.55) | 13 (2.67) | 5 (1.98) | |
| Endocrine, nutritional, and metabolic diseases | 27 (1.98) | 23 (2.04) | 4 (1.69) | | 7 (1.80) | 9 (1.85) | 7 (2.77) | |
| Diseases of the nervous system | 20 (1.47) | 19 (1.68) | 1 (0.42) | | 17 (4.38) | 2 (0.41) | 0 (0) | |
| Certain infectious and parasitic diseases | 8 (0.59) | 5 (0.44) | 3 (1.27) | | 0 (0) | 3 (0.62) | 2 (0.79) | |
| Diseases of the genitourinary system | 6 (0.44) | 4 (0.35) | 2 (0.84) | | 1 (0.26) | 2 (0.41) | 1 (0.40) | |
| Mental and behavioral disorders | 3 (0.22) | 2 (0.18) | 1 (0.42) | | 1 (0.26) | 1 (0.21) | 0 (0) | |
| Diseases of the blood and blood-forming organs, and certain disorders involving the immune mechanism | 2 (0.15) | 2 (0.18) | 0 (0) | | 2 (0.52) | 0 (0) | 0 (0) | |
| Congenital malformations, deformations, and chromosomal abnormalities | 1 (0.07) | 1 (0.09) | 0 (0) | | 0 (0) | 1 (0.21) | 0 (0) | |
| Certain conditions originating in the perinatal period | 1 (0.07) | 1 (0.09) | 0 (0) | | 0 (0) | 0 (0) | 1 (0.40) | |
| Undetermined diseases | 10 (0.73) | 3 (0.27) | 7 (2.95) | | 3 (0.77) | 0 (0) | 0 (0) | |
| Other diseases | 13 (0.95) | 11 (0.98) | 2 (0.84) | | 4 (1.03) | 6 (1.23) | 1 (0.40) | |

Note: Parentheses content explanation: In the “Age (years)” row: Values in parentheses represent the interquartile range (*IQR*) of age distribution. In the “Sex (*n*, %)” and “Economic conditions (*n*, %)” rows: Values in parentheses represent the percentage (%) of each category within the total number of decedents in the corresponding group. In the “Causes of death (*n*, %)” rows: Values in parentheses represent the percentage (%) of each cause of death within the total number of decedents in the corresponding group.

* *P* represents the overall significance of differences in the general characteristics of the decedents across mild, moderate, and severe endemic areas. Continuous variables were compared using the Kruskal–Wallis test, and categorical variables were compared using $\chi^2$ test. All *P* were adjusted.

Abbreviation: ASMR=age-standardized mortality rate; *RR*=rate ratio.

was higher in endemic areas than that in non-endemic areas; however, the difference was not statistically significant. The ASMRs for heart diseases (*RR*=1.80, 95% *CI*: 1.35, 2.54) and ischemic heart diseases (*RR*=1.98, 95% *CI*: 1.46, 2.87) were significantly higher in endemic areas, while cerebrovascular diseases (*RR*=0.62, 95% *CI*: 0.47, 0.85) and cerebral infarction (*RR*=0.52, 95% *CI*: 0.37, 0.79) showed lower ASMRs in endemic areas. The ASMRs for malignancy and malignant neoplasms of the digestive organs were higher in endemic areas, but the difference was not significant. The ASMR for the composite major causes of death in moderate endemic areas was significantly higher than that in non-endemic areas. The ASMRs for heart diseases and ischemic heart diseases were significantly higher in all endemic areas than those in non-endemic areas. The ASMRs for malignant neoplasms and malignant neoplasms of the digestive system were significantly higher in moderate endemic areas, and the ASMRs for cerebrovascular disease and cerebral infarction were significantly lower in mild and severe endemic areas (Table 2). The results of the sensitivity analysis were consistent with these findings (Supplementary Table S1, available at https://weekly.chinacdc.cn/).

The stratified analysis showed that the ASMR for ischemic heart diseases (*RR*=2.79, 95% *CI*: 1.77, 5.38) was significantly higher in endemic areas than that in non-endemic areas among males, while the ASMR for malignant neoplasms of digestive organs (*RR*=4.14, 95% *CI*: 1.63, 16.30) was significantly higher than that in non-endemic areas among females. The ASMRs for ischemic heart disease were consistently higher than those in non-endemic areas among males, while the ASMR for cerebral infarction in severe areas was significantly lower than that in non-endemic areas. Among women, the ASMR for malignant neoplasms of the digestive organs in moderate endemic areas was significantly higher than that in non-endemic areas, and the ASMR for cerebral infarction in severe endemic areas was significantly lower than that in non-endemic areas. Among residents aged <65 years, no significant differences in ASMRs for all-cause deaths were observed between endemic and non-endemic areas. Among residents aged ≥65 years, the ASMR for ischemic heart diseases (*RR*=2.17, 95% *CI*: 1.52, 3.39) was significantly higher in endemic areas than that in non-endemic areas. In different endemic areas, the ASMRs for ischemic heart disease were consistently higher than those in non-endemic areas among residents aged ≥65 years, and the ASMRs for cerebral infarction in severe endemic areas were significantly lower than those in non-endemic areas. In endemic areas, the ASMR for ischemic heart diseases (*RR*=3.00, 95% *CI*: 1.90, 5.93) was significantly higher than that in non-endemic areas among residents in economically developed regions, and the ASMR for cerebral infarction (*RR*=0.32, 95% *CI*: 0.20, 0.55) was significantly lower than that in non-endemic areas. Among residents of economically underdeveloped regions, no significant differences in ASMRs for all causes of death were observed between endemic and non-endemic areas. The ASMRs for ischemic heart disease were consistently higher among residents in economically developed regions, while the ASMRs for cerebral infarction in mild and severe areas were significantly lower than those in non-endemic areas. The ASMR for malignant neoplasms of the digestive organs in moderate endemic areas was significantly higher than that in non-endemic areas among residents of economically developed regions (Supplementary Table S2, available at https://weekly.chinacdc.cn/). The rates of life lost due to ischemic heart disease, cerebral infarction, and malignant neoplasms of the digestive organs in endemic areas were 11.32%, 1.42%, and 1.84%, respectively, compared to 4.22%, 6.36%, and 1.41% in non-endemic areas (Table 3).

## DISCUSSION

ERFs play pivotal roles in the development and progression of KBD and also influence the onset and progression of various diseases through multiple pathways, including oxidative stress and inflammatory responses (*5*–*6*). The high ASMR of ischemic heart disease in endemic areas may be related to selenium deficiency, which induces cellular oxidative stress and inflammatory factor expression (*7*). On the other hand, T-2 toxin can also directly impair the function and structure of cardiomyocytes through its cardiotoxicity (*8*–*9*). The elevated ASMR in malignant neoplasms of the digestive organs may be associated with direct damage to the gastrointestinal tract by the T-2 toxin (*10*). The ASMR for cerebral infarction in endemic areas was significantly lower than that in non-endemic areas, which may be attributable to competing risks posed by the higher ASMRs of heart disease and malignant neoplasms in endemic areas. In addition, local dietary structure, lifestyle, and public health interventions may also reduce the ASMR of this disease. The higher smoking prevalence in males (*11*), combined with exposure to high-level ERFs, further

TABLE 2. ASMRs and *RR*s for major causes of death and subtypes by areas in Heilongjiang Province, 2024.

| Causes of death | $ASMR_{Total}$ (per 100,000) | $ASMR_{Endemic\ areas}$ (per 100,000) | $ASMR_{Non\text{-}endemic\ areas}$ (per 100,000) | $ASMR_{Mild\ endemic\ areas}$ (per 100,000) | $ASMR_{Moderate\ endemic\ areas}$ (per 100,000) | $ASMR_{Severe\ endemic\ areas}$ (per 100,000) | $RR_{Endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Mild\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Moderate\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Severe\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Major causes of death | 416.30 | 430.98 | 356.37 | 404.71 | 508.75 | 356.37 | 1.21 (1.02−1.45) | 1.14 (0.93−1.41) | 1.43 (1.18−1.73)*** | 1.00 (0.81−1.24) |
| Heart diseases | 185.16 | 202.49 | 112.77 | 186.02 | 224.39 | 190.24 | 1.80 (1.35−2.54)*** | 1.65 (1.17−2.41)* | 1.99 (1.45−2.84)*** | 1.69 (1.19−2.47)** |
| Ischemic heart diseases | 169.13 | 187.10 | 94.39 | 176.65 | 197.41 | 185.17 | 1.98 (1.46−2.87)*** | 1.87 (1.31−2.83)*** | 2.09 (1.49−3.14)*** | 1.96 (1.37−2.98)** |
| Hypertensive diseases | 6.94 | 6.16 | 10.73 | 4.60 | 10.21 | 2.01 | 0.57 (0.21−2.94) | 0.43 (0.00−2.40) | 0.95 (0.25−4.91) | 0.19 (0−1.14) |
| Pulmonary heart disease and diseases of pulmonary circulation | 4.71 | 5.35 | 1.76 | 2.42 | 10.28 | 1.46 | 3.04 (0.60−4.85) | 1.37 (0.00−3.39) | 5.84 (0.96−10.10) | 0.83 (0.00−2.49) |
| Cardiac arrhythmias | 3.17 | 2.37 | 5.90 | 1.18 | 3.78 | 1.59 | 0.40 (0.06−1.31) | 0.20 (0−1.00) | 0.64 (0−2.20) | 0.27 (0−1.35) |
| Cardiomyopathy | 0.48 | 0.60 | 0 | 0 | 1.40 | 0 | − | − | − | − |
| Chronic rheumatic heart diseases | 0.42 | 0.53 | 0 | 0 | 1.30 | 0 | − | − | − | − |
| Heart failure | 0.31 | 0.38 | 0 | 1.18 | 0 | 0 | − | − | − | − |
| Cerebrovascular diseases | 98.12 | 88.18 | 141.86 | 87.38 | 110.86 | 61.45 | 0.62 (0.47−0.85)* | 0.62 (0.42−0.90)* | 0.78 (0.56−1.10) | 0.43 (0.28−0.65)** |
| Cerebral infarction | 59.48 | 50.74 | 98.45 | 49.12 | 69.01 | 29.06 | 0.52 (0.37−0.79)** | 0.50 (0.30−0.80)* | 0.70 (0.46−1.09) | 0.30 (0.16−0.51)*** |
| Intracerebral hemorrhage | 38.20 | 36.92 | 43.41 | 36.52 | 41.85 | 32.40 | 0.85 (0.54−1.50) | 0.84 (0.44−1.59) | 0.96 (0.57−1.75) | 0.75 (0.39−1.43) |
| Cerebral aneurysm | 0.43 | 0.53 | 0 | 1.75 | 0 | 0 | − | − | − | − |
| Malignant neoplasms | 133.02 | 140.31 | 101.73 | 131.31 | 173.50 | 104.68 | 1.38 (1.03−1.92) | 1.29 (0.91−1.88) | 1.71 (1.25−2.44)** | 1.03 (0.71−1.51) |
| Malignant neoplasms of digestive organs | 65.01 | 69.59 | 44.56 | 69.08 | 86.61 | 46.71 | 1.56 (1.02−2.71) | 1.55 (0.93−2.78) | 1.94 (1.21−3.40)* | 1.05 (0.59−1.93) |
| Malignant neoplasms of respiratory and intrathoracic organs | 48.42 | 48.35 | 49.63 | 46.23 | 55.25 | 41.75 | 0.97 (0.64−1.63) | 0.93 (0.54−1.64) | 1.11 (0.68−1.95) | 0.84 (0.47−1.53) |
| Malignant neoplasms of urinary tract | 5.10 | 5.90 | 1.78 | 4.41 | 10.58 | 1.27 | 3.32 (0.65−5.35) | 2.48 (0−5.86) | 5.95 (1.01−10.30) | 0.72 (0−2.15) |
| Malignant neoplasms of female genital organs | 4.05 | 4.05 | 3.99 | 0 | 6.50 | 5.07 | 1.01 (0.25−3.18) | − | 1.63 (0.29−5.45) | 1.27 (0−4.89) |
| Malignant neoplasms of lymphoid, hematopoietic, and related tissue | 3.10 | 3.39 | 1.78 | 1.58 | 2.29 | 6.88 | 1.91 (0.30−3.24) | 0.89 (0−2.67) | 1.29 (0−2.97) | 3.88 (0.38−7.63) |
| Malignant neoplasms of eye, brain, and other parts of central nervous system | 2.13 | 2.60 | 0 | 1.18 | 4.24 | 1.50 | − | − | − | − |
| Malignant neoplasms of breast | 1.65 | 2.04 | 0 | 3.09 | 1.40 | 1.50 | − | − | − | − |
| Malignant neoplasms of thyroid and other endocrine glands | 1.16 | 1.42 | 0 | 1.75 | 2.41 | 0 | − | − | − | − |
| Malignant neoplasms of bone and articular cartilage | 1.06 | 1.30 | 0 | 1.24 | 2.41 | 0 | − | − | − | − |
| Malignant neoplasms of lip, oral cavity, and pharynx | 0.72 | 0.88 | 0 | 2.76 | 0 | 0 | − | − | − | − |
| Malignant neoplasms of mesothelial and soft tissue | 0.62 | 0.78 | 0 | 0 | 1.83 | 0 | − | − | − | − |

Note: "−" denotes missing *RR* due to zero ASMR in numerator or denominator.

* $P<0.05$; ** $P<0.01$; *** $P<0.001$ (adjusted).

Abbreviation: ASMR=age-standardized mortality rate; *RR*=rate ratio.

TABLE 3. CELE, PGLEs and the rate of life lost for major causes of death and subtypes by areas in Heilongjiang Province, 2024.

| Causes of death | CELE (years) | | | | | | PGLEs (years) | | | | | | The rate of life lost (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas |
| Heart diseases | 92.52 | 93.23 | 90.21 | 87.05 | 92.47 | 95.00 | 9.90 | 11.02 | 5.50 | 5.40 | 10.91 | 9.27 | 11.98 | 13.41 | 6.49 | 6.61 | 13.38 | 10.82 |
| Ischemic heart diseases | 90.75 | 91.51 | 88.28 | 86.33 | 90.00 | 95.00 | 8.13 | 9.31 | 3.57 | 4.68 | 8.44 | 9.27 | 9.84 | 11.32 | 4.22 | 5.73 | 10.35 | 10.82 |
| Hypertensive diseases | 82.80 | 82.35 | 84.99 | 81.74 | 81.79 | 85.79 | 0.17 | 0.15 | 0.28 | 0.09 | 0.23 | 0.06 | 0.21 | 0.18 | 0.33 | 0.11 | 0.28 | 0.07 |
| Pulmonary heart disease and diseases of pulmonary circulation | 82.75 | 82.34 | 84.75 | 81.69 | 81.79 | 85.77 | 0.13 | 0.13 | 0.04 | 0.04 | 0.23 | 0.04 | 0.15 | 0.16 | 0.05 | 0.05 | 0.28 | 0.05 |
| Cardiac arrhythmias | 82.72 | 82.25 | 85.21 | 81.67 | 81.64 | 85.76 | 0.10 | 0.05 | 0.50 | 0.02 | 0.08 | 0.03 | 0.12 | 0.06 | 0.59 | 0.02 | 0.10 | 0.04 |
| Cardiomyopathy | 82.64 | 82.22 | 84.71 | 81.65 | 81.59 | 85.73 | 0.01 | 0.01 | 0 | 0 | 0.03 | 0 | 0.01 | 0.02 | 0 | 0 | 0.04 | 0 |
| Chronic rheumatic heart diseases | 82.64 | 82.22 | 84.71 | 81.65 | 81.60 | 85.73 | 0.01 | 0.02 | 0 | 0 | 0.04 | 0 | 0.02 | 0.02 | 0 | 0 | 0.05 | 0 |
| Heart failure | 82.63 | 82.21 | 84.71 | 81.67 | 81.56 | 85.73 | 0.01 | 0.01 | 0 | 0.02 | 0 | 0 | 0.01 | 0.01 | 0 | 0.02 | 0 | 0 |
| Cerebrovascular diseases | 86.60 | 85.42 | 95.00 | 84.91 | 84.63 | 89.23 | 3.98 | 3.22 | 10.29 | 3.26 | 3.07 | 3.50 | 4.81 | 3.92 | 12.15 | 3.99 | 3.77 | 4.09 |
| Cerebral infarction | 84.21 | 83.37 | 90.10 | 82.58 | 82.95 | 86.85 | 1.59 | 1.17 | 5.39 | 0.93 | 1.39 | 1.13 | 1.92 | 1.42 | 6.36 | 1.14 | 1.71 | 1.32 |
| Intracerebral Hemorrhage | 83.50 | 83.01 | 86.01 | 82.40 | 82.28 | 86.95 | 0.88 | 0.80 | 1.30 | 0.75 | 0.72 | 1.22 | 1.06 | 0.98 | 1.53 | 0.91 | 0.88 | 1.43 |
| Cerebral aneurysm | 82.63 | 82.21 | 84.71 | 81.68 | 81.56 | 85.73 | 0.01 | 0.01 | 0 | 0.03 | 0 | 0 | 0.01 | 0.01 | 0 | 0.04 | 0 | 0 |
| Malignant neoplasms | 85.90 | 85.51 | 87.74 | 84.25 | 85.63 | 88.45 | 3.27 | 3.31 | 3.03 | 2.60 | 4.07 | 2.72 | 3.96 | 4.03 | 3.57 | 3.19 | 5.00 | 3.17 |
| Malignant neoplasms of digestive organs | 84.09 | 83.71 | 85.91 | 82.89 | 83.38 | 86.93 | 1.46 | 1.51 | 1.20 | 1.24 | 1.82 | 1.21 | 1.77 | 1.84 | 1.41 | 1.52 | 2.24 | 1.41 |
| Malignant neoplasms of respiratory and intrathoracic organs | 83.63 | 83.19 | 85.80 | 82.44 | 82.68 | 86.74 | 1.00 | 0.99 | 1.09 | 0.78 | 1.12 | 1.01 | 1.21 | 1.20 | 1.29 | 0.96 | 1.37 | 1.18 |
| Malignant neoplasms of urinary tract | 82.78 | 82.38 | 84.75 | 81.75 | 81.82 | 85.75 | 0.16 | 0.17 | 0.04 | 0.09 | 0.26 | 0.03 | 0.19 | 0.21 | 0.05 | 0.12 | 0.32 | 0.03 |
| Malignant neoplasms of female genital organs | 82.71 | 82.30 | 84.79 | 81.65 | 81.69 | 85.87 | 0.09 | 0.09 | 0.08 | 0 | 0.13 | 0.14 | 0.11 | 0.11 | 0.09 | 0 | 0.16 | 0.17 |
| Malignant neoplasms of lyphoid, hematopoietic and related tissue | 82.69 | 82.27 | 84.75 | 81.68 | 81.60 | 85.91 | 0.06 | 0.07 | 0.04 | 0.02 | 0.04 | 0.18 | 0.08 | 0.08 | 0.05 | 0.03 | 0.05 | 0.21 |
| Malignant neoplasms of eye, brain and other parts of central nervous system | 82.67 | 82.26 | 84.71 | 81.67 | 81.65 | 85.73 | 0.05 | 0.06 | 0 | 0.02 | 0.09 | 0 | 0.06 | 0.07 | 0 | 0.02 | 0.11 | 0 |

Continued

| Causes of death | CELE (years) | | | | | PGLEs (years) | | | | | The rate of life lost (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas | Total | Endemic areas | Non-endemic areas | Mild endemic areas | Moderate endemic areas | Severe endemic areas |
| Malignant neoplasms of breast | 82.66 | 82.25 | 84.71 | 81.73 | 81.59 | 85.75 | 0.04 | 0.05 | 0 | 0.08 | 0.03 | 0.03 | 0.04 | 0.06 | 0 | 0.10 | 0.04 | 0.03 |
| Malignant neoplasms of thyroid and other endocrine glands | 82.65 | 82.23 | 84.71 | 81.68 | 81.60 | 85.73 | 0.02 | 0.02 | 0 | 0.03 | 0.04 | 0 | 0.03 | 0.03 | 0 | 0.04 | 0.05 | 0 |
| Malignant neoplasms of bone and articular cartilage | 82.64 | 82.23 | 84.71 | 81.67 | 81.60 | 85.73 | 0.02 | 0.02 | 0 | 0.02 | 0.04 | 0 | 0.02 | 0.03 | 0 | 0.03 | 0.05 | 0 |
| Malignant neoplasms of lip, oral cavity, and pharynx | 82.64 | 82.22 | 84.71 | 81.69 | 81.56 | 85.73 | 0.01 | 0.01 | 0 | 0.04 | 0 | 0 | 0.01 | 0.02 | 0 | 0.05 | 0 | 0 |
| Malignant neoplasms of mesothelial and soft tissue | 82.65 | 82.23 | 84.71 | 81.65 | 81.62 | 85.73 | 0.03 | 0.03 | 0 | 0 | 0.06 | 0 | 0.03 | 0.04 | 0 | 0 | 0.07 | 0 |

Abbreviation: CELE=cause-eliminated life expectancy; PGLEs=potential gains in life expectancy.

elevates the mortality risk of ischemic heart disease among male residents in endemic areas. Various carcinogens in tobacco products, such as tobacco-specific nitrosamines, can jointly promote the occurrence and development of malignant neoplasms through mechanisms such as the induction of DNA adduct formation, gene mutations, and chronic inflammation (*12*–*13*). The magnitude of this effect may mask the impact of ERFs, resulting in no difference in ASMR for malignant neoplasms of the digestive organs between the two areas. Aging disrupts the body's oxidative and antioxidant balance, and ERFs exacerbate oxidative stress. This synergy results in a higher ASMR for multiple causes of death among elderly residents in KBD-endemic areas than in non-endemic areas (*14*). Compared with economically developed regions, less developed areas may consume more grain. Phenolic compounds in these grains possess antioxidant and anti-inflammatory properties that can reduce the risk of cardiovascular diseases, malignant neoplasms, and other conditions (*15*), thereby mitigating the impact of ERFs. Consequently, no significant differences in ASMR across causes of death were observed between endemic and non-endemic areas. Furthermore, ischemic heart diseases and malignant neoplasms of the digestive organs caused greater rates of loss of life in endemic areas, whereas cerebral infarction had a more pronounced impact in non-endemic areas. This pattern aligns with the previous findings.

This study had a few limitations. First, the use of stratified sampling carries the risk of sampling errors, which could limit the generalizability of our findings to the overall population of Heilongjiang Province. Second, the data were based on surveillance reports, which may contain underreporting or misreporting, which could compromise the accuracy.

In summary, the ASMR of ischemic heart diseases was significantly higher in endemic areas than that in non-endemic areas, particularly among males, residents aged ≥65 years and residents in economically developed regions. For malignant neoplasms of the digestive organs, ASMR was higher in endemic areas, with a statistically significant difference observed in females between the two regions. For cerebral infarction, ASMR was significantly lower in endemic areas than that in non-endemic areas among residents in economically developed regions. The rate of life lost due to ischemic heart disease and malignant neoplasms of the digestive organs was relatively high in endemic areas, whereas the rate due to cerebral infarction was

relatively high in non-endemic areas. These findings provide scientific evidence for optimizing comprehensive prevention and control strategies for endemic diseases and strengthening interventions for key diseases as well as practical insights for promoting regional health equity. Identifying high-risk populations and implementing targeted interventions can effectively protect the health of vulnerable groups and improve their overall social wellbeing.

**Conflicts of interest**: No conflicts of interest.

**Ethical statement**: Approved by the Ethics Committee of Harbin Medical University, with approval number (hrbmuecdc20221102). This study was conducted in accordance with the ethical guidelines and principles outlined in the Declaration of Helsinki.

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# SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. ASMRs and *RR*s from Poisson regression analysis for composite major causes of death, three major causes of death, and their main subtypes.

| Causes of death | $ASMR_{Total}$ (per 100,000) | $ASMR_{Endemic\ areas}$ (per 100,000) | $ASMR_{Non\text{-}endemic\ areas}$ (per 100,000) | $ASMR_{Mild\ endemic\ areas}$ (per 100,000) | $ASMR_{Moderate\ endemic\ areas}$ (per 100,000) | $ASMR_{Severe\ endemic\ areas}$ (per 100,000) | $RR_{Endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Mild\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Moderate\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ | $RR_{Severe\ endemic\ areas\ vs.\ Non\text{-}endemic\ areas}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Major causes of death | 416.30 | 427.52 | 363.83 | 415.37 | 496.63 | 346.25 | 1.18 (1.00−1.38) | 1.14 (0.94−1.38) | 1.37 (1.14−1.63)*** | 0.95 (0.77−1.16) |
| Heart diseases | 185.16 | 196.32 | 114.54 | 191.32 | 214.15 | 177.23 | 1.71 (1.23−2.29)*** | 1.67 (1.13−2.28)* | 1.86 (1.35−2.57)*** | 1.55 (1.09−2.17)* |
| Ischemic heart diseases | 169.13 | 181.47 | 95.39 | 179.40 | 189.71 | 172.41 | 1.90 (1.42−2.68)*** | 1.88 (1.37−2.68)*** | 1.99 (1.43−2.79)*** | 1.81 (1.25−2.66)*** |
| Cerebrovascular diseases | 98.12 | 89.53 | 141.00 | 87.36 | 111.65 | 61.79 | 0.63 (0.49−0.83)*** | 0.62 (0.46−0.89)* | 0.79 (0.66−1.06) | 0.44 (0.30−0.63)*** |
| Cerebral infarction | 59.48 | 56.97 | 96.66 | 52.64 | 67.88 | 42.07 | 0.59 (0.43−0.87)* | 0.54 (0.35−0.89)* | 0.70 (0.47−1.08) | 0.44 (0.23−0.84)*** |
| Malignant neoplasms | 133.02 | 141.99 | 105.86 | 137.08 | 171.07 | 107.61 | 1.34 (1.00−1.87) | 1.29 (0.89−1.86) | 1.62 (1.17−2.24)* | 1.02 (0.71−1.49) |
| Malignant neoplasms of digestive organs | 65.01 | 68.57 | 45.55 | 71.92 | 82.70 | 46.13 | 1.51 (0.96−2.50) | 1.58 (1.00−2.75) | 1.82 (1.13−3.06)* | 1.01 (0.58−1.84) |

Note: * $P<0.05$; ** $P<0.01$; *** $P<0.001$ (adjusted).
Abbreviation: ASMR=age-standardized mortality rate; *RR*=rate ratio.

SUPPLEMENTARY TABLE S2. ASMRs and *RR*s for major causes of death and subtypes by sex, age and economic conditions in Heilongjiang Province, 2024.

| Variable | Causes of death | $ASMR_{Total}$ (per 100,000) | $ASMR_{Endemic\ areas}$ (per 100,000) | $ASMR_{Non-endemic\ areas}$ (per 100,000) | $ASMR_{Mild\ endemic\ areas}$ (per 100,000) | $ASMR_{Moderate\ endemic\ areas}$ (per 100,000) | $ASMR_{Severe\ endemic\ areas}$ (per 100,000) | $RR_{Endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Mild\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Moderate\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Severe\ endemic\ areas\ vs.\ Non-endemic\ areas}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Male | Major causes of death | 504.54 | 518.13 | 446.81 | 490.54 | 610.47 | 431.32 | 1.16 (0.93−1.48) | 1.10 (0.84−1.45) | 1.37 (1.07−1.78) | 0.97 (0.73−1.29) |
| | Heart diseases | 210.80 | 234.84 | 101.95 | 202.63 | 269.91 | 225.32 | 2.30 (1.51−3.99)** | 1.99 (1.22−3.57)* | 2.65 (1.68−4.62)*** | 2.21 (1.33−3.96)* |
| | Ischemic heart diseases | 189.82 | 215.15 | 77.13 | 188.95 | 236.21 | 219.23 | 2.79 (1.77−5.38)*** | 2.45 (1.44−4.80)** | 3.06 (1.85−5.96)*** | 2.84 (1.67−5.65)*** |
| | Cerebrovascular diseases | 130.74 | 116.80 | 194.41 | 120.64 | 137.96 | 87.38 | 0.60 (0.42−0.92) | 0.62 (0.38−1.01) | 0.71 (0.47−1.13) | 0.45 (0.27−0.75)* |
| | Cerebral infarction | 80.84 | 69.05 | 135.93 | 65.87 | 90.42 | 45.26 | 0.51 (0.32−0.86) | 0.49 (0.26−0.90) | 0.67 (0.39−1.18) | 0.33 (0.15−0.66)* |
| | Malignant neoplasms | 163.00 | 166.49 | 150.44 | 167.27 | 202.59 | 118.63 | 1.11 (0.78−1.69) | 1.11 (0.73−1.74) | 1.35 (0.92−2.07) | 0.79 (0.50−1.28) |
| | Malignant neoplasms of digestive organs | 87.15 | 89.19 | 79.91 | 93.97 | 111.34 | 55.23 | 1.12 (0.70−2.06) | 1.18 (0.65−2.29) | 1.39 (0.83−2.59) | 0.69 (0.34−1.40) |
| Female | Major causes of death | 330.71 | 345.21 | 275.36 | 319.45 | 410.58 | 283.12 | 1.25 (0.97−1.68) | 1.16 (0.84−1.61) | 1.49 (1.12−2.03)* | 1.03 (0.74−1.44) |
| | Heart diseases | 160.11 | 170.61 | 120.80 | 168.67 | 180.69 | 157.34 | 1.41 (0.96−2.32) | 1.40 (0.86−2.35) | 1.50 (0.97−2.48) | 1.30 (0.81−2.19) |
| | Ischemic heart diseases | 148.93 | 159.56 | 107.86 | 163.72 | 160.34 | 153.51 | 1.48 (0.99−2.49) | 1.52 (0.93−2.60) | 1.49 (0.94−2.54) | 1.42 (0.87−2.46) |
| | Cerebrovascular diseases | 67.19 | 60.27 | 97.78 | 54.63 | 84.26 | 35.14 | 0.62 (0.39−1.04) | 0.56 (0.29−1.05) | 0.86 (0.51−1.52) | 0.36 (0.14−0.74)* |
| | Cerebral infarction | 39.48 | 33.11 | 67.56 | 32.56 | 48.51 | 13.88 | 0.49 (0.27−0.97) | 0.48 (0.19−1.06) | 0.72 (0.36−1.47) | 0.21 (0.04−0.55)* |
| | Malignant neoplasms | 103.41 | 114.32 | 56.79 | 96.16 | 145.63 | 90.64 | 2.01 (1.22−4.08)* | 1.69 (0.93−3.57) | 2.56 (1.49−5.33)** | 1.60 (0.86−3.39) |
| | Malignant neoplasms of digestive organs | 42.73 | 49.70 | 11.99 | 44.83 | 61.79 | 37.72 | 4.14 (1.63−16.30)** | 3.74 (1.28−15.70) | 5.15 (1.87−21.10)** | 3.15 (1.00−13.60) |
| <65 years | Major causes of death | 94.45 | 96.77 | 85.02 | 85.94 | 111.83 | 88.30 | 1.14 (0.84−1.64) | 1.01 (0.68−1.55) | 1.32 (0.92−1.95) | 1.04 (0.69−1.60) |
| | Heart diseases | 29.36 | 31.08 | 22.04 | 27.81 | 33.05 | 32.07 | 1.41 (0.81−3.26) | 1.26 (0.60−2.98) | 1.50 (0.77−3.52) | 1.46 (0.70−3.45) |
| | Ischemic heart diseases | 24.78 | 25.94 | 19.97 | 24.45 | 24.09 | 30.48 | 1.30 (0.73−3.23) | 1.22 (0.55−3.08) | 1.21 (0.57−3.02) | 1.53 (0.71−3.86) |
| | Cerebrovascular diseases | 18.82 | 16.8 | 27.88 | 18.89 | 18.38 | 12.52 | 0.60 (0.33−1.29) | 0.68 (0.30−1.55) | 0.66 (0.30−1.50) | 0.45 (0.15−1.11) |
| | Cerebral infarction | 6.61 | 4.77 | 14.73 | 5.86 | 3.92 | 4.70 | 0.32 (0.12−1.02) | 0.40 (0.06−1.55) | 0.27 (0.00−1.07) | 0.32 (0.00−1.29) |
| | Malignant neoplasms | 46.26 | 48.90 | 35.11 | 39.23 | 60.40 | 43.71 | 1.39 (0.87−2.55) | 1.12 (0.61−2.21) | 1.72 (1.01−3.30) | 1.24 (0.67−2.49) |
| | Malignant neoplasms of digestive organs | 24.56 | 27.21 | 12.99 | 25.69 | 32.70 | 21.03 | 2.09 (1.04−6.90) | 1.98 (0.83−7.32) | 2.52 (1.14−9.23) | 1.62 (0.63−5.94) |

Continued

| Variable | Causes of death | $ASMR_{Total}$ (per 100,000) | $ASMR_{Endemic\ areas}$ (per 100,000) | $ASMR_{Non-endemic\ areas}$ (per 100,000) | $ASMR_{Mild\ endemic\ areas}$ (per 100,000) | $ASMR_{Moderate\ endemic\ areas}$ (per 100,000) | $ASMR_{Severe\ endemic\ areas}$ (per 100,000) | $RR_{Endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Mild\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Moderate\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Severe\ endemic\ areas\ vs.\ Non-endemic\ areas}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ≥65 years | Major causes of death | 321.85 | 334.21 | 271.34 | 318.77 | 396.92 | 268.07 | 1.23 (1.01−1.54) | 1.17 (0.93−1.50) | 1.46 (1.18−1.84)** | 0.99 (0.77−1.28) |
| | Heart diseases | 155.80 | 171.42 | 90.74 | 158.21 | 191.34 | 158.17 | 1.89 (1.36−2.81)*** | 1.74 (1.20−2.70)* | 2.11 (1.48−3.19)*** | 1.74 (1.18−2.66)* |
| | Ischemic heart diseases | 144.34 | 161.16 | 74.42 | 152.20 | 173.32 | 154.70 | 2.17 (1.52−3.39)*** | 2.05 (1.37−3.29)** | 2.33 (1.60−3.75)*** | 2.08 (1.38−3.36)** |
| | Cerebrovascular diseases | 79.29 | 71.38 | 113.99 | 68.49 | 92.49 | 48.93 | 0.63 (0.46−0.90) | 0.60 (0.39−0.93) | 0.81 (0.57−1.20) | 0.43 (0.26−0.68)** |
| | Cerebral infarction | 52.88 | 45.96 | 83.72 | 43.25 | 65.10 | 24.35 | 0.55 (0.37−0.86) | 0.52 (0.30−0.88) | 0.78 (0.49−1.24) | 0.29 (0.14−0.53)*** |
| | Malignant neoplasms | 86.76 | 91.41 | 66.62 | 92.08 | 113.10 | 60.98 | 1.37 (0.97−2.12) | 1.38 (0.90−2.20) | 1.70 (1.14−2.66) | 0.92 (0.57−1.50) |
| | Malignant neoplasms of digestive organs | 40.45 | 42.38 | 31.57 | 43.39 | 53.91 | 25.68 | 1.34 (0.81−2.61) | 1.37 (0.75−2.87) | 1.71 (0.97−3.39) | 0.81 (0.39−1.75) |
| Developed regions | Major causes of death | 439.69 | 454.87 | 361.65 | 434.75 | 604.25 | 314.52 | 1.26 (0.99−1.67) | 1.20 (0.90−1.63) | 1.67 (1.29 2.23)*** | 0.87 (0.65−1.19) |
| | Heart diseases | 211.04 | 232.11 | 92.92 | 210.72 | 302.28 | 179.16 | 2.50 (1.62−4.49)*** | 2.27 (1.37−4.19)* | 3.25 (2.09−5.96)*** | 1.93 (1.20−3.52)* |
| | Ischemic heart diseases | 192.16 | 213.79 | 71.22 | 205.54 | 261.57 | 176.59 | 3.00 (1.90−5.93)*** | 2.89 (1.68−5.74)*** | 3.67 (2.24−7.20)*** | 2.48 (1.48−4.87)** |
| | Cerebrovascular diseases | 98.89 | 83.83 | 187.77 | 101.19 | 114.49 | 38.52 | 0.45 (0.31−0.69)*** | 0.54 (0.32−0.90) | 0.61 (0.40−0.97) | 0.21 (0.10−0.37)*** |
| | Cerebral infarction | 56.78 | 43.38 | 136.72 | 54.36 | 70.44 | 6.84 | 0.32 (0.20−0.55)*** | 0.40 (0.20−0.75)* | 0.54 (0.32−0.90) | 0.61 (0.40−0.97)* |
| | Malignant neoplasms | 129.76 | 138.93 | 80.96 | 122.84 | 187.48 | 96.85 | 1.72 (1.11−3.12) | 1.52 (0.89−2.83) | 2.32 (1.45−4.24)** | 1.20 (0.71−2.24) |
| | Malignant neoplasms of digestive organs | 69.51 | 74.54 | 43.77 | 70.71 | 103.20 | 45.47 | 1.70 (0.95−4.23) | 1.62 (0.78−4.19) | 2.36 (1.27−5.77)* | 1.04 (0.48−2.71) |

Continued

| Variable | Causes of death | $ASMR_{Total}$ (per 100,000) | $ASMR_{Endemic\ areas}$ (per 100,000) | $ASMR_{Non-endemic\ areas}$ (per 100,000) | $ASMR_{Mild\ endemic\ areas}$ (per 100,000) | $ASMR_{Moderate\ endemic\ areas}$ (per 100,000) | $ASMR_{Severe\ endemic\ areas}$ (per 100,000) | $RR_{Endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Mild\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Moderate\ endemic\ areas\ vs.\ Non-endemic\ areas}$ | $RR_{Severe\ endemic\ areas\ vs.\ Non-endemic\ areas}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Under-developed regions | Major causes of death | 387.98 | 396.59 | 363.73 | 375.73 | 381.98 | 488.63 | 1.09 (0.87−1.42) | 1.03 (0.79−1.39) | 1.05 (0.79−1.40) | 1.34 (0.96−1.85) |
| | Heart diseases | 152.92 | 159.81 | 133.58 | 163.59 | 129.51 | 229.73 | 1.20 (0.80−1.92) | 1.22 (0.78−2.04) | 0.97 (0.59−1.64) | 1.72 (0.99−3.02) |
| | Ischemic heart diseases | 140.20 | 148.31 | 115.60 | 149.52 | 122.17 | 215.91 | 1.28 (0.85−2.15) | 1.29 (0.81−2.25) | 1.06 (0.63−1.85) | 1.87 (1.04−3.39) |
| | Cerebrovascular diseases | 97.02 | 94.52 | 105.58 | 73.93 | 102.52 | 130.82 | 0.90 (0.59−1.50) | 0.70 (0.38−1.28) | 0.97 (0.57−1.70) | 1.24 (0.64−2.30) |
| | Cerebral infarction | 63.09 | 61.56 | 66.69 | 43.70 | 62.46 | 93.68 | 0.92 (0.54−1.80) | 0.66 (0.30−1.43) | 0.94 (0.47−1.94) | 1.40 (0.62−3.03) |
| | Malignant neoplasms | 138.04 | 142.26 | 124.57 | 138.20 | 149.96 | 128.07 | 1.14 (0.78−1.79) | 1.11 (0.71−1.84) | 1.20 (0.76−2.00) | 1.03 (0.59−1.77) |
| | Malignant neoplasms of digestive organs | 59.00 | 62.42 | 46.28 | 67.17 | 56.26 | 58.22 | 1.35 (0.75−3.09) | 1.45 (0.73−3.45) | 1.22 (0.55−3.02) | 1.26 (0.48−3.22) |

Note: * $P<0.05$; ** $P<0.01$; *** $P<0.001$ (adjusted).

Abbreviation: ASMR=age-standardized mortality rate; *RR*=rate ratio.