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Burden and Risk Factors of Neck Pain in China: A Dual-Database Study of GBD 2021 Population-Level Macro-Trends and CHARLS Individual-Level Prospective Cohort Analyses

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Background: We quantified the burden and temporal trends of neck pain (NP) in China using Global Burden of Disease (GBD) 2021 data and identified populations at higher risk of incident NP using longitudinal data from the China Health and Retirement Longitudinal Study (CHARLS).

Methods: GBD 2021 data were used to estimate NP incidence and prevalence and to assess temporal patterns through joinpoint regression, age–period–cohort modelling, decomposition, and frontier analyses. For the cohort analysis, 6310 CHARLS participants without NP at baseline (2011) and with complete data were followed across five waves through 2020. Incident NP was the outcome. Multivariable Cox regression identified independent predictors. Nonlinear associations, subgroup analyses, trend tests, and mediation analyses were performed, and a nomogram was constructed.

Results: GBD analyses showed that the absolute numbers of prevalent and incident NP cases in China increased, with the largest case counts in the 45–59 age group. Population growth and ageing were the primary drivers of this increase, while age-standardized rates remained stable The 1960–1965 birth cohort had the highest risk, and the 1997–2006 period had the lowest period-related risk. In CHARLS, 1849 (29.3%) participants developed NP. After multivariable adjustment, higher NP risk was associated with middle-aged/older adults, women, ethnic minorities, rural residence, greater chronic disease burden, functional impairment, and elevated depressive symptoms. NP risk showed a nonlinear association with depression severity and chronic disease count. Mediation analyses revealed bidirectional partial mediation: depressive symptoms mediated 19.7% of the chronic disease count-NP association, while chronic disease count (17.0%) mediated the depressive symptoms-NP association.

Conclusion: China' s NP burden is rising. Prioritize prevention for: ethnic minorities, middle-aged/older adults, women, rural residence, and individuals with chronic diseases, functional impairment, or depression. Critically, bidirectional mediation between depression and chronic diseases underscores the need for integrated interventions.

Keywords: neck pain, depression, chronic diseases, joinpoint regression analysis, mediation analyses

Introduction

Neck pain (NP) is one of the most common musculoskeletal disorders,[1] characterized by self-reported pain and functional limitation. It ranked ninth among 354 conditions causing years lived with disability (YLDs)[2] and fourth among global causes of disability,[3] posing a major public-health challenge.[4] Modern lifestyles—prolonged occupational sitting, widespread smartphone use, and reduced physical activity—are expected to further amplify the NP burden,[5] with global prevalence projected to rise by 32.5% to 269 million cases by 2050.[4] Therefore, enhancing NP prevention and early intervention is imperative.

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Disease distribution varies substantially across regions and populations due to differences in environmental exposures and unequal health-care resources.[6] As a developing nation with over 1.4 billion people experiencing rapid aging, China exhibits distinct regional disparities in natural resources and economic development, shaping unique epidemiological patterns of NP.[7] Systematic characterization of NP epidemiology in China is essential for designing nationwide, scalable health-management strategies. Although the Global Burden of Disease (GBD) provides a valuable global overview of NP, it offers limited insight into individual-level risk relationships for precision prevention. Moreover, existing studies on NP risk factors in Chinese populations are predominantly cross-sectional or retrospective, with a lack of large-scale prospective cohort evidence to establish exposure–outcome temporality, thereby constraining the development of targeted prevention strategies.

To address these gaps, our study uniquely integrates GBD macro-trends with longitudinal data from the China Health and Retirement Longitudinal Study (CHARLS). This dual-database approach offers two key advantages: (1) the first longitudinal cohort analysis of NP using the latest CHARLS waves, and (2) combined macro- and micro-level analyses that enable multi-angle characterization and mutual validation of population trends and individual risk factors.

Within this framework, we focus particularly on depressive symptoms and multimorbidity for two main reasons. First, both are highly prevalent among middle-aged and older adults and may influence NP through behavioral, biological, and social pathways, such as reduced physical activity, altered pain perception, and functional decline. Second, accumulating evidence[8] suggests potentially bidirectional relationships among pain, depression, and chronic disease, whereby each condition may exacerbate the others over time. Accordingly, using longitudinal data, we examine associations between depressive symptoms, multimorbidity, and incident NP, and further explore mediation and possible bidirectional mediation between these factors in relation to NP.

By integrating macro- and micro-level evidence, this study provides comprehensive, evidence-based support for NP prevention and management, public health policy evaluation, and healthcare resource allocation planning.

Methods

Data Collection and Study Population

The GBD database provides estimates of incidence, prevalence, mortality, years of life lost (YLL), YLD, and disability-adjusted life years (DALY) for 370 diseases and injuries across 204 countries and territories from 1990–2021. GBD database provides population-level data aggregated at the national and regional levels. Detailed methodologies for data acquisition and burden estimation are described in prior publications,[9] and this study adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting.[10] Due to patient information desensitization in the GBD study, the Institutional Review Board of the University of Washington approved the waiver of informed consent.[11] For this analysis, we extracted comprehensive data on population-level NP in China from 1990 to 2021, obtained from the GBD 2021 study via the Global Health Data Exchange (https://www.healthdata.org/research-analysis/gbd; released May 16, 2024; accessed January 20, 2025). The search criteria for this study were: GBD Estimate - cause of death or injury; Measure - DALYs, prevalence and incidence; Metric - number, percent, rate; Cause - neck pain; Location - China, as well as other BRICS countries including Brazil, Russian Federation, South Africa, Indonesia, Egypt, India, Iran (Islamic Republic of), Ethiopia, United Arab Emirates; Age - all ages, age-standardized, 5 years to >95 years; Sex - both, male, female; Year - 1990 to 2021.

The CHARLS is a nationally representative survey of Chinese adults aged ≥45 years that employs multistage sampling and probability-proportional-to-size sampling in urban and rural administrative units. The baseline survey began in 2011 and covered 28 provinces, 150 counties, 450 villages/communities, and approximately 17000 individuals from 10000 households. CHARLS collected individual-level data through comprehensive personal interviews and health assessments. Biennial follow-up surveys were conducted in 2013 (Wave 2), 2015 (Wave 3), 2018 (Wave 4), and finally in 2020 (Wave 5) for data collection. Our longitudinal analysis used the five-wave dataset spanning 2011–2020, with the 2011 survey serving as the baseline to ascertain incident NP over nine years. After applying the inclusion and exclusion criteria shown in Figure 1, a total of 6310 participants with complete baseline data, aged ≥ 45 years at baseline and with no NP at baseline, were included in the cohort analysis.

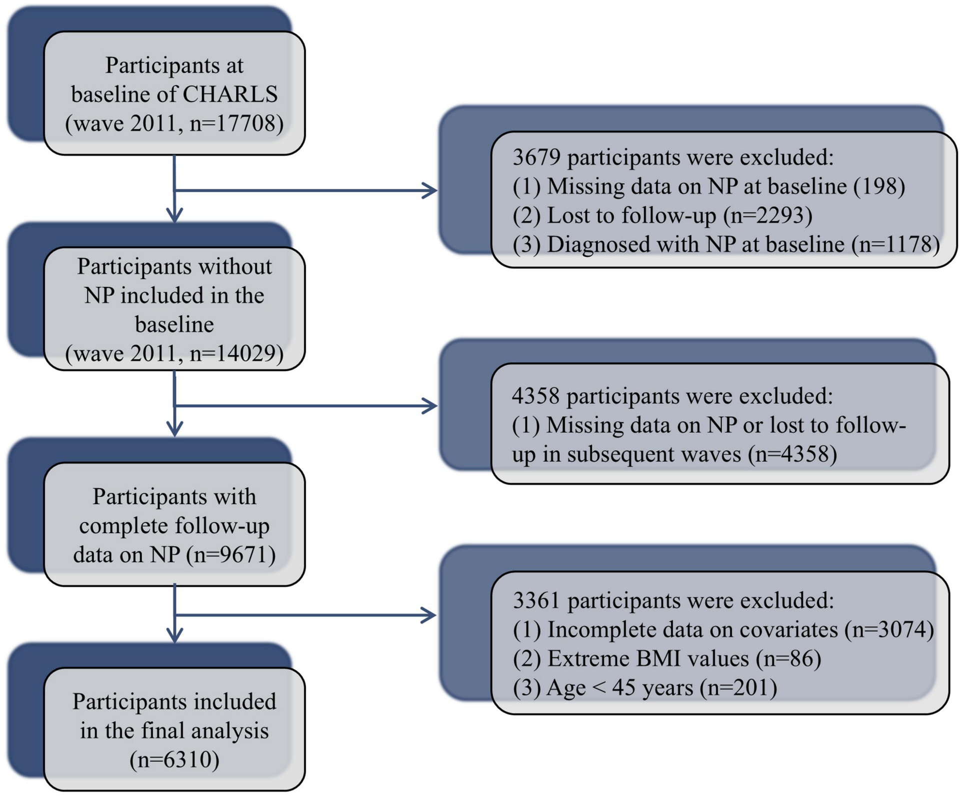

Figure 1 Flowchart of the Study Design.
Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; NP, Neck Pain; BMI, Body Mass Index.

Neck Pain

The GBD reference case definition for NP was pain (with or without referral into the upper limb [or limbs]) that lasts for at least 1 day. The ICD-9 code is 723.1, and the ICD-10 code is M54.2. The GBD study employed empirical redistribution algorithms, which enhance the cross-country comparability and validity of NP estimates.[9,12]

In the CHARLS Health Status and Functioning module, participants were first asked, "Are you frequently troubled by body pains?" (the questionnaire item code for 2020 is DA027; for 2018 is DA041_W4; for 2015 is DA041; for 2013 is DA041_WB16; for 2011 is DA041) with five response options: "None," "A little," "Somewhat," "Quite a bit," and "Very much." Respondents who reported any pain (any answer other than "None") were then prompted to identify affected body regions from a predefined list (multiple responses permitted): head, neck, shoulders, arms, wrists, fingers, chest, stomach, back, waist, buttocks, legs, knees, ankles, and toes (The questionnaire item code for 2020 is DA028; for 2018 is DA042; for 2015 is DA042; for 2013 is DA042; for 2011 is DA042). Participants who selected "neck" on this follow-up question were classified as having NP.

Study Variables

The primary outcome was incident NP. Time-to-event was measured from the baseline survey (2011) to the first report of NP or to censoring at study end (Wave 5, 2020); participants who remained free of NP contributed NP-free time. Baseline (2011) values of the following variables were used in all analyses.

Previous cross-sectional and small-sample studies have suggested that depression and chronic disease burden influence somatic pain.[13,14] We therefore treated the Center for Epidemiologic Studies Depression Scale-10 items (CESD-10) and Chronic Disease Count (CDC) as core exposures. CHARLS assessed depressive symptoms using the CESD-10 (score range 0–30; higher scores indicate greater depressive symptom burden); the scale's overall Cronbach's $\alpha = 0.815$.[15] CHARLS also recorded physician-diagnosed chronic conditions.[16] Fourteen conditions were screened: high blood pressure, diabetes, cancer, lung disease, heart problem, stroke, psych problem, psych problem, dyslipidemia, liver disease, kidney disease, digestive

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disease, asthma, and memory problem. A "yes" response to having ever been clinically diagnosed with any listed condition indicated presence of that disease. CDC was calculated as the total number of these chronic conditions present at baseline for each participant. In subsequent analyses CESD-10 and CDC were treated as ordinal variables; for multilevel regression tables and subgroup analyses we also used categorical definitions based on prior literature:[13] CESD-10 ≥10 denoted high depression risk, and chronic disease count was grouped as 0, 1–2, and ≥3.

We included the following covariates (baseline, 2011): age, gender, sleep time, nation (Han/Minority), place of residence (rural/urban), marital status (married/other), education (primary school and below, junior high school, senior high school, university and above), current smoking (yes/no), current alcohol use (yes/no), and household per-capita consumption (yuan). Body mass index (BMI) was calculated by dividing weight in kilograms by height in metres squared (kg/m^2). Participants' ability to perform routine tasks was assessed with the Katz Index of Independence in Activities of Daily Living (ADL),[17] covering bathing, dressing, toileting, transferring, continence, and feeding; needing help or being unable to perform a task was scored as an impairment, and scores range from 0 to 6 (higher scores = greater ADL impairment).[18]

Participant Characteristics

Participants in CHARLS were divided into two groups according to incident NP. Continuous variables with a normal distribution are presented as mean (SD) and compared between groups using Student's t-tests; non-normally distributed continuous variables are presented as median [IQR] and compared using the Mann–Whitney *U*-test. Categorical variables are reported as n (%) and compared with the chi-square test. All statistical analyses were performed using R Studio 4.2.1 (R Development Core Team, Vienna, Austria). A two-tailed p-value < 0.05 was considered statistically significant.

Neck Pain Burden Trends

The Joinpoint regression model was applied to analyze the overall and stage-specific trends of NP burden. This model identifies inflection points in the time series and fits each segment using linear regression, dividing the entire temporal sequence into distinct periods with divergent linear trends. Core metrics include the Annual Percentage Change (APC), which reflects the relative annual variation in DALYs between adjacent intervals (APC > 0 indicates an increase, while APC < 0 signifies a decrease), and the Average Annual Percent Change (AAPC), calculated as the weighted average of APC values across multiple intervals to evaluate the overarching trend. The age-standardized DALYs were selected, and their corresponding standard error was calculated. The processed data were then imported into Joinpoint (version 5.3.0; National Cancer Institute, Rockville, MD, USA) for analysis using the Permutation Test. Differences in APC across intervals were calculated, while AAPC was used to assess overall trend changes, with a significance level of $\alpha = 0.05$.

The age-period-cohort model can decompose epidemiological data into period, birth cohort, and age effects. Based on population estimates from the GBD database from 1990 to 2021, data were divided into 5-year intervals. Data from 1990–1991 were excluded from the analysis as they did not span a full 5-year interval. The Age Period Cohort Analysis Web Tool (https://dceg.cancer.gov/tools/analysis/apc) was used to construct the APC model. Drift (%/year) was used to quantify the long-term trend of disease incidence, while local drift was calculated to indicate trend variations over specific time periods. Relative risk (RR) was computed for each period and birth cohort. All statistical analyses were conducted using the Wald chi-squared test, with a significance level of $\alpha = 0.05$.

We applied Das Gupta's decomposition method to apportion changes in incident and prevalent case counts of NP in China from 1990 to 2021 to three drivers: population ageing, population growth, and epidemiological change.[19]

Frontier analysis was conducted based on the Socio-Demographic Index (SDI) constructed by the GBD, combined with NP disease burden data. Using techniques such as non-parametric data packet network analysis and local polynomial regression, the optimal practice frontier between socio-demographic development levels and disease burden was constructed. This frontier represents the minimum achievable age-standardized disease burden at different SDI levels. A bootstrap of 100 iterations was set to calculate the average disease burden (age-standardized DALYs rate) for each SDI value. The study focused on the BRICS countries (including Brazil, China, Egypt, Ethiopia, India, Indonesia, Iran, Russian Federation, South Africa, and United Arab Emirates). The distance (ie., effective difference) between each country's DALYs rate and the corresponding frontier boundary of SDI indicates the health benefits that the country or region has yet to realize based on its current development level.

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Influencing Factors

Cox proportional hazards regression was performed using the coxph function from the "survival" package in R Studio 4.2.1 (R Development Core Team, Vienna, Austria). Variables with $p < 0.05$ in univariable regression were considered candidate predictors and entered into multivariable models. To address collinearity between CDC, CESD-10, and specific disease statuses, a separate multivariable model including the 14 individual chronic conditions was also specified. Variables with $p < 0.05$ in the fully adjusted models were considered independent risk factors for incident NP. We estimated the hazard ratios (HR) and absolute risks for each independent influencing factor. The Kaplan-Meier method was employed to calculate the cumulative incidence rates at the specified follow-up time points (2, 4, 7, and 9 years) across groups stratified by different influencing factors. Optimal cut-points for continuous and ordinal predictors were estimated with surv_cutpoint function to identify thresholds that best discriminate risk groups. A nomogram for individualized risk prediction was constructed using the "rms" and "Hmisc" packages. Internal validation was performed with 500 bootstrap resamples to assess model calibration. Good agreement between the calibration curve and the 45° reference line indicated close concordance between predicted probabilities and observed outcomes.

Covariates were added sequentially to build nested models, allowing evaluation of how adjustment affected the association strength between CESD-10/CDC and NP and the robustness of the proportional-hazards assumption. For trend testing, CESD-10 and CDC were categorized into quartiles and the median value of each quartile was used to test for linear trends. To assess potential nonlinearity, restricted cubic splines (RCS) were fitted in the fully adjusted models with four knots placed at the 5th, 35th, 65th, and 95th percentiles of the exposure distribution.

Subgroup analyses were performed by adding interaction terms to the fully adjusted model to examine effect modification across covariate strata. Time-to-event outcomes were analyzed using the accelerated failure time model, which quantifies the relative shortening or prolongation of NP and allows intuitive decomposition of total, direct, and indirect effects. Compared with logistic regression or Cox-based mediation, accelerated failure time better and facilitates clinical interpretation. Based on prior literature and subgroup analysis results, variables of interest were selected from the independent risk factors for NP. Bidirectional mediation analyses were then conducted in strict accordance with the following temporal sequence: exposure variables → mediator variables → outcome event (NP). Mediation analyses were conducted using the "mediation" package to quantify indirect and direct pathways. The total effect (TE) was decomposed into the Average Direct Effect (ADE) and the Average Causal Mediation Effect (ACME); the mediation proportion was calculated as ACME/(ACME + ADE). Statistical significance of mediation estimates was evaluated by bootstrap resampling with 1000 iterations.

Results

National Prevalence and Incidence

China accounted for roughly 23.8% of absolute global incident NP cases, 23.5% of prevalent cases, and 23.6% of NP-related DALYs. The age-standardized incidence rate (567 [95% UI 449–700] vs. 519 [95% UI 408–633]), age-standardized prevalence rate (2550 [95% UI 2008–3142] vs. 2443 [95% UI 1923–3002]), and age-standardized DALY rate (255 [95% UI 167–358] vs. 242 [95% UI 163–343]) were all higher than the global averages (Supplementary Table S1). Although age-standardized incidence and prevalence have been relatively stable in recent years, absolute numbers of incident and prevalent cases continue to rise. The largest absolute burden of both prevalent and incident NP occurred in the 45–59 age group. In 2021, people aged ≥45 years accounted for 65.2% of absolute incident cases (vs. 39.5% in 1990), 71.5% of prevalent cases (vs. 46.9% in 1990), and 70.5% of DALYs (vs. 45.7% in 1990), indicating a marked shift toward older-age burden. Before age 80, NP incidence and prevalence were higher in women than men; after age 80, these rates were higher in men (Figure S1).

In the CHARLS cohort (Supplementary Table S2), 1849 participants (29.3%) developed incident NP during follow-up (mean follow-up 8.09 years). Baseline characteristics of the overall cohort were: mean age 58.08 years, 3315 (52.5%) female and 2995 (47.5%) male. Median CESD-10 score was 7; 4141 (65.6%) had CESD-10 <10 and 2169 (34.4%) had CESD-10 ≥10 (high depression risk). At baseline, 2165 (34.3%) participants reported no chronic conditions, 3184 (50.5%) had 1–2 conditions, and 961 (15.2%) had ≥3 chronic conditions.

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Joinpoint Regression Analysis

From 1990 to 2021, the age-standardized DALY rate of NP in China showed an overall upward trend (AAPC > 0, P < 0.05), with notable fluctuations across periods and distinct sex differences (Table 1). Among men, a plateau was observed from 1990 to 1995, followed by the lowest APC (indicating a temporary decline in burden) during 1995–2000. Thereafter, a sustained increase was noted from 2000 to 2012, peaking in 2006–2009 with the fastest growth rate, before stabilizing again in 2012–2021. Women experienced a prolonged, gradual rise over 1990–2006, after which the trend aligned with men, showing a marked increase followed by stabilization (Figure 2A).

Age-Period-Cohort Analysis

Net drift indicated a slow long-term upward trend in NP burden, with an estimated annual change of 0.120% (95% CI: −0.019, 0.260). The Wald chi-squared test yielded a χ^2 value of 2.857 (P = 0.091). Local drift analysis revealed significant heterogeneity across age groups (χ^2 = 133.897, P < 0.001) (Figure 2B). A shift from negative to positive values occurred between ages 42.5 and 47.5, suggesting that NP incidence began to rise after 47.5 years and peaked at age 62.5 [0.576% per year (95% CI: 0.458–0.694)].

The longitudinal age curve (Figure 2C) showed that within the same birth cohort, NP incidence rose sharply between ages 37.5 and 42.5, from 787.844 per 100000 (95% CI: 770.155, 805.940) to 1008.628 per 100000 (95% CI: 988.968, 1028.679), marking the steepest increase. This was followed by a plateau phase (42.5–62.5 years), then a steady rise from 62.5 to 72.5 years, peaking at 72.5 years with an incidence of 1306.410 per 100000 (95% CI: 1269.374, 1344.528), after which the incidence declined.

The cohort effect analysis demonstrated significant differences in NP risk across birth cohorts (ALL cohort RR, χ^2 = 144.252, P < 0.05). The 1960–1965 cohort exhibited the highest NP risk (Figure 2D). Risks steadily increased in earlier birth cohorts, while in later cohorts, risks declined year by year (P < 0.05). The period effect also showed significant variation (ALL period RR, χ^2 = 15.717, P = 0.008). NP risk decreased progressively before the reference period (2001–2006), then increased in subsequent years (Figure 2E), with 1997–2006 representing the lowest-risk period.

Decomposition Analysis

For incident cases, all three driving factors (population aging, population growth, and epidemiological changes) contributed positively to the increasing NP burden (Figure 3A). For prevalent cases, population aging and growth contributed positively, whereas epidemiological changes exerted a negative impact (Figure 3B). The distribution patterns were similar across sexes. After quantification, population aging and growth emerged as the primary determinants of the overall NP burden, while the contribution of epidemiological changes was minimal (Supplementary Table S3).

Frontier Analysis

Frontier analysis revealed a heterogeneous distribution of the association between NP burden and SDI across BRICS countries (Figure 3C). Ethiopia had the smallest efficiency gap among low-SDI countries, while Iran had the largest among higher-SDI countries (Figure 3D).

Table 1 Joinpoint Regression Analysis Based on Age-Standardized DALYs

Trend	Both			Male			Female		
	Interval	APC (95% CI)	P	Interval	APC (95% CI)	P	Interval	APC (95% CI)	P
Trend 1	1990–1995	0.039(0.021,0.058)	<0.001	1990–1995	0.036(0.021,0.051)	<0.001	1990–2006	0.042(0.038,0.047)	<0.001
Trend 2	1995–2001	−0.097(−0.116,-0.079)	<0.001	1995–2000	−0.378(−0.399,-0.357)	<0.001	2006–2009	0.949(0.835,1.064)	<0.001
Trend 3	2001–2006	0.084(0.058,0.111)	<0.001	2000–2006	0.052(0.037,0.067)	<0.001	2009–2012	0.087(−0.024,0.198)	0.117
Trend 4	2006–2009	0.887(0.804,0.970)	<0.001	2006–2009	0.821(0.754,0.887)	<0.001	2012–2021	−0.029(−0.039,-0.019)	<0.001
Trend 5	2009–2012	0.103(0.022,0.185)	0.016	2009–2012	0.068(0.004,0.133)	<0.001	——	——	——
Trend 6	2012–2021	−0.029(−0.036,-0.021)	<0.001	2012-2021	−0.029(−0.035,-0.023)	<0.001	——	——	——
AAPC	1990–2021	0.088(0.076,0.100)	<0.001	1990–2021	0.032(0.023,0.042)	<0.001	1990–2021	0.113(0.098,0.128)	<0.001

Abbreviations: DALYs, Disability-Adjusted Life Years; APC, Annual Percentage Change; CI, Confidence Intervals; AAPC, Average Annual Percentage Change.

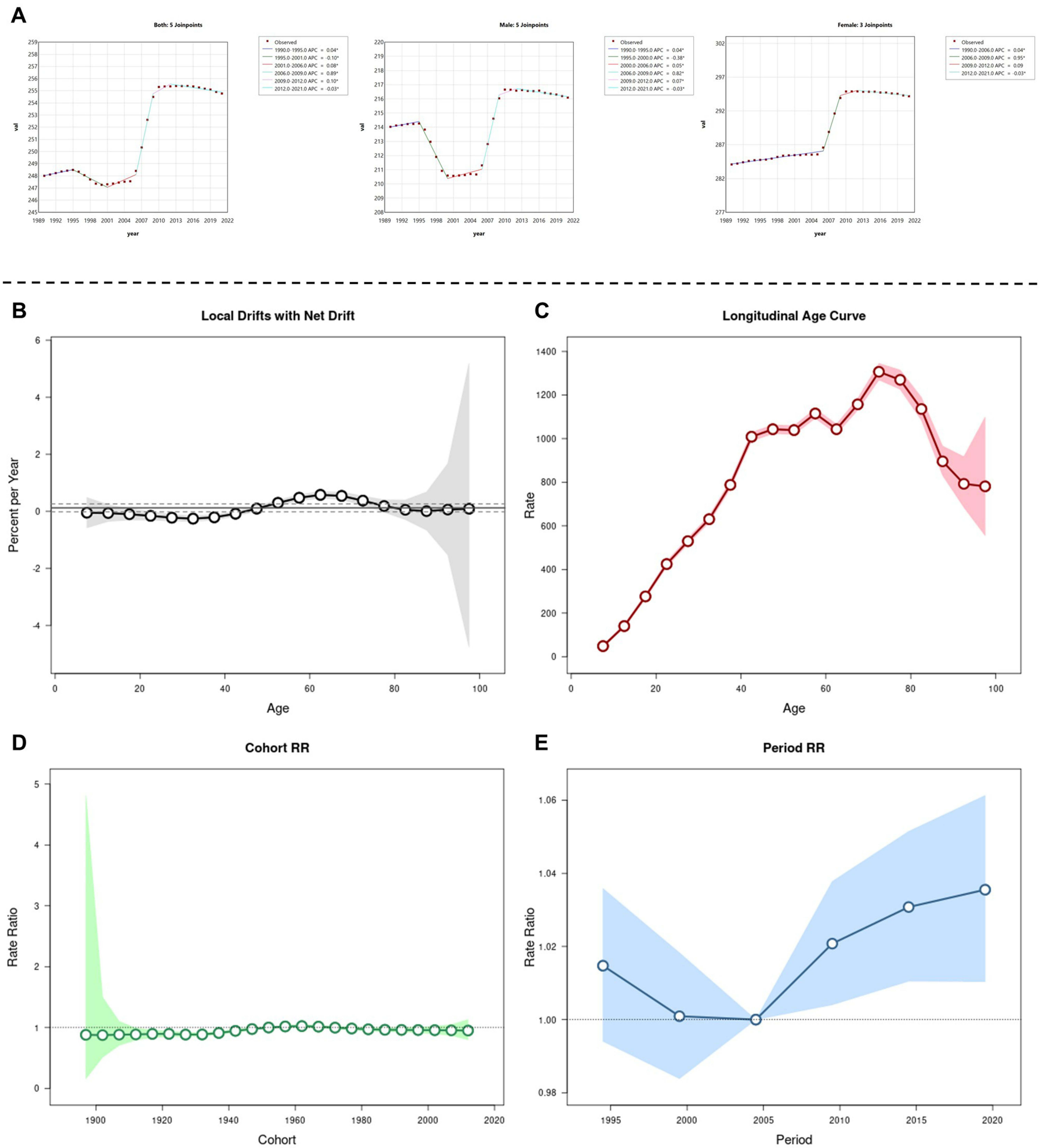

Figure 2 Temporal and cohort analyses of neck pain burden in China. (**A**) Joinpoint regression of age-standardized disability-adjusted life years rate for neck pain (1990–2021). *Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level. (**B**) Local drifts with net drift from age-period-cohort modeling (1992–2021). (**C**) Age effect on neck pain incidence. (**D**) Cohort effect on neck pain incidence. (**E**) Period effect on neck pain incidence.

Risk Factors for Neck Pain

A total of 11 variables with $P < 0.05$ in the univariate regression analysis (Supplementary Table S4) were included in the multivariate regression, which ultimately identified 7 independent predictors of NP (Table 2). The nomogram constructed from these results (Figure 4A), which exhibited coherent directional alignment with established risk effects: its predictive trends consistently mirrored both the NP absolute risk associations detailed in Supplementary Table S5, and the

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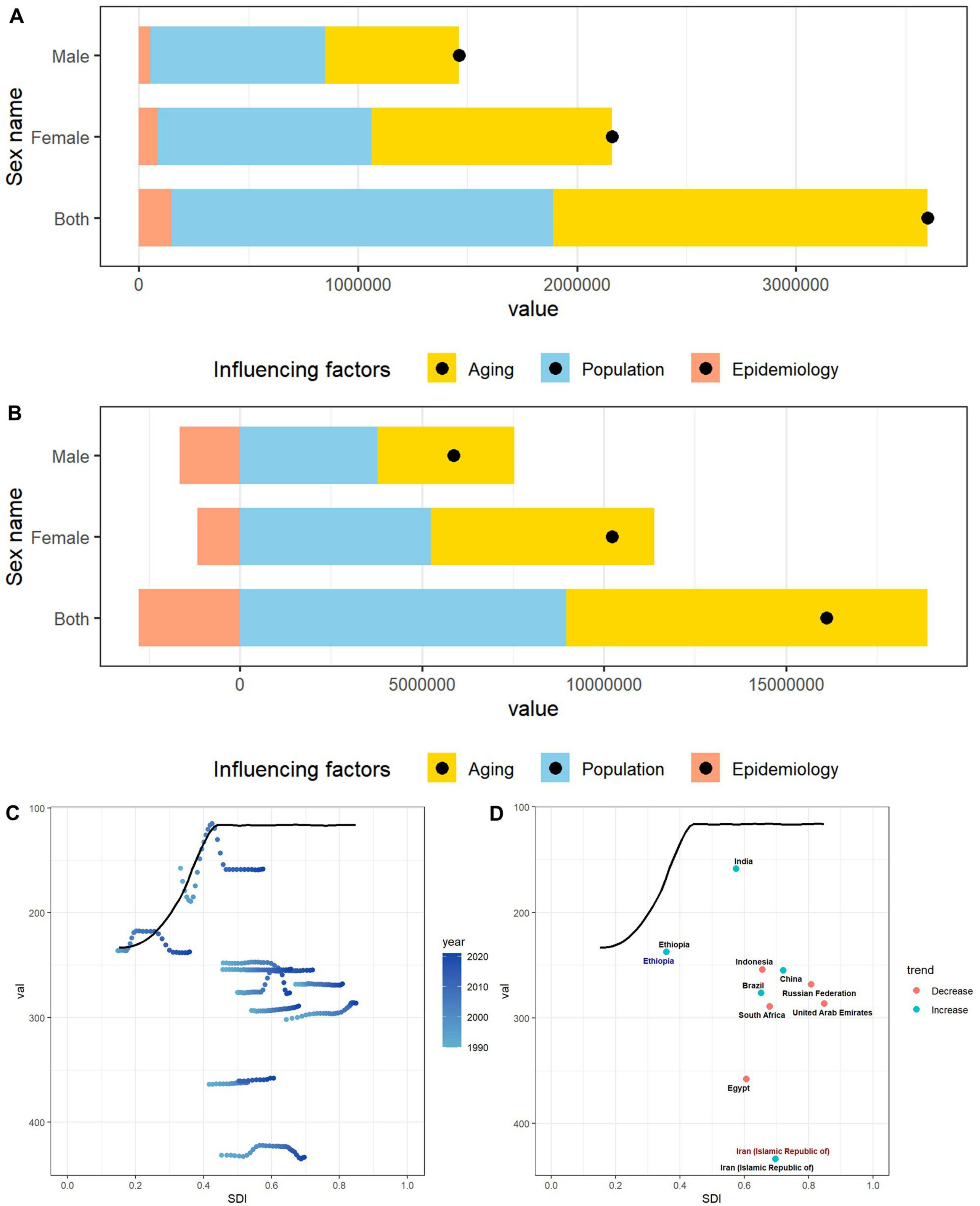

Figure 3 Decomposition of NP Burden and Frontier Analysis of SDI-NP in China, 1990–2021. (**A** and **B**) Population-attributable decomposition of changes in NP incidence (**A**) and prevalence (**B**) in China from 1990 to 2021, stratified by aging, population growth, and epidemiological changes. Black dots represent the total net change. (**C**) Frontier analysis based on the SDI and age-standardized DALY rates for NP. The black line represents the frontier boundary. Blue beads trace the dynamic trajectories of SDI and NP burden across countries from 1990 to 2021. (**D**) Countries and regions are plotted as individual points. Red points indicate a decline in age-standardized DALY rates for NP from 1990 to 2021, whereas green points indicate an increase. Countries with the largest effective gaps are highlighted in red (Iran).

Abbreviations: NP, Neck Pain; SDI, Socio-Demographic Index; DALYs, Disability-Adjusted Life Years.

cumulative incidence dynamics visualized in Figure S2. The cut-off values for continuous or ordinal variables were: age 51 years, CDC = 1, and CESD-10 = 6. In the calibration curves for the 4-year and 7-year NP probabilities corresponding to the nomogram, the calibration curves closely aligned with the ideal 45°reference line (Figure 4B and C), indicating minimal average deviation between predicted and actual values. In addition, multivariate regression results for 14 chronic diseases excluded from the main model due to collinearity (Table 2) indicated that individuals with arthritis, psychological problems, digestive disease, kidney disease, or heart problems had a higher risk of comorbid NP (Figure 4D).

To avoid bias from reverse causation, participants who had NP at baseline (n=198) were excluded. Following reference,[13] categorical transformations were applied to highlight clinically meaningful group differences: depressive status (CESD-10≥10) and strata of chronic disease count (CDC: 0/1-2/≥3). In Cox regression analyses, both CESD-10 and CDC remained significantly associated with incident NP after adjustment for confounders. In the fully adjusted models (CESD-10 Model 3A and CDC Model 3B), participants with CESD-10≥10 had a 1.361-fold higher risk of NP compared with those scoring<10 (HR 1.361, 95% CI: 1.236–1.498). Compared with the disease-free group, participants with 1–2 chronic diseases had an increased NP risk (HR 1.697, 95% CI: 1.518–1.897), and those with≥3 diseases had an NP risk of 2.601 (95% CI: 2.273–2.975). A P for trend < 0.05 — calculated using medians of quartile intervals — indicated a dose-response relationship: NP risk increased with higher CESD-10 scores and greater CDC (Table 3).

Restricted Cubic Spline

Fully adjusted models revealed statistically significant nonlinear associations of both CESD-10 scores and CDC with NP risk (P for nonlinear < 0.05). CESD-10 < 7 was associated with HR < 1 (no extra risk), whereas scores > 7 were linked to increasing NP risk with attenuation at higher scores (Figure 5A). CDC < 1 corresponded to HR < 1, but each additional chronic disease above this threshold produced progressively larger HR increases, implying synergistic effects of multimorbidity (Figure 5B).

Subgroup and Mediation Analyses

Subgroup analyses showed that the positive associations of CESD-10 score and CDC with incident neck pain were broadly consistent (Figure 5C and D). A statistically significant interaction by sex was observed for the CESD-10-NP association (stronger effect in men; P for interaction<0.05), while CDC's effect varied by depressive level (stronger association among participants with CESD-10 <10; P for interaction<0.05).

Based on the variables identified through the Cox regression model, accelerated failure-time mediation models (survreg) were applied. The results showed that CESD-10 shortened pain-free survival (TE=−0.549), with 19.7% of this effect mediated

Table 2 Results from Cox Regression

Variables	HR (95% CI for HR)	P
Regression excluding specified disease conditions		
Age	0.982 (0.978–0.988)	<0.001
Gender	0.594 (0.539–0.655)	<0.001
ADL	1.135 (1.078–1.195)	<0.001
Nation	0.757 (0.643–0.892)	<0.001
CESD-10	1.039 (1.031–1.046)	<0.001
CDC	1.298 (1.259–1.340)	<0.001
Place of residence	1.136 (1.026–1.258)	0.014
Regression for only 14 diseases		
Heart problem	1.480 (1.293–1.694)	<0.001
Psych problem	1.904 (1.324–2.737)	<0.001
Arthritis	2.079 (1.892–2.283)	<0.001
Kidney disease	1.540 (1.297–1.828)	<0.001
Digestive disease	1.577 (1.426–1.744)	<0.001

Abbreviations: CI, Confidence Intervals; HR, Hazard Ratio; ADL, Activity of Daily Living Scale; CESD-10, Center for Epidemiologic Studies Depression Scale-10 items; CDC, Chronic Disease Count.

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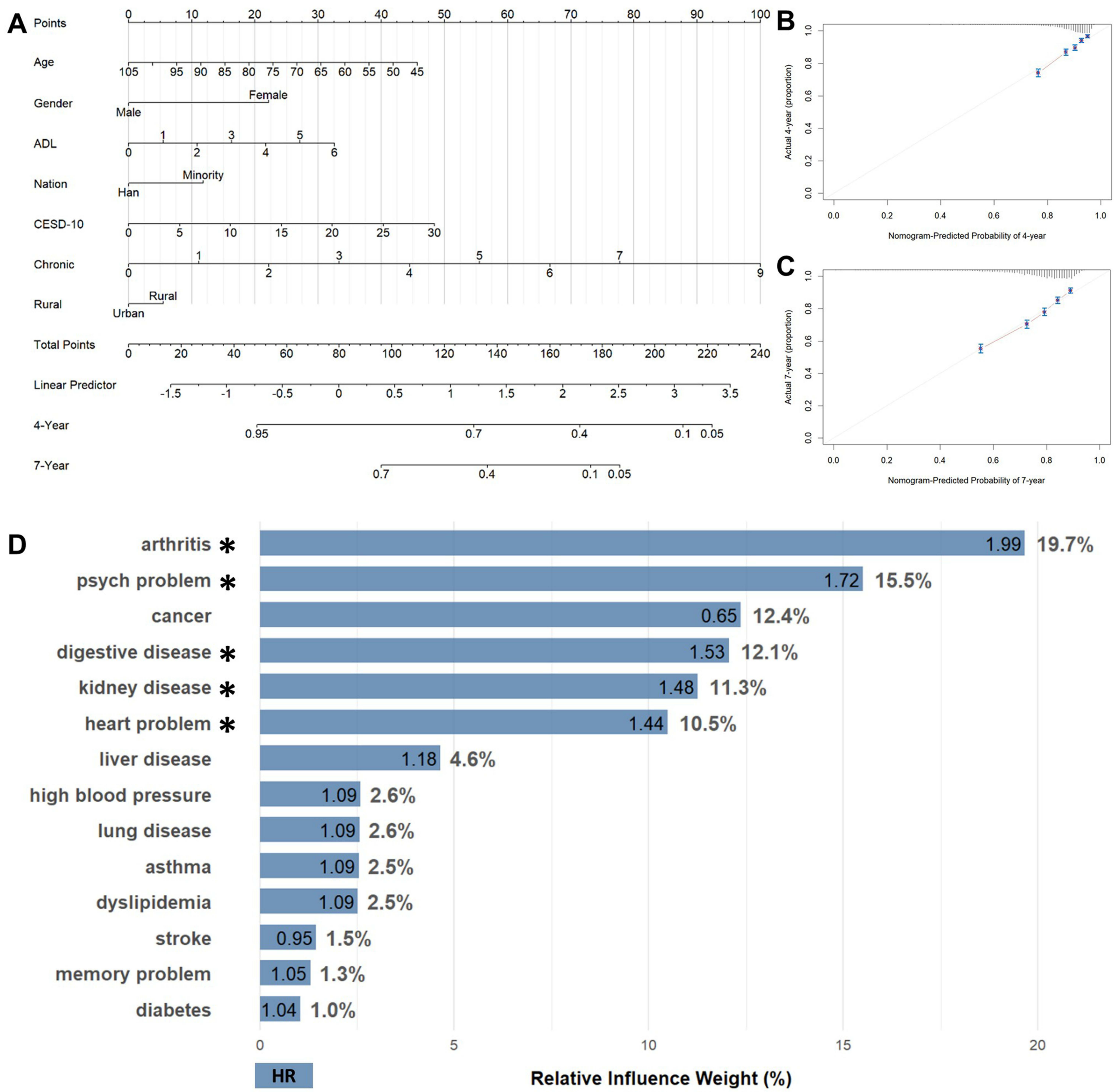

Figure 4 Multivariate Cox regression. (**A**) Nomogram: each prognostic factor was assigned a score, and the total score corresponded to the probability of an individual patient remaining NP-free at specific time points. NP, neck pain; ADL, Activity of Daily Living Scale; CESD-10, Center for Epidemiologic Studies Depression Scale-10 items. (**B** and **C**) Calibration curves of the nomogram for 4-year (Panel (**B**) and 7-year (Panel (**C**) NP prediction. The x-axis represents the nomogram predicted probability of NP at the corresponding follow-up time point, while the y-axis indicates the observed NP probability estimated by the Kaplan-Meier method and validated using 500 bootstrap resamples. Blue error bars represent the 95% confidence interval. The red solid line shows the actual calibration curve, and the gray dashed line refers to the ideal calibration line (y = x, indicating perfect agreement between predicted and observed probabilities). (**D**) Multivariate Cox regression results based on the presence of 14 chronic diseases; *Indicates P < 0.05; HR, Hazard Ratio; $\mathrm{Weight} = \frac{|\beta_i|}{\sum_{k=1}^{p}|\beta_k|}100\%$; $|\beta_i|$, absolute value of a single variable's regression coefficient; $\sum|\beta_k|$, sum of absolute regression coefficients across all variables.

by chronic disease accumulation and 10.1% mediated by sex. CDC also shortened pain-free survival (TE=−2.468), 17.0% of which was mediated through depressive symptoms (Figure S3). The sex pathway revealed a bidirectional mechanism: males (coded = 1) experienced delayed NP onset associated with lower CESD-10 scores, whereas females (coded = 0) experienced earlier NP onset associated with higher CESD-10 scores. These contributions were similar in magnitude but opposite in direction (Table 4).

Table 3 Multivariate-Adjusted Cox Regression and Linear Trend Analysis for CESD-10 and CDC

Variables	Model 1A		Model 2A		Model 3A		Model 4A	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
CESD-10								
< 10	1.000 (Reference)	——	1.000 (Reference)	——	1.000 (Reference)	——	1.000 (Reference)	——
≥10	1.877 (1.722–2.046)	<0.001	1.733 (1.584–1.896)	<0.001	1.389 (1.262–1.529)	<0.001	1.361 (1.236–1.498)	<0.001
P for linear trend (quartile-based)	1.072 (1.063–1.081)	<0.001	1.064 (1.055–1.073)	<0.001	1.045 (1.035–1.055)	<0.001	1.039 (1.029–1.048)	<0.001
	Model 1B		Model 2B		Model 3B			
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P		
CDC								
0	1.000 (Reference)	——	1.000 (Reference)	——	1.000 (Reference)	——		
1–2	1.807 (1.618–2.019)	<0.001	1.830 (1.639–2.043)	<0.001	1.697 (1.518–1.897)	<0.001		
≥3	3.028 (2.666–3.440)	<0.001	3.110 (2.737–3.535)	<0.001	2.601 (2.273–2.975)	<0.001		
P for linear trend (quartile-based)	1.483 (1.423–1.546)	<0.001	1.498 (1.436–1.562)	<0.001	1.421 (1.360–1.485)	<0.001		

Notes: Model 1A: Crude; Model 2A: Adjust: Age + Gender + Place of residence + Education level + Marital status + Nation + Household consumption per capita; Model 3A: Adjusting for Smoke + Drink + Sleep time + BMI + ADL + CDC based on Model 2; Model 4A: Replace CDC in Model 3A with the morbidity status of 14 specific chronic diseases. Model 1B: Crude; Model 2B: Adjust: Age + Gender + Place of residence + Education level + Marital status + Nation + Household consumption per capita; Model 3B: Adjusting for Smoke + Drink + Sleep time + BMI + ADL + CESD-10 based on Model 2.

Abbreviations: CESD-10, Center for Epidemiologic Studies Depression Scale-10 items; CDC, Chronic Disease Count; CI, Confidence Intervals; BMI, Body Mass Index; ADL, Activity of Daily Living Scale.

Discussion

The 2021 GBD ranked neck and back pain as the fourth leading cause of DALYs globally.[3] Although the burden of low back pain in China has declined,[20] the overall burden of neck pain (NP) has not shown comparable improvement, suggesting that current prevention and control measures may not have achieved their desired impact. By integrating macro-level GBD trends with individual-level CHARLS cohort data, this study characterizes NP from complementary epidemiological and risk-factor perspectives, strengthening causal inference.

Macro-level analyses indicate that China contributes substantially to global NP incidence and prevalence. GBD 1990–2021 data show significant increases in crude (non-age-standardized) NP metrics, while the CHARLS nine-year follow-up observed a cumulative NP incidence of 29.3%. However, these estimates require cautious interpretation due to methodological distinctions. The GBD integrates multisource data—including administrative claims, hospital records, and population-based surveys across all age groups—whereas CHARLS relies exclusively on self-reported pain, which may introduce ascertainment bias and potential overestimation. Furthermore, the CHARLS cohort (aged ≥45 years) represents a demographic at peak risk for degenerative NP, with a relatively recent and shorter follow-up period. Consequently, NP estimates derived from CHARLS are likely modestly higher than those from GBD analyses. The age-period-cohort analysis yielded a Net Drift of 0.120%, suggesting relatively modest changes in age-standardized rates and that the “true” underlying risk has not markedly worsened. Decomposition analysis attributes most of the absolute burden increase to population growth and aging. Given China’ s large population base and accelerated aging, the absolute number of NP cases is likely to rise further, underscoring the need for proactive allocation of healthcare resources. Joinpoint analysis showed declines in male age-standardized DALYs in 1995–2000 and increases in 2006–2009, whereas female rates rose slowly over a 16-year span with no clear decline. Rapid industrialization and mechanization since the late 1990s may have reduced heavy physical labor exposure among men, while women—overrepresented in clerical and service roles—were less affected. The spread of computers and smartphones around 2006–2009 likely exacerbated neck strain, highlighting the importance of public education on ergonomic device use.[21] The age–period–cohort model identified 1997–2006 as the period of lowest NP risk, reinforcing the role of occupational transitions in shaping population burden. Cohort analysis identified the 1960–1965 birth cohort as having the highest NP risk. Early-life nutritional deprivation during infancy in this cohort may have impaired musculoskeletal development and later increased susceptibility to degenerative changes from chronic mechanical loading in adulthood.[22] Prior studies linking famine exposure to higher adult cardiovascular disease,[23] hypertension,[24] and diabetes[25] are consistent with the “thrifty

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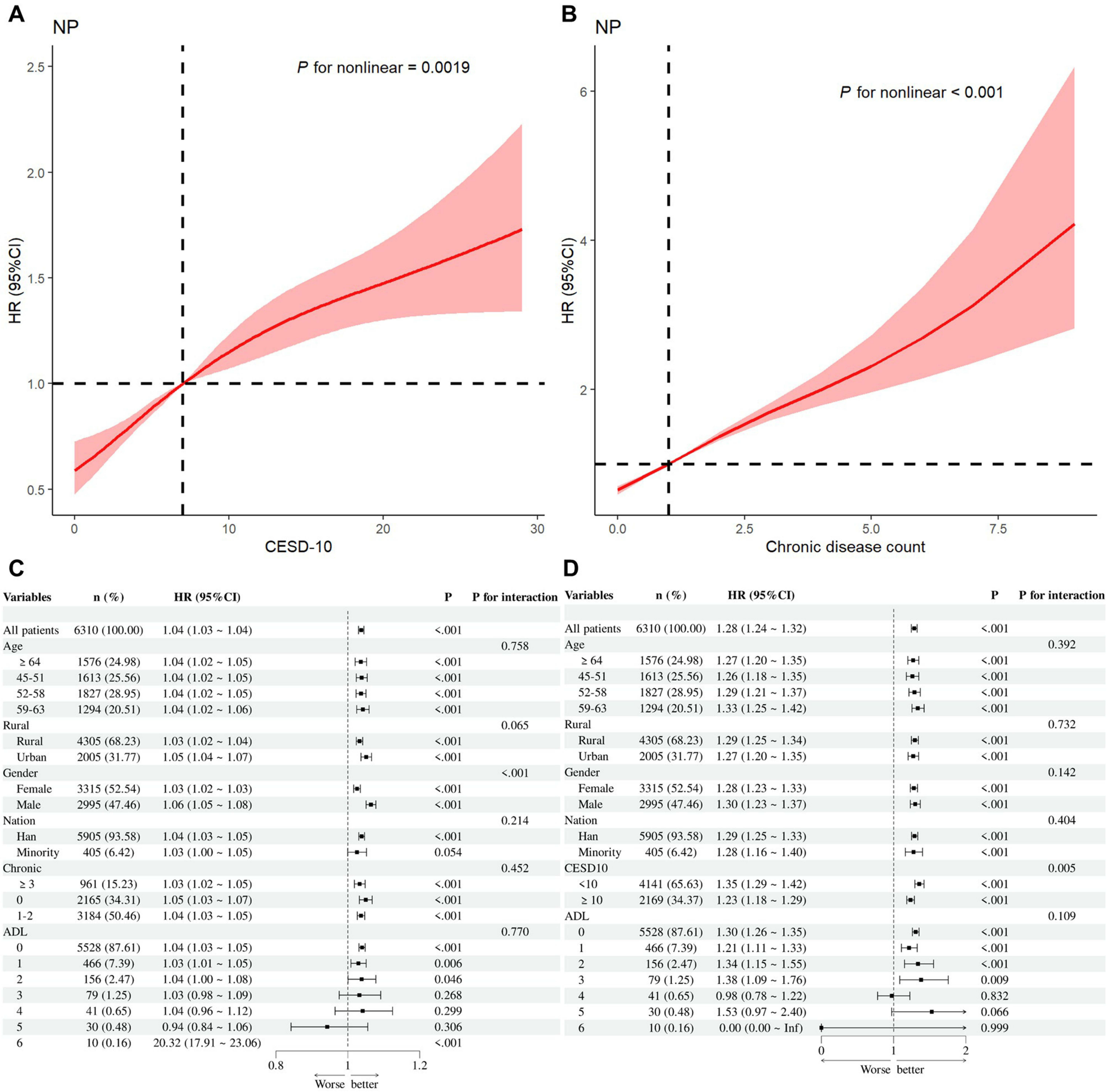

Figure 5 Restricted cubic spline curves (**A** and **B**) and subgroup-analysis forest plots (**C** and **D**). (**A**) Exposure-response association between CESD-10 score and NP. (**B**) Exposure-response association between CDC and NP. (**C**) Subgroup analysis of the association between CESD-10 and NP risk, adjusted for age, place of residence, sex, nation, CDC, and ADL. (**D**) Subgroup analysis of the association between CDC and NP risk, adjusted for age, place of residence, sex, nation, CESD-10, and ADL.
Abbreviations: HR, Hazard Ratio; CI: Confidence intervals; CESD-10, Center for Epidemiologic Studies Depression Scale-10 items; NP, Neck Pain; CDC, Chronic Disease Count; ADL, Activity of Daily Living Scale.

phenotype" (Barker) hypothesis.[26] Finally, although higher SDI typically correlates with stronger health systems and better chronic disease control,[27] cross-country differences in NP burden among BRICS nations imply that development level alone does not determine NP trends—culturally and structurally tailored prevention strategies remain necessary.

We synthesized individual susceptibility patterns for NP. People aged 45–59 accounted for the largest number of prevalent and incident cases, consistent with global patterns.[28] The longitudinal age curve identified 37.5–42.5 years as a critical window of rapidly increasing incidence, possibly reflecting accelerated cervical disc degeneration[29] and heightened risk of neuroinflammation in fiber-dense regions.[30] Incidence declined markedly after age 75; CHARLS analyses (age range 45–105) showed a similar trend (HR=0.982), echoing cross-sectional findings of lower reported NP prevalence in the oldest-old.[13] This decline

Table 4 Mediation Analysis of the Association Between Key Factors and Neck Pain

Independent Variable	Mediator	TE (95% CI)	ACME (95% CI)	ADE (95% CI)	Mediation Proportion (95% CI)
CESD-10	CDC	−0.549 (−0.638, −0.459)	−0.108 (−0.130, −0.088)	−0.441 (−0.524, −0.361)	0.197 (0.164, 0.237)
	Gender	−0.550 (−0.642, −0.463)	−0.056 (−0.072, −0.041)	−0.494 (−0.579, −0.408)	0.101 (0.077, 0.132)
CDC	CESD-10	−2.468 (−2.818, −2.134)	−0.417 (−0.510, −0.337)	−2.051 (−2.362, −1.756)	0.170 (0.137, 0.202)
Gender	CESD-10	4.697 (3.879, 5.529)	0.683 (0.520, 0.842)	4.014 (3.184, 4.839)	0.145 (0.110, 0.185)

Abbreviations: TE, Total Effect; CI, Confidence Intervals; ACME, Average Causal Mediation Effect; ADE, Average Direct Effect; CESD-10, Center for Epidemiologic Studies Depression Scale-10 items; CDC, Chronic Disease Count.

may partly reflect reduced pain sensitivity, cognitive impairment, or underreporting due to comorbidity in very old adults. Sex differences were pronounced: women had higher incidence than men before age 80, after which the pattern reversed. Regression results in CHARLS indicate that, overall, women aged ≥45 have higher NP risk than men. Explanations include hormonal effects lowering pain thresholds and delaying recovery in women,[31] greater cervical biomechanical stability in men,[32] and higher prevalence of sedentary clerical occupations among women. We also observed that sex substantially mediates/moderates the depression-NP link, with women more likely to somaticize depressive symptoms as pain.[33] Rural residence and minority status were associated with higher NP risk. The rural excess aligns with a community-based cross-sectional study in rural Gadchiroli[34] and likely reflects shortages in healthcare access, greater manual labor, and sustained head-down postures; rural-to-urban migration has also exacerbated rural aging.[35] Elevated NP risk among some minority populations (notably in western and northern regions)[36] may relate to cold climates, challenging terrain, and local cultural practices.[37] In summary, rational allocation of public health resources is required to optimize the prevention and control framework for high-risk populations of NP (eg., women aged 45–75 years), with prioritized enhancement of medical resource distribution and health education in ethnic minority communities and rural areas.

We confirmed that comorbid chronic conditions—particularly cardiovascular disease, arthritis, kidney and digestive disorders—and depressive symptoms are important risk factors for NP, with NP risk rising nonlinearly as multimorbidity or depression severity increases.[14] Approximately 28.8% of Chinese adults aged ≥40 score >10 on the CESD-10. Depression may amplify pain through catastrophizing, reduced activity, and increased muscle tension.[38] In China, chronic conditions affect nearly 50% of middle-aged and older adults.[39] A Saskatchewan population-based study reported significant associations between NP and both cardiovascular and digestive diseases.[40] Chronic inflammation appears to be a central mechanism linking pain and cardiovascular disorders: it promotes heart disease by inducing endothelial dysfunction and dysregulating lipid metabolism, while also sensitizing the central nervous system and peripheral nociceptors, thereby increasing pain perception and persistence.[41] Digestive disorders may influence NP via neural referral, systemic inflammation, or malnutrition, and gut-microbiota dysbiosis can modulate central pain processing.[42,43] Kidney disease may contribute indirectly through altered bone metabolism,[44] and arthritis directly produces shoulder–neck symptoms (it showed the largest regression coefficient in multivariable models).[45] Furthermore, chronic disease accumulation induces frailty and amplifies pain perception sensitivity, indirectly promoting neck pain through elevated depression risk.[46] As evidenced by Moussavi S et al, the depression prevalence was 3.2% in disease-free individuals versus 23% in those with multimorbidity.[47] Multimorbidity and depression mutually reinforce each other—via inflammation, adverse health behaviors, and medication effects—forming a vicious cycle that amplifies pain.[48] Our subgroup and mediation analyses identified reciprocal mediation patterns between CDC and depressive symptoms (CESD-10), highlighting the potential relevance of integrated, person-centered multidisciplinary care. These findings generate the hypothesis that early management strategies addressing both multimorbidity and depressive symptoms—particularly through nonpharmacologic biopsychosocial approaches such as structured exercise programs combined with psychological interventions—may be beneficial, rather than focusing exclusively on pain treatment.[49] However, given the observational design, causal inferences cannot be made. Whether treating depression or slowing multimorbidity progression reduces NP incidence requires confirmation in prospective interventional studies.

Unlike a prior cross-sectional analysis based on 2018 CHARLS data,[13] our study used a prospective design and excluded prevalent NP cases at baseline, thereby reducing the risk of reverse causation. We found no strong association

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between sleep duration and incident NP, suggesting that earlier cross-sectional links may partly reflect NP causing sleep disturbance. Concerning functional limitation (activity ability), previous work[13] often treated it as a consequence of NP; in contrast, after excluding baseline NP we observed that activity impairment also predicts subsequent NP, implying bidirectional influence. Low activity may promote frailty or coexist with severe musculoskeletal/neurological conditions that increase pain risk. Consistent with guidelines, we recommend ≥150 minutes/week of moderate-intensity or ≥75 minutes/week of vigorous aerobic activity plus ≥2 days/week of muscle-strengthening exercise to alleviate NP.[50]

Strengths of this study include the use of the nationally representative CHARLS cohort with longitudinal follow-up and a prospective design, supported by rigorous sampling protocols to ensure data robustness. By integrating data from both GBD and CHARLS, we were able to comprehensively examine burden trajectories and individual risk profiles of NP in China, thereby providing valuable evidence to inform targeted prevention strategies. Several limitations of this study should be acknowledged. First, methodological differences between the CHARLS and GBD datasets—including variations in case definitions, measurement strategies, and regional data quality—may limit direct comparability. CHARLS relies on self-reported neck pain outcomes, which may introduce recall bias and diagnostic heterogeneity; in contrast, GBD estimates are derived from statistical modeling with imputation for missing data, which entails inherent uncertainties related to such imputation. Second, inherent design constraints of the CHARLS database include fixed follow-up intervals, which prevent precise ascertainment of the exact timing of neck pain onset. In addition, survey-related biases may inevitably introduce further residual biases. Third, our study population was limited to Chinese adults aged 45 years and older, which restricts the generalizability of our findings to younger age groups. External validation using independent, population-based datasets is therefore warranted. Furthermore, despite adjustment for a wide range of covariates, residual confounding from unmeasured or incompletely assessed factors cannot be entirely ruled out. Finally, the absence of real-time updates in publicly available datasets limits our ability to capture the most recent epidemiological trends of neck pain. Future well-designed randomized controlled intervention trials are warranted to validate our findings and provide high-quality evidence for the prevention and clinical management of neck pain.

Conclusion

NP constitutes a substantial and growing public health burden in China. Although age-standardized incidence and prevalence rates have remained relatively stable, the absolute number of affected individuals has risen markedly, primarily driven by population growth and demographic ageing. Distinct disparities in burden were observed across population subgroups, with middle-aged and older adults, women, rural residents, and ethnic minority populations experiencing disproportionately higher risk, underscoring the need for targeted prevention and resource allocation strategies. In the longitudinal cohort, depressive symptoms, chronic disease accumulation, and impaired activities of daily living were consistently associated with incident NP, indicating that NP commonly co-occurs with psychological distress and multimorbidity. Importantly, the observed bidirectional partial mediation between depressive symptoms and chronic disease burden in relation to NP suggests that effective prevention and management may require integrated strategies addressing both mental health and multimorbidity, rather than focusing exclusively on musculoskeletal symptoms. Collectively, these findings support the adoption of integrated, biopsychosocial approaches to NP prevention and management. Strengthening access to preventive healthcare, mental health services, and coordinated chronic disease management—particularly in underserved rural and ethnic minority communities—may be critical to mitigating the expanding absolute burden of NP in China.

Abbreviations

NP, Neck Pain; YLDs, Years Lived with Disability; GBD, Global Burden of Disease; CHARLS, China Health and Retirement Longitudinal Study; YLL, Years of Life Lost; DALYs, Disability Adjusted Life Years; CDC, Chronic Disease Count; CESD-10, Center for Epidemiologic Studies Depression Scale-10 items; BMI, Body Mass Index; ADL, Activities of Daily Living; APC, Annual Percentage Change; AAPC, Average Annual Percent Change; RR, Relative Risk; SDI, Socio-Demographic Index; RCS, Restricted Cubic Splines; TE, Total effect; ADE, Average Direct Effect; ACME, Average Causal Mediation Effect; UI, Uncertainty Intervals; CI, Confidence intervals; HR, Hazard Ratio.

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Data Sharing Statement

The data sources and codes used in the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 are publicly available on the Internet (https://ghdx.healthdata.org/gbd-results-tool). The CHARLS data reported in this paper is available from: https://charls.pku.edu.cn.

Ethics Approval and Consent to Participate

This study used de-identified, publicly available data from the CHARLS and the GBD database. According to Item 1 and Item 2 of Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects (China, February 18, 2023), research based on legally obtained public data or anonymized data that does not involve sensitive personal information or cause harm to individuals is exempt from additional ethical review. Therefore, this study was exempt from approval by our Institutional Review Board or local ethics committee. The original CHARLS project was approved by the Biomedical Ethics Review Committee of Peking University (IRB No.: IRB00001052-11015), and all participants provided written informed consent. The GBD database provides aggregated data without individual identifiers. All data were used in compliance with relevant data access and usage policies.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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