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The Association Between the Frailty Index and Arthritis Among Middle-Aged and Older Chinese Adults (≥45 Years): Evidence From the GBD 2023, CHARLS, and Mendelian Randomization Analyses

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Abstract

Background

Arthritis is a common musculoskeletal disorder affecting more than 600 million people worldwide. It substantially impairs quality of life and mental health and increases reliance on opioid medications. Despite its high prevalence, effective prevention and management remain limited. Growing evidence suggests an association between frailty—reflecting reduced physiological reserve—and the risk of arthritis. This study aimed to quantify the burden of arthritis among Chinese adults aged ≥ 45 years and to examine the causal relationship between frailty and arthritis risk.

Methods

We used data from the Global Burden of Disease (GBD) 2023 to estimate incidence, prevalence, and disability-adjusted life years (DALYs) of arthritis among Chinese adults aged ≥ 45 years, including temporal trends (1990–2023), spatial patterns, and age-standardized rates, with subgroup analyses by sex and age. Associations between frailty and arthritis were assessed using China Health and Retirement Longitudinal Study (CHARLS) data with multivariable logistic regression and progressive adjustment for demographic, socioeconomic, and health-related confounders. Subgroup and sensitivity analyses were conducted to evaluate robustness. Two-sample Mendelian randomization (MR) using genetic instruments for frailty was performed to investigate potential causal effects on overall arthritis and osteoarthritis.

Results

From 1990 to 2023, age-standardized rates of arthritis among Chinese adults aged ≥ 45 years remained relatively stable, whereas the absolute burden increased substantially. In 2023, an estimated 154.8 million individuals (95% uncertainty interval: 133.9–177.6 million) were affected, accounting for nearly one-third of the global burden in this age group. The burden was higher in women and older adults. Higher frailty was strongly associated with increased arthritis risk. Compared with the lowest frailty quartile, individuals in the highest quartile had a more than twofold increased risk (odds ratio = 2.68, 95% confidence interval: 1.65–4.35; $p < 0.001$) after full adjustment. MR analyses provided additional evidence consistent with a potential causal effect of frailty on arthritis.

Conclusions

Arthritis remains a major and growing public health challenge among middle-aged and older Chinese adults. Frailty shows strong predictive value for arthritis risk and may serve as an effective tool for risk

stratification. Integrating frailty assessment into clinical practice and public health strategies may enable earlier prevention and improved management.

Introduction

Arthritis are major chronic arthritic disorders and constitute a substantial and growing public health burden due to persistent pain, progressive functional limitation, and long-term disability. According to the Global Burden of Disease (GBD) 2021 estimates, approximately 595 million individuals worldwide were living with OA in 2020, representing 7.6% of the global population and making it the most prevalent form of arthritis, particularly in high-income countries [1]. The burden of RA has also increased, with an estimated 17.9 million patients globally in 2021, affecting about 0.22% of adults [2].Arthritis leads to chronic pain, joint swelling, stiffness, and functional limitations, substantially impairing quality of life and mental health. It also imposes a considerable economic burden through both direct costs, including medical care, medications, and surgical interventions, and indirect costs, such as productivity loss, work absenteeism, and income reduction due to disability [3–5]. In China, where demographic transition is accelerating and the proportion of adults aged 45 years and older is expanding rapidly, the overall burden attributable to arthritis is expected to rise both in absolute numbers and in healthcare needs, underscoring the importance of identifying actionable, modifiable risk factors [7].

Frailty is increasingly viewed as a multidimensional clinical syndrome reflecting diminished physiological reserve and heightened vulnerability to adverse health outcomes. Unlike single-dimension biomarkers, the frailty index (FI) operationalizes frailty as the cumulative burden of deficits across multiple domains (e.g., physical function, symptoms, chronic diseases, and mental health). FI therefore captures an individual's overall "health deficit accumulation," which may plausibly influence subsequent health trajectories. Importantly, there are biologically and clinically credible pathways linking frailty to arthritis risk: frailty may reflect systemic inflammation, reduced muscle strength and physical capacity, impaired recovery and adaptation, and shared downstream pathways such as reduced mobility and metabolic dysregulation[10, 11]. However, the direction of association is not always straightforward. Arthritis symptoms and functional decline can also lead to worsening health deficits, creating a risk of reverse causation in observational studies. In addition, observational associations between FI and incident arthritis may be affected by residual confounding (e.g., socioeconomic status, lifestyle factors, and comorbidity profiles) if not carefully addressed[12–16].

To improve causal interpretation, our study integrates three complementary approaches. First, we quantified the trends and magnitude of arthritis burden among Chinese adults aged ≥ 45 years using GBD 2023 results, including incidence, prevalence, YLD, YLL, and DALYs, and further examined patterns by sex and age. Second, we leveraged the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative prospective cohort, to examine the association between FI and incident arthritis[17]. Arthritis onset was ascertained across follow-up waves, and participants with pre-existing arthritis at baseline were excluded to strengthen temporality. We further applied multivariable regression models with stepwise adjustment for demographic, lifestyle, and comorbidity-related covariates, and

conducted sensitivity analyses to assess robustness. Third, to assess whether genetically predicted frailty may causally influence OA risk, we applied two-sample Mendelian randomization (MR)[18]. By using genetic variants as instruments for FI, MR can reduce bias from reverse causation and many forms of unmeasured confounding under standard assumptions, thereby providing additional evidence for causality[19].

By combining burden estimation, longitudinal observational analysis, and MR-based causal inference, this study aims to clarify whether frailty is associated with-and may contribute causally to-the risk of arthritis, particularly osteoarthritis, among older adults in China. Ultimately, identifying such links may support earlier risk stratification and targeted interventions (e.g., frailty assessment and multidomain health management) to mitigate the expanding arthritis burden.

Methods

Study Population and Data Sources

Global Burden of Disease Database

The Global Burden of Disease (GBD) database provides estimates of incidence, prevalence, mortality, years of life lost (YLL), years lived with disability (YLD), and disability-adjusted life years (DALY) for 375 diseases and injuries from 1990–2021[20]. The GBD offers nationally aggregated data at both national and regional levels. Arthritis estimates are derived from systematic reviews of epidemiological studies and national health surveys. Data used in this study were obtained from the Global Health Data Exchange (GHDx) online platform (https://vizhub.healthdata.org/gbd-results/).

In this study, arthritis encompassed OA, RA, and other forms of arthritis. In GBD 2023, hip and knee OA were defined as symptomatic OA confirmed by radiographic evidence with Kellgren–Lawrence grades 2–4 (International Classification of Diseases [ICD]-9 code 715; ICD-10 codes M16 and M17). Hand OA was defined as symptomatic, imaging-confirmed OA affecting at least one hand joint (ICD-10 code M15), while OA in other anatomical sites was classified under ICD-10 code M19 [1]. RA was defined according to the 1987 American College of Rheumatology (ACR) classification criteria, which include clinical symptoms such as joint pain and swelling, imaging evidence of joint damage, and serological positivity for rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibodies (ACPA) (ICD-9 code 714; ICD-10 codes M05 and M06) [2]. All GBD data are anonymized, and informed consent was waived following approval by the Institutional Review Board of the University of Washington.

China Health and Retirement Longitudinal Study (CHARLS)

The CHARLS is a nationally representative cohort survey of Chinese adults aged 45 years and older, using a multistage, probability-proportional-to-size sampling strategy across urban and rural areas [21]. CHARLS covers 28 provincial-level regions, 150 county-level units, and 450 communities or villages. The

baseline survey was conducted in 2011, with follow-up assessments every two years using face-to-face, computer-assisted interviews to collect data on demographics, health conditions, psychological status, and physical measurements [22]. Five survey waves have been completed to date (2011, 2013, 2015, 2018, and 2020).The CHARLS study was approved by the Biomedical Ethics Committee of Peking University (IRB00001052-11015), and all participants provided written informed consent. From the 2011 baseline wave, 17,705 participants were initially identified. After excluding individuals younger than 45 years, those with pre-existing arthritis, and participants with missing FI data or key covariates, a total of 4,615 individuals were included in the final analysis. The participant selection process is illustrated in Fig. 1.

Mendelian Randomization Analysis

Genetic instruments for the FI and OA used in the MR analyses were obtained from the IEU OpenGWAS database. All genome-wide association study (GWAS) datasets were derived primarily from populations of European ancestry and were publicly available through the IEU OpenGWAS platform (https://gwas.mrcieu.ac.uk/). The MR analyses evaluated the potential causal effect of FI on multiple OA phenotypes, including clinically diagnosed OA, generalized OA, and self-reported OA from the UK Biobank.

Variable Definitions

Incident arthritis was identified based on participants' self-reported physician diagnoses during follow-up surveys conducted in 2013, 2015, and 2018. At each follow-up, participants were asked, "Have you ever been diagnosed with arthritis by a doctor?" An affirmative response was considered indicative of arthritis. To ensure an arthritis-free baseline cohort, individuals reporting arthritis at baseline (2011) were excluded. Participants who first reported a diagnosis during follow-up were classified as having incident arthritis and were censored at the time of diagnosis to accurately determine disease onset. Participants without arthritis were followed until the end of the study period or loss to follow-up [23].

The primary exposure was frailty, assessed using the FI. The FI was calculated as the ratio of the number of health deficits present to the total number of age-related deficits assessed. Health deficits were defined as physical or psychological impairments associated with aging that increase vulnerability to adverse outcomes. The FI incorporated multiple domains, including activities of daily living (ADL) and instrumental activities of daily living (IADL; 11 items), physical function limitations (9 items), chronic diseases (9 items), mental health indicators (5 items), and subjective health assessments. Each deficit was coded as 0 (absence) or 1 (presence); intermediate responses (e.g., "sometimes" or "possibly") were assigned a value of 0.5 to reflect partial impairment. The full list of FI components is provided in Supplementary Table.1 [24].

Covariates were extracted from the CHARLS database and included demographic characteristics (age, sex, urban or rural residence), socioeconomic factors (education level: illiterate, junior high school or below, high school or above; marital status), lifestyle factors (body mass index, smoking status, alcohol consumption), and comorbid conditions (hypertension, diabetes, dyslipidemia). All covariates were collected using standardized household interview questionnaires.

Data completeness was systematically evaluated. Multiple imputation was applied for variables with missingness exceeding 10%. Sensitivity analyses were performed to assess the robustness of the findings.

Statistical Analysis

This study analyzed the incidence, prevalence,DALYs, age-standardized rates (ASRs), and corresponding estimated annual percentage changes (EAPCs) in arthritis patients aged 45 and above in China from 1990 to 2021 using data from the GBD 2023 database. The analysis was stratified by gender (male/female) and age group (e.g., 65–69 years, 70–74 years). Descriptive statistics were computed for all key variables, and results are presented as means with 95% uncertainty intervals (UIs).

In the CHARLS database, participant characteristics were summarized using descriptive statistics. Normally distributed continuous variables were reported as means and standard deviations (SD), while non-normally distributed variables were presented as medians with interquartile ranges (IQR). Categorical variables were described by frequency and percentage. Between-group comparisons were performed using the chi-square test for categorical variables and the Mann-Whitney U test for continuous variables.The relationship between FI (both continuous and categorical) and arthritis was evaluated using univariable and multivariable logistic regression models. Four models were used for analysis: the crude model (without covariate adjustment); Model 1 (adjusting for age, sex, residence, education level, marital status, and body mass index [BMI]); Model 2 (further adjusting for smoking and alcohol consumption); and Model 3 (additionally adjusting for chronic conditions such as hypertension, diabetes, and dyslipidemia). Subgroup analyses were conducted to assess the robustness of the results. Restricted Cubic Spline (RCS) curves were used to explore the nonlinear relationship between FI and NP, with piecewise regression identifying inflection points.

For the MR analysis, two-sample MR was performed using the TwoSampleMR R package to assess the causal relationship between FI and OA outcomes. Independent genetic variants with genome-wide significance ($P < 5 \times 10^{-8}$) were selected as instrumental variables, and linkage disequilibrium (LD) pruning was applied ($r^2 < 0.001$, within a 10,000 kb window). The inverse variance weighted (IVW) method was used as the primary analysis approach, with MR-Egger regression, weighted median (WME), and weighted mode methods serving as secondary analyses to evaluate the robustness of the IVW results. An F statistic > 10 was used to ensure that weak instrumental variable bias was absent. Homogeneity tests were conducted using both the IVW and MR-Egger methods, and multiplicity was addressed using the MR-PRESSO method. Sensitivity analysis was performed using the leave-one-out

method, with results visualized to assess the influence of individual SNPs on the final estimates. A Bonferroni correction was applied, with a threshold of $P < 0.002$ (for the IVW method) considered statistically significant to account for multiple testing.

All statistical tests were two-sided, with $P < 0.05$ indicating statistical significance. Statistical analyses and graphical representations were conducted using R software (version 4.3.3).

Results

Global Burden of Arthritis

From 1990 to 2023, the ASRs of arthritis among Chinese adults aged ≥ 45 years remained relatively stable, whereas the absolute disease burden increased substantially in both sexes (Figure. 2). In 2023, the ASRs of incidence, prevalence, and DALYs were 1,613.58 per 100,000 (95% UI: 1,240.63–2,027.41), 23,938.37 per 100,000 (95% UI: 20,707.62–27,442.73), and 836.09 per 100,000 (95% UI: 398.19–1,794.62), respectively. The corresponding EAPCs were 0.55 (95% CI: 0.48–0.62), 0.58 (95% CI: 0.51–0.66), and 0.66 (95% CI: 0.58–0.73).In absolute terms, China recorded 10,192,878 incident cases (95% UI: 7,842,076–12,806,519), 154,816,703 prevalent cases (95% UI: 133,909,543–177,591,958), and 5,410,926 DALYs (95% UI: 2,576,016–11,610,937) in 2023, accounting for approximately 25–26% of the global burden in the same age group. Compared with 1990, these figures increased by 189.73%, 215.22%, and 222.28%, respectively.

Subgroup analyses showed marked increases in absolute disease burden across all sexes and age groups, while ASRs changed modestly over time (Figure. 3 and Figure.4). Females consistently exhibited higher ASRs and absolute burdens than males. In 2023, female incidence and ASR were 6,096,729 (95% UI: 4,687,304–7,699,596) and 1,915.47 per 100,000 (95% UI: 1,472.32–2,417.51), representing 1.05- and 1.50-fold those of males, respectively. Female prevalence and ASR were 93,796,724 (95% UI: 80,997,193–107,569,549) and 28,297.89 per 100,000 (95% UI: 24,418.96–32,457.26), corresponding to 1.46- and 1.43-fold those of males. Similarly, female DALYs and ASR were 3,290,296 (95% UI: 1,569,633–7,089,211) and 672.99 per 100,000 (95% UI: 320.21–1,438.22), 1.47- and 1.55-fold higher than in males.Across age strata, the arthritis burden was primarily concentrated in individuals younger than 74 years, with a peak in the 55–59-year group. Age-standardized incidence rates were higher and increased more rapidly in younger groups, whereas age-standardized prevalence and DALY rates were greater in older age groups (Figure. 4).

Baseline Characteristics of the CHARLS Population

Baseline characteristics of the CHARLS participants are summarized in Table.1. Among 4,615 participants, 1,219 (26.41%) developed arthritis during follow-up. The mean age was 57.76 ± 8.62 years, 52.24% were female, and 64.85% resided in rural areas. Arthritis prevalence was significantly higher among women, individuals with greater frailty, those with pre-existing chronic conditions, participants

with lower educational attainment, rural residents, and those who did not consume alcohol (all P < 0.001).

Association Between the Frailty Index (FI) and Arthritis

Multivariable logistic regression showed a robust association between FI and arthritis risk (Table.2). Compared with the robust group, pre-frailty (OR = 1.40, 95% CI: 1.19–1.64; p < 0.001) and frailty (OR = 1.84, 95% CI: 1.19–2.83; p < 0.001) were associated with significantly higher odds of arthritis. When FI was modeled as a continuous variable, each 1-point increase in FI was associated with higher odds of arthritis (crude model OR = 1.10, 95% CI: 1.07–1.13), and the association remained after adjustment (Models 1–3: OR = 1.08, 95% CI: 1.05–1.12). When FI was analyzed per IQR increase, the ORs were 1.58 (95% CI: 1.38–1.81) in the crude model and 1.51 (95% CI: 1.29–1.74), 1.48 (95% CI: 1.28–1.73), and 1.50 (95% CI: 1.29–1.75) in Models 1–3, respectively (all p < 0.0001).

In quartile analyses, a clear dose–response relationship was observed (Table.2). In the fully adjusted model (Model 3), compared with Q1, the ORs were 1.47 (95% CI: 1.22–1.78) for Q2, 1.56 (95% CI: 1.31–1.87) for Q3, and 2.68 (95% CI: 1.65–4.35) for Q4. Trend tests were significant regardless of whether quartiles were modeled by rank or median values (all p for trend < 0.0001). Consistent stepwise risk gradients across FI quartiles were observed across models (Figure. 5).

RCS analyses adjusted for covariates further supported an approximately linear association between FI and arthritis risk (P-overall < 0.001; P-nonlinear > 0.05) (Figure. 6). Although the curve attenuated slightly with progressive confounder adjustment, FI remained positively associated with arthritis risk, particularly at higher FI levels (FI > 28), and this pattern was consistent across subgroups.

Subgroup Analyses

Subgroup analyses showed directionally consistent associations across prespecified strata (Table.3). Relative to frailty, pre-frailty and robustness were generally associated with progressively lower arthritis risk, with statistically significant linear trends in most subgroups (most p for trend < 0.001). No significant effect modification was detected by sex, age, marital status, education level, residence, BMI, smoking, alcohol use, or multimorbidity (all interaction p > 0.05), indicating that the FI–arthritis association was broadly stable across population subgroups.

Mendelian Randomization Results

Two-sample MR analyses supported a positive causal effect of FI on OA across multiple OA definitions (Table.4). Using SPA-corrected OA as the outcome, the IVW estimate was OR = 1.537 (95% CI: 1.132–2.088;P = 0.006). For generalized OA, the IVW estimate was OR = 1.019(95% CI: 1.003–1.036; P = 0.016). For self-reported OA from the UK Biobank, the IVW estimate was OR = 1.039(95% CI:1.017–1.061;P = 0.001), supported by the weighted median method (OR = 1.027, 95% CI: 1.002–1.053;P = 0.028). Other sensitivity methods provided less consistent support for the SPA-corrected and generalized OA outcomes.

Heterogeneity and pleiotropy assessments are summarized in Table.5. Modest heterogeneity was observed only for the SPA-corrected OA analysis (IVW Q P = 0.029), whereas no significant heterogeneity was detected for the other outcomes. There was no evidence of directional pleiotropy for any outcome (MR-Egger intercept p > 0.05) (Supplementary Figures.S1–S3). Leave-one-out analyses indicated that IVW estimates were robust to exclusion of individual SNPs (Supplementary Figure. S4). Overall, these findings support a positive causal association between FI and OA risk, with the most consistent evidence observed for self-reported OA.

Discussion

This study, utilizing GBD 2023 data and CHARLS cohort information, provides a comprehensive analysis of the epidemiological characteristics of arthritis among individuals aged 45 and above in China. For the first time, multivariate adjustment and MR analysis were employed to confirm the causal relationship between FI and the risk of arthritis. Our findings highlight key characteristics of arthritis burden in China, such as a higher burden in females, earlier onset age, and greater disability in older populations. Additionally, an increase in frailty status was significantly associated with an elevated risk of arthritis. As a multidimensional health indicator, FI holds promise as an important tool for future arthritis risk assessment.

The results from the GBD 2023 analysis demonstrated notable gender and age disparities in the arthritis burden among Chinese individuals aged 45 and above. The absolute number and ASRs for females were consistently higher than those for males, a pattern in line with global trends [25]. Several factors likely contribute to the higher disease burden in females. First, postmenopausal estrogen decline and changes in cartilage and bone metabolism, coupled with increased autoimmune susceptibility, elevate the risk of OA and RA (RA) [26, 27]. Second, females are more likely to engage in repetitive physical labor and caregiving tasks, which result in greater musculoskeletal injuries and a higher likelihood of seeking medical treatment, thereby increasing the reporting burden of arthritis [28, 29].Additionally, the significantly higher age-standardized incidence rates (ASIRs) observed in younger age groups suggest that arthritis in China is not merely a “disease of old age,” but rather is increasingly affecting younger individuals. This shift may be attributed to the accumulation of risk factors during middle age. Key contributors include sedentary lifestyles, insufficient physical activity, and the rising prevalence of overweight and obesity, which subject joints to both metabolic and mechanical stresses [30–32]. Moreover, repetitive occupational activities, poor posture, and early joint injuries likely trigger degenerative changes in younger individuals, leading to earlier onset of arthritis [33, 34].In contrast to the ASIRs patterns, the study found that age-standardized prevalence rates (ASPRs) and age-standardized death rates (ASDRs) peaked in older age groups. This reflects the chronic and irreversible nature of arthritis, with disease duration extending as individuals age. Consequently, functional impairment and loss of quality of life become more pronounced in older populations. The concentrated burden of arthritis among individuals under 74 years of age also corresponds to the age distribution of the population, suggesting that arthritis impacts a substantial proportion of the working-age and early retirement-aged individuals in China.

Previous studies have suggested a close relationship between frailty and arthritis; however, the strength of this association remains to be further validated in large-scale studies due to variations in frailty scales and study populations [17–19]. This study, based on the CHARLS cohort, found that the prevalence of arthritis was 26.41%, with significantly higher rates observed in females, rural populations, illiterate individuals, and those with frailty or pre-frailty. These findings highlight the combined influence of biological susceptibility and social determinants on the burden of arthritis.Multivariate logistic regression analysis showed a consistent and positive association between frailty (whether treated as a categorical or continuous variable) and the risk of arthritis. Quartile analysis revealed a gradual increase in risk as FI levels rose, with the association remaining significant after full adjustment for confounding factors. Trend tests and IQR effects further supported the dose-response relationship between frailty and arthritis risk. RCS analyses suggested that the association was approximately linear, with a more stable positive effect when FI exceeded 28. This may reflect a threshold effect, where the accumulation of health deficits leads to a confluence of factors—such as chronic low-level inflammation, immune aging, sarcopenia, and limited mobility—that mutually reinforce each other, thereby exacerbating arthritis-related pain, structural damage, and functional decline [35, 36].Subgroup analyses did not reveal significant interactions, suggesting that the positive association between FI and arthritis risk was robust across different gender, age, BMI, and multimorbidity groups. This further supports the potential of FI as a comprehensive risk tool for arthritis, extending beyond single risk factors.

It is important to note that arthritis and frailty may have a bidirectional causal relationship, which is also supported by the MR analysis in this study. Potential mechanisms for this relationship include: First, arthritis can contribute to frailty through chronic pain and functional limitations. Longitudinal studies have shown that knee pain can significantly predict the development of frailty, even after adjusting for demographic characteristics and comorbidities, suggesting that pain may act as an initiating factor in the cascade of functional decline [37]. Persistent pain can result in "homeostenosis"—a reduction in physiological reserve and stress tolerance—thereby increasing susceptibility to frailty. Additionally, pain-related avoidance of physical activity can lead to reduced mobility, slower walking speed, and increased fatigue, all of which accelerate the development of the frailty phenotype.Conversely, frailty may also accelerate the occurrence and progression of arthritis. Frailty is often accompanied by sarcopenia and decreased muscle strength, resulting in inadequate joint stability and abnormal load distribution, which increases the risk of biomechanical injury and pain. This creates a cycle of "pain – reduced activity – sarcopenia – joint instability." Inflammation appears to be a key mechanism linking these two conditions: studies on OA have shown that IL-6 can predict radiographic knee OA, and early knee OA is associated with elevated levels of C-reactive protein (CRP), suggesting that low-level inflammation plays a role in structural damage [39, 40]. Frail individuals also exhibit elevated levels of pro-inflammatory markers such as IL-6, CRP, and TNF-α, which are associated with the degree of frailty and increased mortality risk [41, 42]. In chronic inflammatory diseases like RA, systemic inflammation combined with muscle atrophy and "sarcopenic obesity" diminishes physical reserves and exacerbates functional impairment, resulting in earlier and more frequent onset of frailty.Based on this evidence, incorporating frailty assessment (e.g., FI) into the arthritis management framework could be beneficial in clinical practice. This approach

would enable more comprehensive interventions, including pain management, exercise rehabilitation, nutritional support, and management of inflammation and comorbidities. Such strategies could help interrupt the bidirectional amplification pathway between frailty and arthritis, ultimately reducing the risk of disability and improving patient outcomes.

Despite the comprehensive data sources and rigorous analytical methods used in this study, several limitations should be acknowledged. First, the accuracy of GBD estimates depends heavily on the completeness and quality of regional health statistics in China. Underrepresentation of low-income or resource-limited areas may lead to underestimation of the true disease burden, particularly given higher exposure to physical labor and limited access to healthcare in these populations. Second, both arthritis status and FI in the CHARLS database were based on self-reported information, which may introduce measurement error and information bias. Although these measures have demonstrated acceptable reliability and validity, discrepancies between subjective reports and objective assessments may affect the precision of effect estimates [21, 43]. Third, the study population was predominantly Chinese. Although MR analyses incorporated genetic data from European populations, the generalizability of these findings to other ethnic and cultural contexts requires further validation. Finally, arthritis encompasses heterogeneous subtypes, including RA, OA, and OA at different anatomical sites. The inability to distinguish these subtypes within the CHARLS data may have obscured subtype-specific associations with FI.

Conclusions

In conclusion, this study demonstrates a significant positive association between frailty and arthritis and supports the potential utility of the FI as a risk assessment tool. Future research should include prospective, multi-ethnic cohort studies to evaluate the clinical effectiveness and cost-efficiency of FI-based personalized management strategies. Additionally, further investigation into the molecular and biological mechanisms linking frailty and arthritis is needed to inform precision medicine approaches. A multidisciplinary, integrative framework may ultimately help clarify the complex pathophysiology of arthritis and improve its clinical management.

Abbreviations

ACPA
Anti-cyclic citrullinated peptide antibodies
ACR
American College of Rheumatology
ADL
Activities of daily living
ASIR
Age-standardized incidence rate
ASPR

Age-standardized prevalence rate
ASR
Age-standardized rate
BMI
Body mass index
CHARLS
China Health and Retirement Longitudinal Study
CI
Confidence interval
CRP
C-reactive protein
DALY
Disability-adjusted life year
EAPC
Estimated annual percentage change
FI
Frailty Index
GBD
Global Burden of Disease
GWAS
Genome-wide association study
IADL
Instrumental activities of daily living
ICD
International Classification of Diseases
IL-6
Interleukin-6
IQR
Interquartile range
IVW
Inverse variance weighted
LD
Linkage disequilibrium
MR
Mendelian randomization
OA
Osteoarthritis
OR
Odds ratio
PsA

Psoriatic arthritis
RA
Rheumatoid arthritis
RCS
Restricted cubic spline
RF
Rheumatoid factor
SD
Standard deviation
SNP
Single nucleotide polymorphism
TNF-α
Tumor necrosis factor-alpha
UI
Uncertainty interval
YLD
Years lived with disability
YLL
Years of life lost

Declarations

Clinical trial number:

Not applicable

Author Contribution

XC, JT, SZ, and YH contributed to the conceptualization and design of the study. SZ and CX designed and wrote the entire manuscript. SZ, XC, JT, and CX collected the references for the manuscript and prepared the figures. JT, YH, and SZ completed the subsequent revisions of the manuscript. All authors contributed to the manuscript revision and reviewed the final version of the manuscript.

Data Availability

The Global Burden of Disease Study 2023 data supporting the findings of this study are publicly available from the Institute for Health Metrics and Evaluation (IHME) at https://vizhub.healthdata.org/gbd-results/. The China Health and Retirement Longitudinal Study data are publicly available from Peking University at http://charls.pku.edu.cn/. No new datasets were generated during the current study.

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Tables

Tables 1 to 5 are available in the supplementary files section

Figures

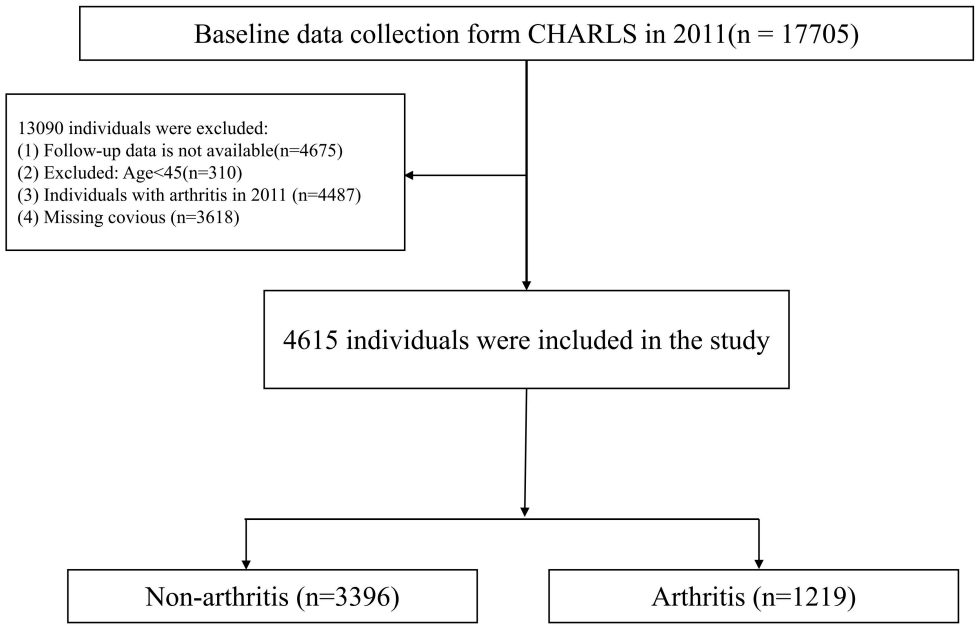


Figure 1

Flow chart of study participants.

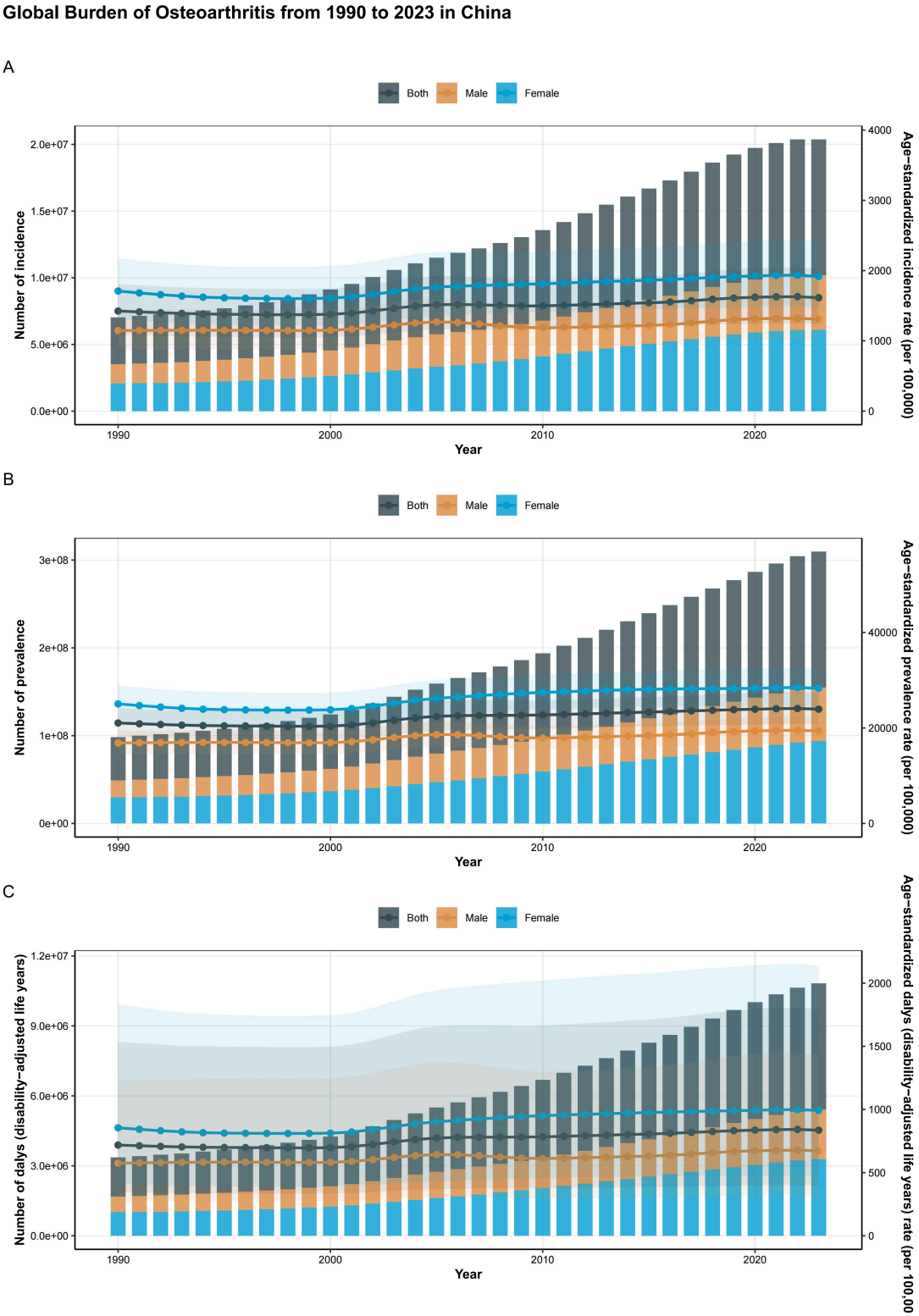


Figure 2

Trends in the disease burden of arthritis among individuals aged 45 years and older in China over time (A. Incidence; B. Prevalence; C. DALYs).

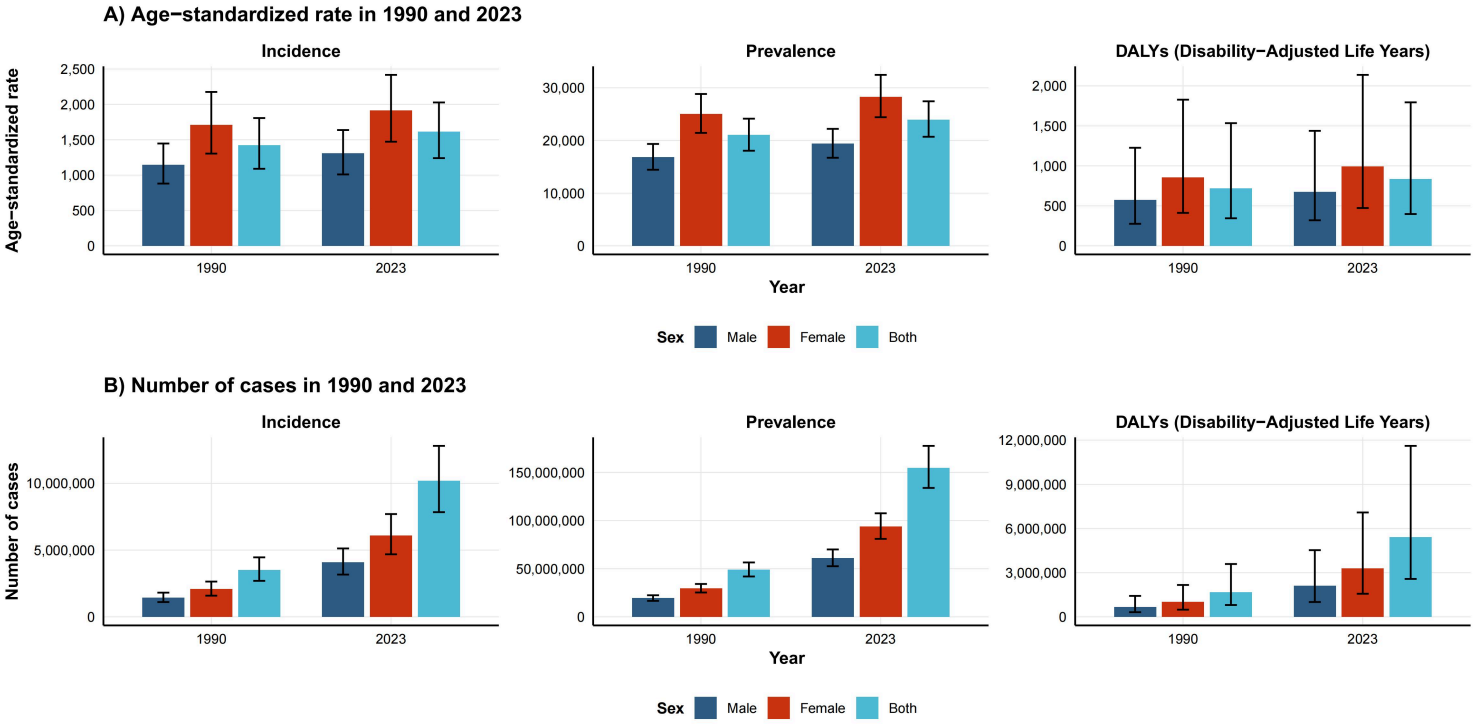


Figure 3

Comparison of the burden of arthritis disease by gender in China between 1990 and 2023(A. Incidence; B. Prevalence; C. DALYs).

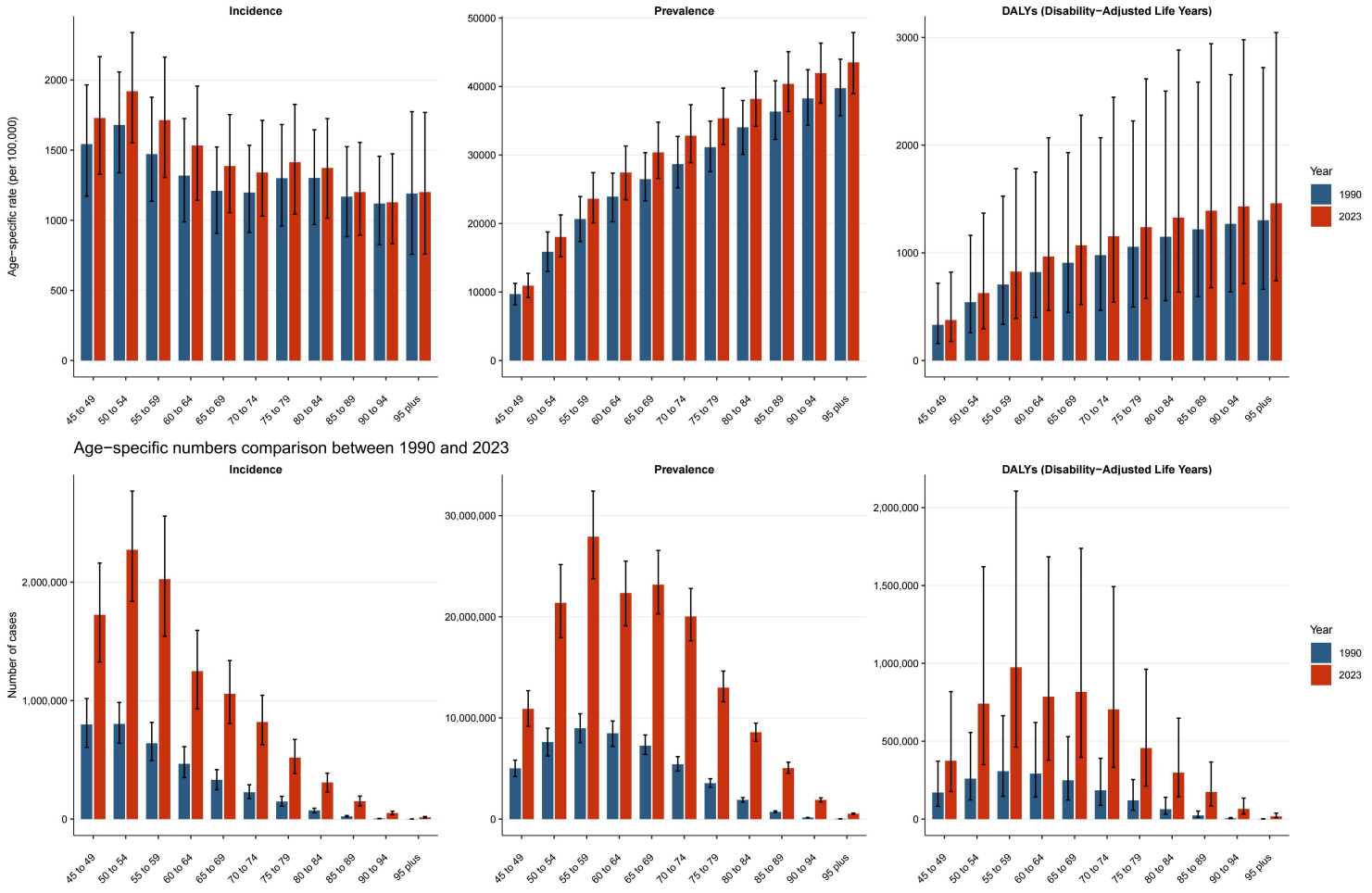


Figure 4

Comparison of the burden of arthritis disease by age group in China between 1990 and 2023.

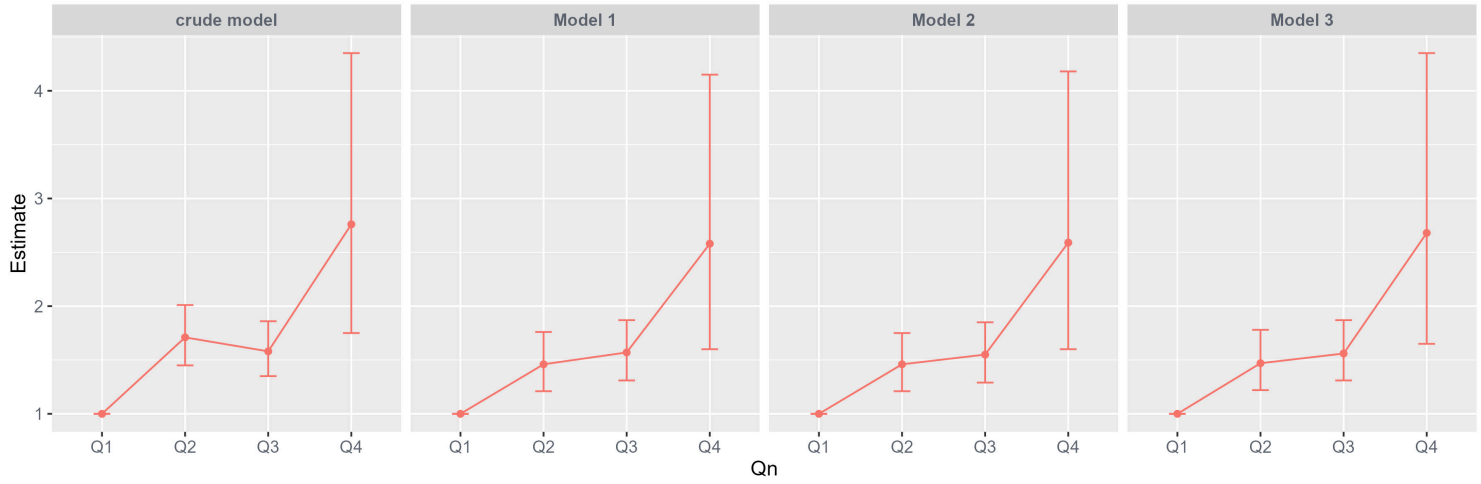


Figure 5

The risk gradient of neck pain across frailty index levels in all analytical models.

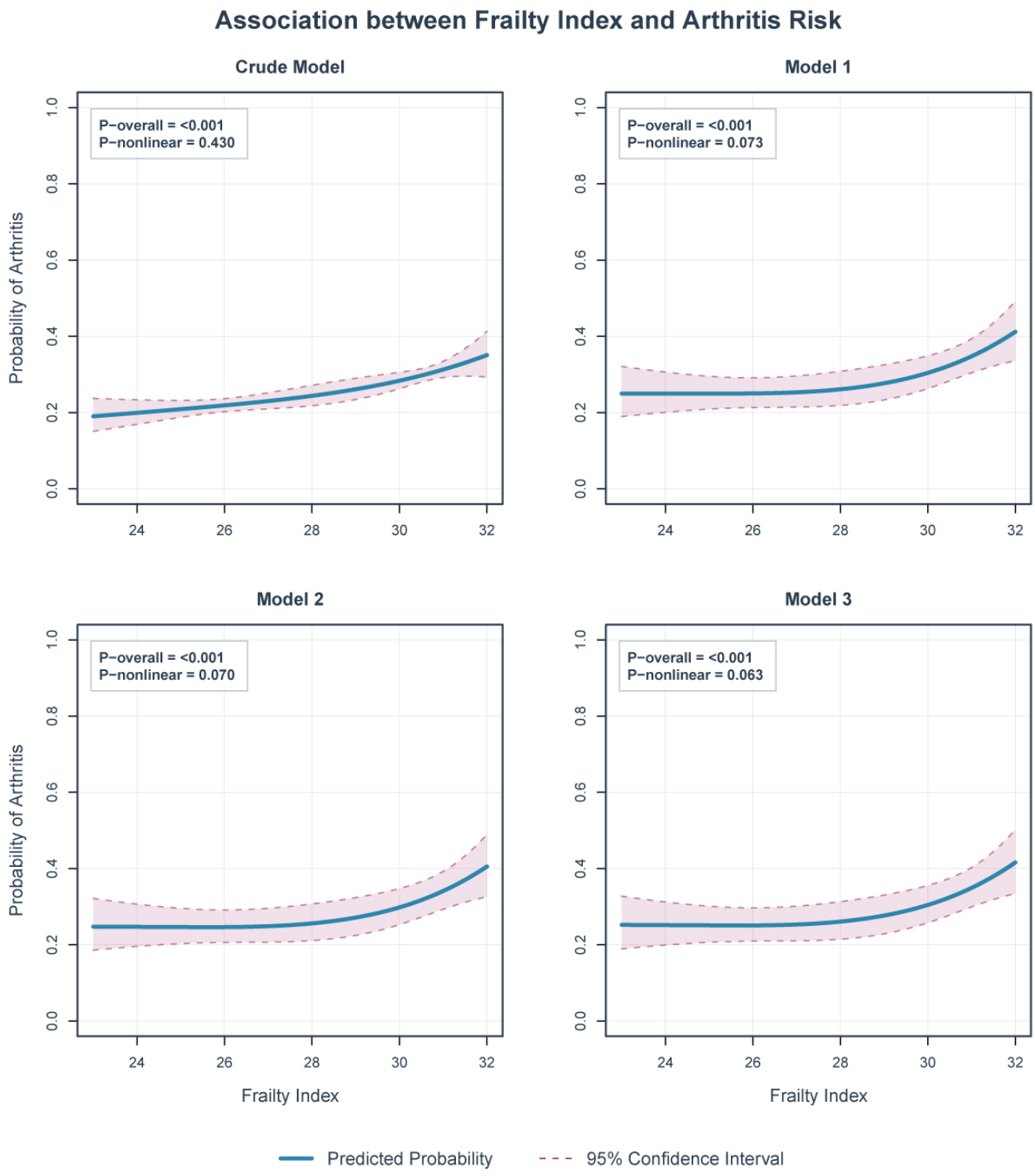


Figure 6

RCS Analysis of arthritis and Frailty Index in Different Models.

Supplementary Files

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