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# Nonlinear age-related differences in adult knee extension strength reveal sex-specific early warning windows

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**Abstract**

We analyzed isometric knee extension strength in 6,761 adults to determine how lower-limb strength varies with age and whether age-related patterns differ by sex. Isometric knee extension strength was positively associated with back strength, grip strength, height, vertical jump, and body weight, and negatively associated with age. Men had substantially higher strength than women. Restricted cubic spline, first-derivative, and piecewise regression analyses showed a clear nonlinear and sex-specific age pattern. In men, the relationship changed around 38 years and the steepest decline occurred around 45 years. In women, age-related decline became more pronounced after 50 years, although the oldest-age derivative estimate was boundary-sensitive. The association remained significant after adjustment for height, weight, and grip strength. These findings support sex-specific monitoring of lower-limb strength and earlier intervention windows across adulthood.

**Keywords:** knee extension strength; age; sex; restricted cubic spline; lower-limb strength

# 1 Introduction

With accelerating population ageing, maintaining functional ability in later adulthood and old age has become a major public health priority. The World Health Organization has emphasized that healthy ageing is fundamentally defined by the maintenance of functional ability, which is built on intrinsic capacity, with motor and muscular functions serving as key components [1]. Declines in lower-limb strength not only impair basic activities such as walking, rising from a chair, and stair negotiation, but are also closely associated with adverse outcomes including falls, disability, hospitalization, and mortality; accordingly, they are of clear public health and preventive-medicine relevance [1, 2].

Among the many indicators of muscle strength, isometric knee extension strength directly reflects the functional status of the knee extensors, particularly the quadriceps. Compared with the widely used handgrip strength measure, knee extension strength is more closely aligned with lower-limb functional performance and, in some contexts, may even outperform grip strength in predicting functional limitation [3, 4]. Previous studies have shown that quadriceps weakness is strongly associated with pain and disability in patients with knee osteoarthritis and may contribute to the progression of structural joint damage [5, 6]. In frailty and sarcopenia research, low muscle strength is regarded as a core phenotype, and knee extension strength, as a lower-limb strength indicator, is highly informative for identifying reductions in functional reserve [7, 8].

Nonetheless, several important gaps remain. First, most previous studies have focused on older adults or disease-specific populations, whereas comparatively little is known about age-related differences in lower-limb strength across adulthood, particularly regarding whether a period of more marked cross-sectional age differences emerges around midlife [3, 4, 8]. Second, handgrip strength has often been used as a surrogate for overall muscle strength, yet accumulating evidence suggests that age-related differences in knee extension strength may emerge earlier, be more pronounced, and more closely mirror functional deterioration [3, 4]. Third, from a modeling perspective, continuous variables such as age are often categorized or treated as purely linear terms, which may obscure their true nonlinear relationships with outcomes. Restricted cubic splines (RCS) can flexibly characterize dose-response relationships while preserving the continuity of the exposure, and are therefore better suited to identifying potential age windows of more pronounced cross-sectional change.

From public health and biostatistical perspectives, identifying the age window in adulthood during which lower-limb strength shifts from relative stability to more marked age-related differences could facilitate earlier risk identification, functional monitoring, and stratified intervention. If this process follows different temporal

patterns in men and women, the use of a single age threshold may underestimate early risk in part of the population [1, 7]. Accordingly, using a large cross-sectional dataset collected directly by our research team, this study systematically characterized the distribution of isometric knee extension strength and its associations with anthropometric and physical fitness indicators, and applied restricted cubic splines, first-derivative analysis, and piecewise regression to examine the nonlinear association between age and isometric knee extension strength as well as its potential turning ages. Quantile regression was additionally used to depict continuous cross-sectional age patterns across strength strata, thereby complementing the evidence from the perspectives of heterogeneous, nonuniform age-related differences and practical application. We hypothesized that age would show a significant nonlinear association with isometric knee extension strength and that this pattern would differ clearly by sex.

# 2 Results

## 2.1 Basic Characteristics of the Sample

A total of 6,761 adults were included, comprising 3,020 men and 3,741 women. The overall mean age was 39.4 ± 10.8 years, and the mean isometric knee extension strength was 318.2 ± 131.1 N. Men had higher height, weight, grip strength, back strength, vertical jump, and isometric knee extension strength than women. The basic characteristics of the sample are shown in Table 1.

## 2.2 Correlates of Isometric Knee Extension Strength

Correlation analyses showed that isometric knee extension strength was significantly positively associated with back strength, grip strength, height, vertical jump, and body weight, with the strongest correlation observed for back strength (r = 0.578), followed by grip strength (r = 0.562) and height (r = 0.484). Age was significantly negatively associated with isometric knee extension strength (r = -0.194). Multiple linear regression further showed that after adjustment for sex, age, and anthropometric and physical fitness indicators, back strength, grip strength, vertical jump, sit-ups, body weight, and push-ups/knee push-ups remained independently associated with isometric knee extension strength, whereas height showed a small but statistically significant negative association. This change in direction relative to the unadjusted correlation likely reflects conditional adjustment effects after simultaneous inclusion of sex, body weight, and other strength-related indicators, rather than a simple inverse unadjusted association. Both the main effect of age and the age-by-sex interaction were statistically

significant. Men had significantly greater mean isometric knee extension strength than women, with an average difference of 142.8 N. To further clarify whether the relationship between age and isometric knee extension strength was nonlinear and whether potential turning features were present, restricted cubic spline and piecewise regression analyses were performed, with the main results summarized in Table 3. As a supplementary analysis, quantile regression was used to test the consistency and heterogeneity of the age effect across different strength levels. In both men and women, relative isometric knee extension strength showed increasingly negative cross-sectional age gradients at all quantiles (Q10–Q90), and the curves were steeper at higher quantiles, suggesting that age exerts a stronger negative influence among individuals with greater baseline strength reserves. Quantile regression was treated as a supplementary analysis describing heterogeneity in the age effect across strength quantiles, whereas identification of key age windows relied primarily on RCS, first-derivative analysis, and piecewise regression. Detailed quantile-regression and sex-specific normative grading results are provided in the Supplementary Information (Tables S7 and S8).

## 2.3 Covariate-Adjusted Restricted Cubic Spline (RCS) Age-Effect Curves

After adjustment for height, weight, and grip strength, age showed a significant nonlinear association with isometric knee extension strength in both men and women. The RCS analyses indicated that the optimal model for men used 5 degrees of freedom with knots at [30, 40, 50], whereas the optimal model for women used 4 degrees of freedom with knots at [40, 50]. Both the F-tests and likelihood ratio tests for nonlinearity were statistically significant in men and women (all $P < 0.001$), confirming the presence of significant nonlinear age effects. The covariate-adjusted RCS curves further showed clear sex differences in cross-sectional age patterning. In men, isometric knee extension strength remained relatively stable from early adulthood through the late 30s and then showed more evident age-related differences, with the cross-sectional age gradient becoming steeper by the mid-40s. In women, age-related differences were more gradual across adulthood and became more pronounced after 50 years. Overall, although the association between age and isometric knee extension strength was significantly nonlinear in both sexes, the cross-sectional pattern differed clearly by sex: men showed steeper age gradients earlier, whereas women showed later but progressively greater age-related differences with advancing age. Candidate-model selection results and the full multivariable spline coefficients are provided in Supplementary Information (Tables S3 and S4).

## 2.4 Piecewise Regression Results

Piecewise regression further verified the nonlinear nature of the age effect and provided more structured estimates of age thresholds for men and women. In men, the model identified a breakpoint at approximately 38 years. The age slope before the breakpoint was not statistically significant, indicating that isometric knee extension strength remained broadly stable before the late 30s. The change in slope after the breakpoint was highly significant ($P < 0.001$), indicating that men showed more pronounced age-related differences after 38 years.

In women, the model identified a breakpoint at approximately 50 years. The main effect of age was statistically significant ($P < 0.001$), and the change in slope after the breakpoint was likewise significant ($P < 0.001$), indicating that women exhibited cross-sectional age differences across adulthood that became more pronounced after 50 years.

The piecewise regression results were broadly consistent with the RCS and derivative analyses. Whereas the RCS analysis emphasizes smooth curvature in the age effect, piecewise regression approximates this continuous pattern as a structural turning point. The two approaches therefore reached directionally concordant conclusions from different statistical perspectives: men showed stronger age gradients earlier, whereas more marked age-related differences emerged later in women. The full piecewise coefficients and breakpoint-search profile are provided in the Supplementary Information (Table S5 and Supplementary Figure S1).

## 2.5 First Derivative of the Age-Effect Curves

To further characterize age-related differences across the observed age range, first-derivative analysis was used to evaluate the cross-sectional age gradient in isometric knee extension strength. In men, the derivative curve became more negative after 38 years and reached its minimum at 45.4 years, indicating that this age corresponded to the steepest cross-sectional age gradient in isometric knee extension strength. This suggests that cross-sectional differences in lower-limb strength among men are not uniform across adulthood, but appear more marked around midlife.

In women, the derivative curve likewise became progressively more negative with age, indicating increasingly marked cross-sectional differences at older ages. However, the minimum derivative occurred near the upper boundary of the observed age range, at approximately 57.0 years. Because this estimate lies close to the upper age limit of the sample, it is clearly boundary-sensitive and should not be interpreted directly as a stable physiological turning age. A more appropriate interpretation is that in women,

particularly after 50 years, cross-sectional age-related differences in strength become more pronounced, although more precise localization of the turning age will require samples including a larger number of older participants.

First-derivative analysis supplemented and reinforced the findings of the RCS curves, further showing that both the timing and the magnitude of cross-sectional age differences differ by sex: men exhibited earlier and more marked age gradients, whereas women showed later but progressively stronger age-related differences. Key derivative-based numeric estimates are provided in the Supplementary Information (Table S6).

# 3 Discussion

## 3.1 Principal Findings and Overall Significance

Using a large dataset of directly measured field data from adults, this study systematically analyzed the distribution of isometric knee extension strength and its associations with age, sex, and multiple physical fitness indicators. Four principal findings emerged. First, isometric knee extension strength was significantly associated with back strength, grip strength, height, vertical jump, and body weight, suggesting that it reflects not only local knee extensor function but also, to some extent, overall body size and global muscle strength. Second, the association between age and isometric knee extension strength was significantly and robustly nonlinear rather than a simple linear pattern. Third, men showed stronger age gradients earlier, whereas women showed a relatively delayed but progressively more marked pattern of age-related differences. Fourth, quantile regression further indicated that the age effect was heterogeneous across different baseline strength strata, and that both the absolute level of strength and the pattern of age-related differences differed substantially by sex.

From a public health perspective, lower-limb strength is not merely a kinematic indicator, but a key foundation of functional ability. The World Health Organization has emphasized that healthy ageing is centered on maintaining functional ability, which in turn is grounded in intrinsic capacity, with motor and muscular function being core components [1, 17]. The EWGSOP2 consensus further identifies low muscle strength as a defining hallmark of sarcopenia, indicating that strength loss is not only a feature of ageing but also a potential early signal of future adverse health outcomes [7]. Meta-analytic evidence has also shown that muscle strength is significantly associated with all-cause mortality risk [18]. Therefore, identifying key age windows of lower-limb strength differences in adulthood has clear practical significance for early screening, risk

stratification, and timely intervention from public health and preventive-medicine perspectives.

## 3.2 Isometric Knee Extension Strength and Physical Fitness Status

The present study showed that isometric knee extension strength was strongly correlated with back strength and grip strength, suggesting that it reflects not only local knee extensor function but also an important manifestation of the overall neuromuscular system. Previous work has focused largely on older populations and has shown that knee extension strength may outperform traditional grip strength when predicting functional capacity, leading to recommendations that it be incorporated into comprehensive geriatric assessment [5,6]. Our multivariable results extend this value into earlier adulthood: after adjustment for covariates, adult knee extension strength remained independently associated with multidimensional fitness indicators including back strength, grip strength, and vertical jump. This suggests that across adulthood, the measure integrates maximal strength, explosive power, and local muscular endurance, making it a core lower-limb marker for tracking overall physical fitness status throughout the adult lifespan.

From physiological and biomechanical perspectives, the quadriceps serve as the primary engine for antigravity movements such as walking, standing up, and climbing stairs, and their strength directly determines lower-limb functional reserve. Within a life-course health management framework, declines in physical function are not abrupt events confined to old age, but rather gradual accumulative processes that begin during adulthood. Compared with grip strength, losses in knee extension strength often begin earlier and more closely parallel the deterioration of lower-limb mobility. Accordingly, incorporating isometric knee extension strength into routine monitoring may not only improve screening for disability risk in advanced age, but also provide valuable early warning signals during the transition from adulthood to midlife, thereby informing life-course physical fitness surveillance and earlier resistance-training intervention [5,6].

## 3.3 Overview of Nonlinear Age-Related Change and Sex Differences

The most important finding of this study is that the association between age and isometric knee extension strength is significantly **nonlinear**, and that this nonlinearity follows different temporal patterns in men and women. The RCS models showed that the age effect could not be adequately described as a simple linear pattern; instead, it

more closely resembled a pattern of increasingly marked cross-sectional age differences. Men showed stronger age gradients earlier, whereas women showed relatively delayed but progressively more pronounced age-related differences. Thus, lower-limb strength variation does not appear to reflect "uniform ageing," but is more likely the result of multiple physiological processes accumulating across different stages of the life course [16].

From an interpretive standpoint, the approximately 38-year breakpoint identified by piecewise regression and the approximately 45.4-year minimum in the first derivative suggest that lower-limb strength in men may show two related but nonidentical windows in cross-sectional age patterning: an early structural transition and a later age of steepest cross-sectional gradient. In women, age-related differences became more clearly marked after 50 years. In other words, the present study does not merely show that strength differs by age; it indicates when men and women may begin to show more pronounced age-related differences in lower-limb strength, thereby providing more explicit physiological and public health meaning to the findings.

## 3.4 Key Age Windows in Men and Neuromuscular Cross-talk Mechanisms

The more marked cross-sectional age differences in lower-limb strength observed in men between approximately 38 and 45 years are likely to reflect the combined influence of gradual endocrine changes, neuromuscular remodeling, deterioration of the skeletal muscle microenvironment, and increasingly sedentary midlife lifestyles. First, age-related androgen change provides an important biological background for this process. Previous reviews have shown that, with ageing, men tend to experience mild reductions in total testosterone, increases in sex hormone-binding globulin (SHBG), and more marked reductions in free testosterone; these changes may gradually impair muscle protein synthesis, maintenance of muscle mass, and neuromuscular homeostasis [19–21]. Therefore, the turning pattern observed around 40 years in men more plausibly reflects the cumulative impact of age-related endocrine change together with metabolic and comorbidity burdens, rather than a single hormonal threshold event.

Second, early remodeling of the neuromuscular system may be a key mechanism underlying the structural change observed during this male midlife window. Existing studies indicate that ageing is accompanied by motor unit loss, structural and functional alterations of the neuromuscular junction (NMJ), and a greater susceptibility of type II muscle fibers to denervation. Although some compensatory reinnervation may occur initially, continued ageing may allow motor neuron loss and NMJ instability to outpace such compensation, leading to reductions in maximal force production and

explosive performance [22–25]. Because lower-limb extensor function depends heavily on the recruitment of large motor units and the output of fast-twitch fibers, this neuromuscular remodeling may be projected relatively early onto age-related differences in knee extension strength.

Importantly, the relationship between nerve and muscle is not unidirectional but characterized by sustained bidirectional **cross-talk**. The NMJ is a dynamic interface composed of motor neurons, muscle fibers, terminal Schwann cells, and extracellular matrix components. Neural input determines recruitment and contractile behavior, whereas the metabolic state of muscle, mitochondrial function, and local signaling can in turn influence NMJ stability and motor neuron integrity. Recent reviews suggest that ageing and disuse may simultaneously lead to muscle atrophy, mitochondrial dysfunction, NMJ instability, and motor unit loss, and that mitochondrial dysfunction within muscle may itself contribute to NMJ deterioration and impaired neural drive [32, 33]. Thus, long-term reductions in muscle strength may not only result from weakened neural regulation, but may also further compromise neural control and neuromuscular transmission efficiency, creating a vicious cycle of weakening neural control, reduced strength, and further neuromuscular instability.

At the same time, the lower-limb extensor system may already be entering a phase of reduced compensatory reserve in midlife. Emerging evidence on muscle ageing suggests that anabolic resistance, mitochondrial imbalance, low-grade inflammation, and impaired regeneration can begin before overt sarcopenia becomes clinically apparent [26]. Accordingly, the approximately 38-year structural transition identified in men may represent an early inflection point at which the lower-limb strength system shifts from a relatively stable and compensatory state toward a pattern of more evident age-related differences with weakening compensatory capacity, whereas the approximately 45-year age of the steepest cross-sectional gradient may indicate that these differences are most marked by midlife.

From a public health perspective, these findings imply that surveillance of lower-limb strength and resistance-training intervention in men should be moved forward to around midlife rather than waiting until old age for passive identification. In practical terms, the interval from 38 to 45 years may represent a biologically and behaviorally relevant window during which lower-limb strength is especially vulnerable to the combined effects of endocrine ageing, neuromuscular remodeling, and reduced physical activity.

### 3.5 Female Age-Related Pattern, Midlife Transition Hypothesis, and Boundary Sensitivity

The age-related pattern in women differed from that in men. The RCS curves showed that isometric knee extension strength differed across adulthood overall and showed a more negative slope after 50 years. The piecewise regression breakpoint was approximately 50 years, indicating that age-related differences became more pronounced beyond this age. Compared with men, women appeared to enter this more marked phase later. This finding is not only statistically meaningful but also temporally consistent with the age range during which many women experience the menopausal transition. However, because menopausal status and circulating hormone levels were not measured in the present study, any interpretation linking the approximately 50-year breakpoint to menopause should be regarded as an association-based hypothesis rather than as direct evidence of a causal endocrine mechanism [27–31].

Mechanistically, estrogen and estrogen receptor signaling are involved in the regulation of skeletal muscle protein metabolism, satellite cell activation, mitochondrial homeostasis, and muscle contractile function. A low-estrogen state after menopause may lead to reduced muscle mass, greater intramuscular fat infiltration, and worsening mismatch between muscle mass and muscle strength, thereby lowering lower-limb functional reserve [28–30]. Longitudinal studies have further suggested that deterioration in physical performance and muscle strength may already emerge during the menopausal transition rather than only becoming apparent at advanced age [27]. These prior findings provide a plausible biological context for the female age pattern observed here, but the current data can support only a cautious hypothesis that the stronger age-related differences after 50 years may be related to menopausal transition-associated endocrine changes.

In addition, the minimum derivative in women occurred near the upper boundary of the sampled age range and was therefore clearly boundary-sensitive. Accordingly, the more marked age-related differences identified in women are more likely to reflect a broader midlife pattern rather than a single precise and fixed turning age. In other words, an age of around 50 years may be a more appropriate public health warning window for entry into a more evident phase of lower-limb strength differences in women, whereas the 57-year minimum derivative should be interpreted as a statistical signal within the current sample range and requires confirmation in samples containing more older adults and in longitudinal follow-up studies.

From an applied perspective, these findings indicate that midlife women, especially those around the age range commonly associated with the menopausal transition, may represent an important target period for lower-limb strength monitoring and

intervention. Because endocrine changes during this life stage may affect both skeletal muscle and the skeletal system, the lower strength observed during this period may not only increase the future risk of functional limitation and frailty but may also be related to higher fall risk and declining mobility. Therefore, strengthening resistance training, functional physical activity, and integrated health management around the age of 50 years may have particular preventive value in women [27, 29, 31].

## 3.6 Strengths and Limitations

The primary strength of this study lies in the originality and reliability of its data source. Relying on a large adult field-measured cohort designed and collected entirely by our research team, the study avoided the measurement heterogeneity frequently encountered in secondary database analyses. This enabled us to move the observational window for lower-limb strength differences substantially forward—from the conventional focus on old age to adulthood and even midlife—thereby providing a high-fidelity empirical basis for early functional warning and earlier intervention across the life course. Methodologically, we combined restricted cubic splines, first-derivative analysis, and piecewise regression to triangulate the nonlinear age effect from the complementary perspectives of continuous smooth fitting, cross-sectional age gradients, and structural breakpoint detection, thereby improving the robustness of both the overall age-related pattern and the estimated turning ages.

Several limitations should nevertheless be acknowledged. First, because of the cross-sectional design, the age-related patterns described here cannot establish causal temporality and cannot fully exclude potential cohort effects. For example, lower strength in today's older participants may partly reflect generational differences in lifetime physical activity, nutrition, occupational demands, and broader social conditions rather than physiological ageing alone. Second, participants were concentrated primarily between 20 and 59 years of age; the relative paucity of older adults ($\geq$60 years) contributed to the evident boundary sensitivity of the female high-age extremum estimate, and its precise nonlinear pattern will need confirmation in cohorts including broader older-age distributions. Third, menopausal status, reproductive stage, and circulating hormone measures were not available in the current dataset. As a result, the apparent correspondence between the female breakpoint around 50 years and the menopausal transition can be interpreted only as an association-based hypothesis rather than a direct causal inference. Fourth, although the multivariable models carefully adjusted for core anthropometric and fitness indicators, BMI was excluded from the final multivariable models because of collinearity with height and body weight, and residual confounding from unmeasured factors such as

long-term exercise habits, occupational physical load, protein intake, and prior musculoskeletal injury history cannot be completely ruled out. Finally, the identified age breakpoints and windows of more marked differences are, by nature, group-level statistical phenotype windows. This study was not based on a nationally representative sample; rather, it was derived from a field-measured Chinese adult cohort recruited and tested directly by our research team. Accordingly, the current findings are most directly applicable to similarly measured Chinese adults in community or field-testing settings. Their representativeness and external generalizability to other regions, ethnic and sociocultural contexts, adults aged $\geq$60 years, clinical populations, and frail older adults should be interpreted cautiously. In particular, the stability, screening utility, and clinical predictive value of these age windows in geriatric or patient populations remain to be established in prospective longitudinal studies and in cohorts deliberately enriched for older and clinically vulnerable participants [16].

## 3.7 Public Health and Practical Implications

The translational value of this study lies in converting the nonlinear cross-sectional age-related pattern of isometric knee extension strength into concrete intervention targets for chronic musculoskeletal disease prevention and life-course health management. Previous studies have shown that quadriceps weakness is not merely a concomitant feature of ageing, but also a core risk factor driving pain, functional limitation, and structural deterioration in knee osteoarthritis. Against this background, the sex-specific age-related difference windows identified in the present study—the structural transition and steeper age gradient in men between approximately 38 and 45 years, and the more pronounced differences after 50 years in women—should be regarded as key early warning windows in public health practice. Lower knee extensor strength observed during these periods may indicate not only general reductions in physical fitness, but also substantially elevated long-term risks of knee symptoms, impaired activity, and chronic musculoskeletal disease. In addition, the quantile regression results showed that age exerted a stronger negative effect in high-quantile strength groups. This suggests that even adults with relatively high lower-limb strength reserves may still show substantial age-related differences in strength, challenging the traditional assumption that functional maintenance efforts need focus only on those with low fitness. At the same time, the marked heterogeneity in the absolute distribution of strength between men and women indicates that risk assessment based on a uniform threshold may lead to major misclassification. Based on these findings, the present study supports the following strategies for public health and clinical practice, while recognizing that the present evidence is most directly relevant to a field-measured Chinese adult cohort rather than to nationally representative, clinical, or

frail older populations:

First, precision resistance-training interventions should be implemented around the identified age-related difference windows. The timing of preventive intervention should be moved substantially earlier than old age. During the compensatory window around the age of 40 years in men and during the corresponding midlife window in women, timely introduction of high-load resistance training and neuromuscular control training may maximize the delay of motor unit loss and deterioration in skeletal muscle function.

Second, stratified health management pathways should be constructed according to heterogeneity in baseline strength. In light of the quantile regression findings, one-dimensional generic health guidance should be replaced by risk-stratified management. Individuals with low baseline strength may benefit more from foundational strength rebuilding and fall prevention, whereas those with high baseline strength may require greater emphasis on maintaining muscular power and higher-order physical performance, thereby allowing precision intervention concepts to be implemented throughout life-course lower-limb function maintenance.

# 4 Methods

## 4.1 Study Design and Participants

This was a cross-sectional study. Participants were adults who were recruited and tested on site by our research team. All data were collected in the field according to standardized testing procedures, rather than obtained from an existing database or secondary data compilation. Study design, implementation, and reporting were organized with reference to the STROBE statement for observational studies [9].

Eligible participants were adults aged 20–60 years who were able to complete the physical fitness tests independently and had valid measurements of isometric knee extension strength as well as relevant anthropometric and physical fitness indicators. Exclusion criteria were missing age or primary outcome data, clearly abnormal records during testing, and failed or invalid isometric knee extension measurements. After data cleaning, all indicators were converted to numeric variables; obvious outliers and records flagged as measurement failures were treated as missing values. After excluding individuals with missing age or isometric knee extension strength data, 6,761 participants were retained for analysis, including 3,020 men and 3,741 women. The participant flow is shown in Supplementary Figure S1 in the Supplementary Information.

The study protocol was approved by the institutional ethics committee of Shanghai

University of Sport (approval No. 102772024RT091). All methods were performed in accordance with the relevant guidelines and regulations. Before testing, all participants were fully informed of the purpose of the study and its potential risks, and written informed consent was obtained from all participants.

## 4.2 Data Collection and Measurements

All participants were assessed by uniformly trained examiners following standardized procedures. The test battery included basic demographic and anthropometric indicators as well as multiple physical fitness measures. To ensure data quality, all measurements were obtained under standardized conditions; devices were inspected and calibrated before testing, and results were recorded during testing by designated examiners using uniform procedures. After testing, the research team reviewed, cleaned, and coded the raw data.

Isometric knee extension strength was the primary outcome and was used to characterize the functional level of the knee extensors. Previous work has shown that knee extension strength is closely related to functional performance and, in some settings, is at least as informative as or more informative than grip strength for predicting functional capacity; it has therefore been recommended as part of comprehensive functional assessment [3, 4]. Anthropometric variables included height, weight, and body mass index (BMI). Physical fitness indicators included grip strength, back strength, vertical jump, push-ups/knee push-ups, and sit-ups. To reduce confounding by body size and general strength level when estimating age effects, height, weight, and grip strength were further included as covariates in the multivariable nonlinear models. BMI was retained for descriptive and correlation analyses but excluded from the final multivariable models because of collinearity with height and body weight.

Isometric knee extension strength was measured with a portable isometric dynamometer on the dominant leg. During testing, participants sat on a chair with a backrest, with the back against the support and both hands holding the sides of the seat to stabilize the trunk. The test-side thigh was kept in contact with the seat, while the lower leg hung naturally so that the hip and knee were positioned in a standardized flexed posture, with the lower leg forming an angle of approximately 90° with the thigh. A tape measure was used to locate a point 5 cm above the medial malleolus, which served as the fixation point for the dynamometer strap. Before testing, participants were instructed to keep the test leg at the starting position and not to swing it backward before exerting force forward. On a standardized verbal cue, participants pushed the leg forward with maximal effort and maintained the contraction for 3 s; the highest force

recorded during the trial was taken as the result for that attempt. Previous studies have shown that the isometric knee extension test is a practical and repeatable field-based tool for assessing lower-limb strength and is useful in functional assessment and sarcopenia-related research [10–12]. To reduce random error, each participant completed 3 repeated trials with adequate rest between trials, and the maximum value was used in the final analyses. Trials were discarded and repeated if movement quality was poor, compensatory body motion was obvious, or the device fixation was unstable. Throughout testing, examiners monitored posture and force application to ensure consistency and reliability. Previous studies also support the reliability and validity of portable or fixed dynamometer systems for measuring knee extension strength [11–14].

## 4.3 Statistical Analysis

### 4.3.1 Descriptive Statistics and Preliminary Association Analyses

Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency and percentage. Baseline characteristics are reported in the Results section as summary tables. Pearson correlation analysis was used to evaluate linear associations between isometric knee extension strength and anthropometric and physical fitness indicators, and multiple linear regression was further used to examine their independent associations with isometric knee extension strength.

As a supplementary analysis, quantile regression was used to examine differences in the age effect across strength quantiles and to establish sex-specific normative grading in order to enhance the practical interpretability and applied value of the findings. In line with the SAMPL guidelines, statistical reporting should emphasize effect estimates and their uncertainty rather than relying solely on P values; accordingly, effect estimates, 95% confidence intervals, and P values are reported for the main models [15].

### 4.3.2 Nonlinear Analysis of Age and Isometric Knee Extension Strength

To explore the potentially nonlinear relationship between age and isometric knee extension strength, age was modeled continuously using restricted cubic splines (RCS), with separate models fitted for men and women. Isometric knee extension strength was the dependent variable, the spline function of age was the primary independent variable, and height, weight, and grip strength were included as covariates. The model was specified as follows:

$$Y = \beta_0 + f(\text{Age}) + \beta_1 \text{Height} + \beta_2 \text{Weight} + \beta_3 \text{Grip strength} + \varepsilon$$

where $Y$ denotes isometric knee extension strength and $f(\text{Age})$ denotes the restricted cubic spline function of age. RCS permits flexible modeling of nonlinear exposure-outcome relationships while preserving the continuity of the exposure, and is therefore suitable for identifying smooth turning patterns and change windows in age effects [16]. To enhance model robustness, the degrees of freedom and prespecified knot combinations were selected using five-fold cross-validation, with preference given to models with lower prediction error. F-tests and likelihood ratio tests were then used to evaluate whether the age term showed significant nonlinearity.

#### 4.3.3 Identification of Age Turning Points

After fitting the RCS models, the first derivative of the predicted age-effect curve—holding covariates at their mean values—was calculated to characterize the cross-sectional age gradient in isometric knee extension strength across age. The age corresponding to the minimum first derivative was defined as the age of steepest cross-sectional gradient and used to identify a potential age turning point. Because derivative extrema may be influenced by the age distribution boundaries of the sample, minima occurring near the boundary of the observed age range were classified as boundary-sensitive results and interpreted cautiously rather than directly regarded as stable physiological thresholds [16].

#### 4.3.4 Piecewise Regression Analysis

To verify the structural turning characteristics of the age effect from an additional perspective, a single-breakpoint piecewise regression model was fitted for the relationship between age and isometric knee extension strength. The optimal breakpoint was identified by scanning candidate ages and comparing residual sums of squares. After the breakpoint had been determined, the age slope before the breakpoint and the change in slope after the breakpoint were estimated and their corresponding P values were reported. To assess uncertainty in the breakpoint estimate, bootstrap resampling was further used to calculate the 95% confidence interval of the breakpoint.

#### 4.3.5 Software and Significance Criteria

All statistical analyses were performed in Python. Data management was conducted primarily using pandas; linear regression, quantile regression, restricted cubic spline modeling, and piecewise regression were implemented using statsmodels and patsy; scikit-learn was used for cross-validation; and matplotlib was used for visualization. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant. In

accordance with the STROBE and SAMPL recommendations, the statistical analysis section emphasizes variable handling, model specification, tests of nonlinearity, effect estimation, and measures of uncertainty [9, 15].

# Data availability

The de-identified participant-level datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. Derived supplementary tables supporting the conclusions of this article are included in the Supplementary Information and Supplementary Tables files.

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# Author contributions

Zhen Ling completed all data analyses and drafted the manuscript. Yunhe Zhou completed data provision and on-site data collection. All authors reviewed the manuscript and approved the final version.

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# Competing interests

The authors declare no competing interests.

# Figure legends

**Figure 1. Age-related RCS curves for isometric knee extension strength.** Panel A shows men and Panel B shows women. Curves were generated with height, weight, and grip strength fixed at their mean values. Shaded areas represent 95% confidence intervals, and the red dashed line indicates the age of the steepest cross-sectional gradient. The age effect was significantly nonlinear in both sexes, with stronger age-related differences emerging earlier in men and later but progressively more marked differences in women. *Boundary-sensitive estimate in women; interpret cautiously because the minimum derivative occurred near the upper boundary of the observed age range.

**Figure 2. Piecewise regression breakpoints for age-related strength differences.** Panel A shows men and Panel B shows women. Gray points represent observed values, the solid blue line represents the fitted piecewise regression, and the red dashed line indicates the estimated breakpoint. The estimated breakpoint was approximately 38 years in men and 50 years in women, supporting sex-specific structural turning features in the age-related differences of lower-limb strength.

**Figure 3. First-derivative curves of age-related change in strength.** Panel A shows men and Panel B shows women. The first derivative represents the cross-sectional age gradient in predicted isometric knee extension strength. In men, the derivative reached its minimum at 45.4 years, indicating the age of the steepest cross-sectional gradient. In women, the derivative became progressively more negative

with age and reached its minimum near the upper boundary of the observed age range, indicating a boundary-sensitive estimate and suggesting that age-related differences become more pronounced at older ages.

# Tables

**Table 1. Basic Characteristics of the Study Participants (mean ± SD)**

| Indicator | All | Male | Female |
|---|---|---|---|
| Age (years) | 39.4 ± 10.8 | 38.3 ± 11.1 | 40.3 ± 10.4 |
| BMI (kg/m$^2$) | 24.4 ± 4.4 | 25.7 ± 4.5 | 23.4 ± 4.1 |
| Back strength (kg) | 84.0 ± 31.9 | 109.7 ± 27.0 | 63.0 ± 16.6 |
| Grip strength (kg) | 33.4 ± 10.4 | 42.4 ± 7.9 | 26.1 ± 5.4 |
| Height (cm) | 165.8 ± 8.7 | 172.7 ± 6.6 | 160.3 ± 5.8 |
| Isometric knee extension strength (N) | 318.2 ± 131.1 | 397.2 ± 136.0 | 254.4 ± 83.7 |
| Push-ups/knee push-ups (repetitions) | 19.3 ± 9.6 | 20.7 ± 10.4 | 18.2 ± 8.7 |
| Sit-ups (repetitions) | 21.0 ± 8.4 | 23.6 ± 8.5 | 19.0 ± 7.7 |
| Vertical jump (cm) | 27.3 ± 8.7 | 32.8 ± 8.1 | 22.9 ± 6.3 |
| Body weight (kg) | 67.7 ± 14.3 | 76.8 ± 13.4 | 60.3 ± 10.1 |

**Table 2A. Pearson correlations with isometric knee extension strength**

| Variable | Pearson $r$ | $P$ value |
|---|---|---|
| Back strength (kg) | 0.578 | $< 0.001$ |
| Grip strength (kg) | 0.562 | $< 0.001$ |
| Height (cm) | 0.484 | $< 0.001$ |
| Vertical jump (cm) | 0.462 | $< 0.001$ |
| Body weight (kg) | 0.450 | $< 0.001$ |
| Sit-ups (repetitions) | 0.322 | $< 0.001$ |
| BMI (kg/m$^2$) | 0.235 | $< 0.001$ |
| Push-ups/knee push-ups (repetitions) | 0.205 | $< 0.001$ |
| Age (years) | -0.194 | $< 0.001$ |

**Table 2B. Multiple linear regression for isometric knee extension strength**

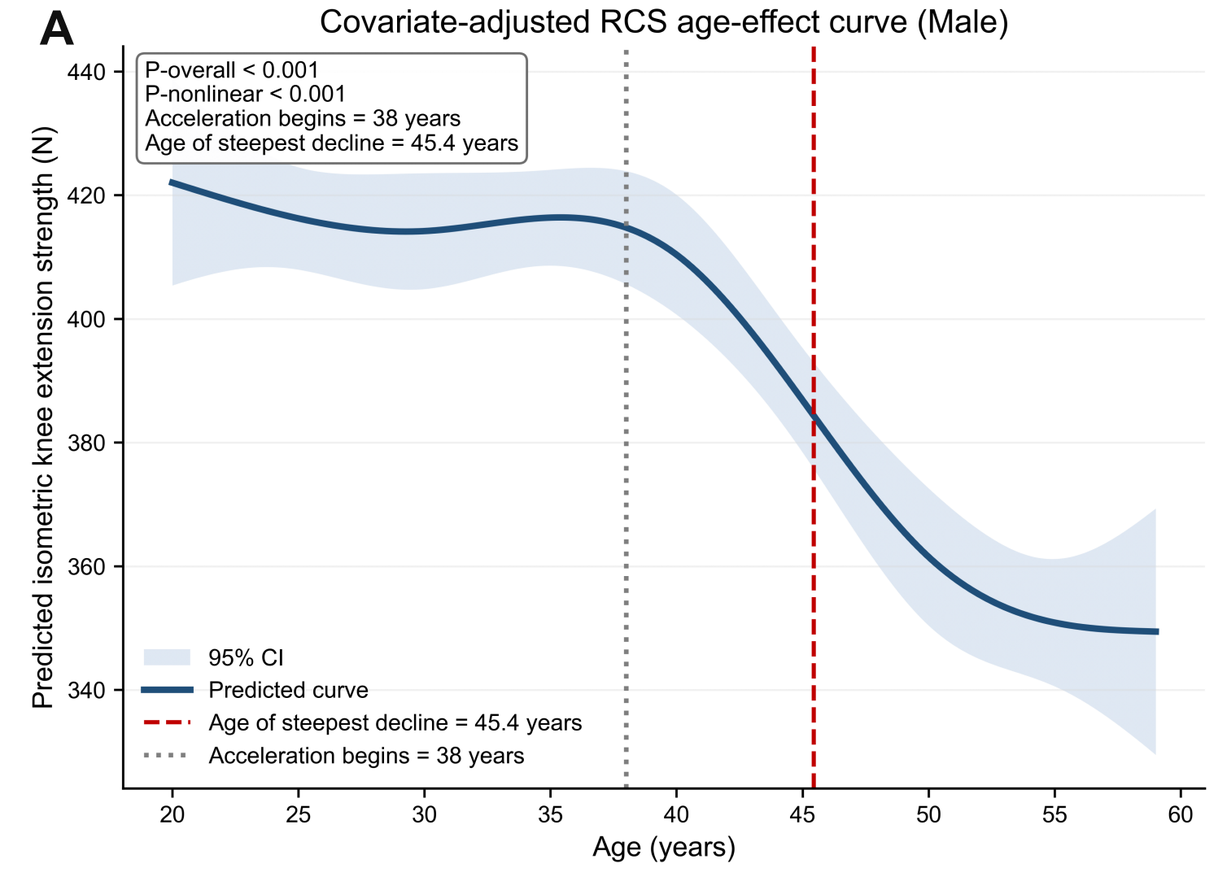
| Variable | Adjusted beta | 95% CI | *P* value |
|---|---|---|---|
| Age | -0.568 | (-0.908, -0.229) | 0.001 |
| Sex (male vs female) | 52.510 | (31.611, 73.409) | $< 0.001$ |
| Age × sex interaction | -0.643 | (-1.107, -0.180) | 0.007 |
| Height | -0.565 | (-1.035, -0.094) | 0.019 |
| Body weight | 1.576 | (1.327, 1.825) | $< 0.001$ |
| Grip strength | 1.800 | (1.367, 2.233) | $< 0.001$ |
| Back strength | 0.931 | (0.796, 1.066) | $< 0.001$ |
| Vertical jump | 1.461 | (1.062, 1.861) | $< 0.001$ |
| Push-ups/knee push-ups | 0.484 | (0.196, 0.771) | $< 0.001$ |
| Sit-ups | 1.236 | (0.872, 1.600) | $< 0.001$ |

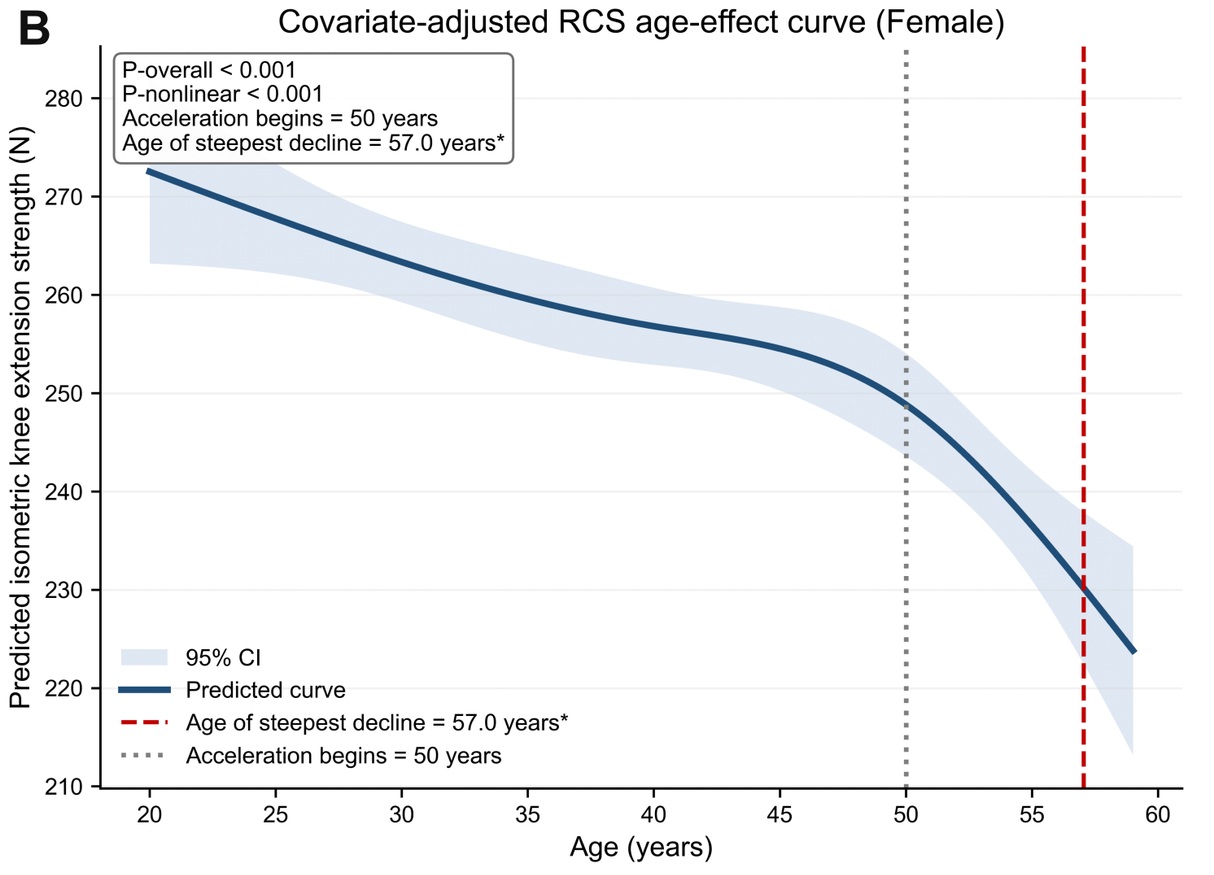
**Table 3. Main nonlinear age-effect results for knee extension strength**

| Sex | Optimal RCS model | Nonlinearity | Age of steepest cross-sectional gradient (years) | Piecewise breakpoint (95% CI) | Post-break slope-change P |
|---|---|---|---|---|---|
| Male | df=5; knots 30, 40, 50 | Both tests P<0.001 | 45.4 | 38.0 (29.0, 40.5) | <0.001 |
| Female | df=4; knots 40, 50 | Both tests P<0.001 | 57.0* | 50.0 (36.9, 53.0) | <0.001 |

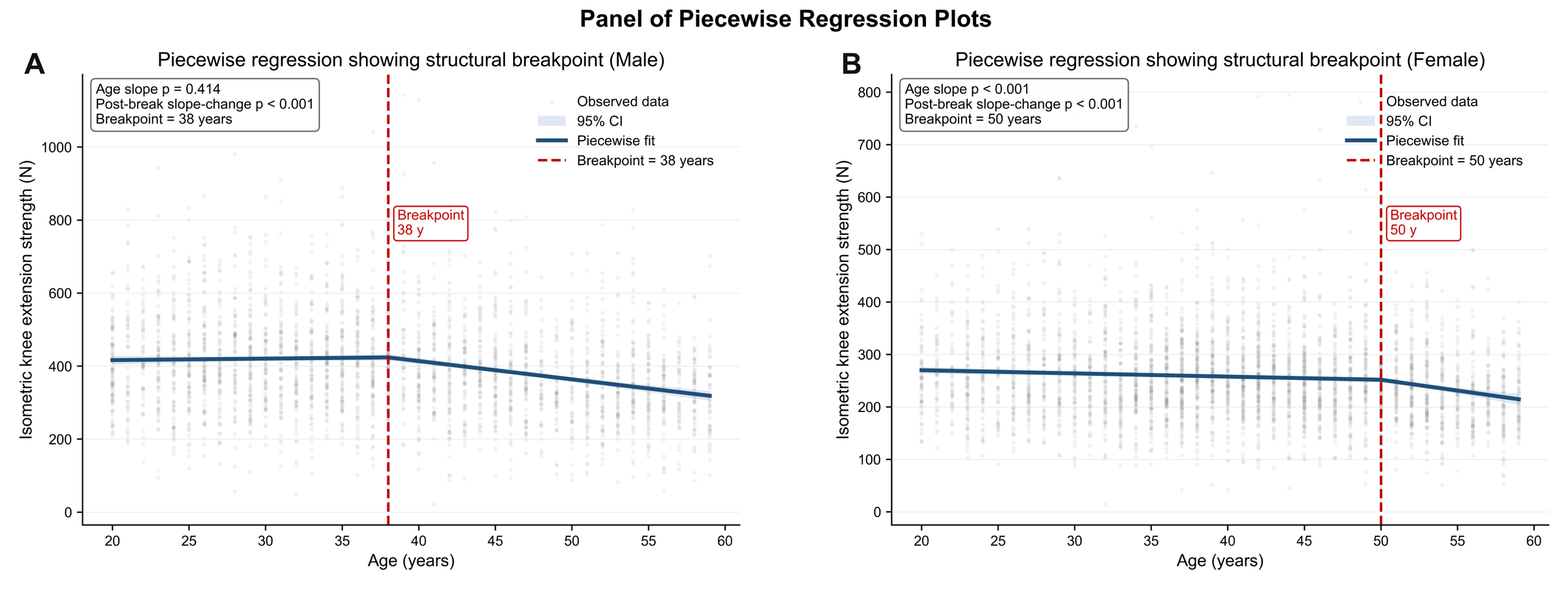
*Note:* *Boundary-sensitive estimate; interpret cautiously because the minimum derivative occurred near the upper boundary of the observed age range.

# Panel of Covariate-adjusted RCS Age-effect Curves

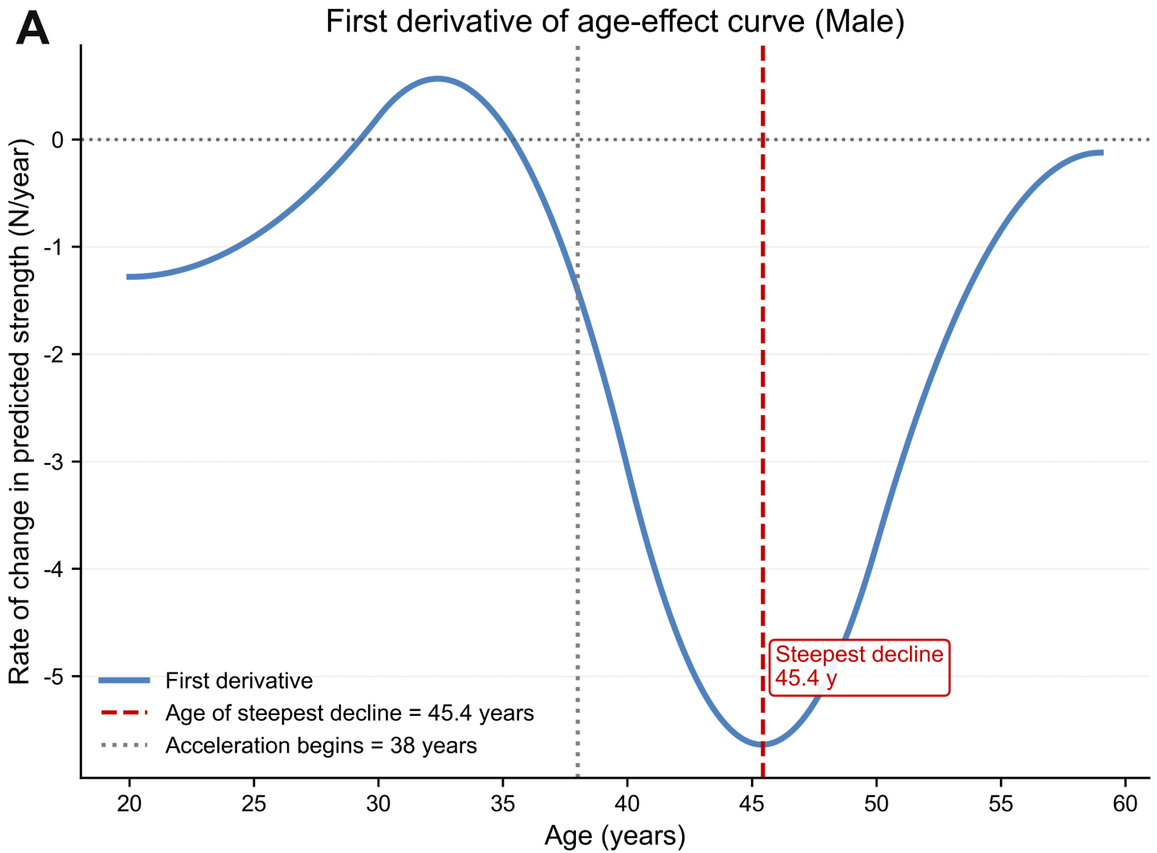


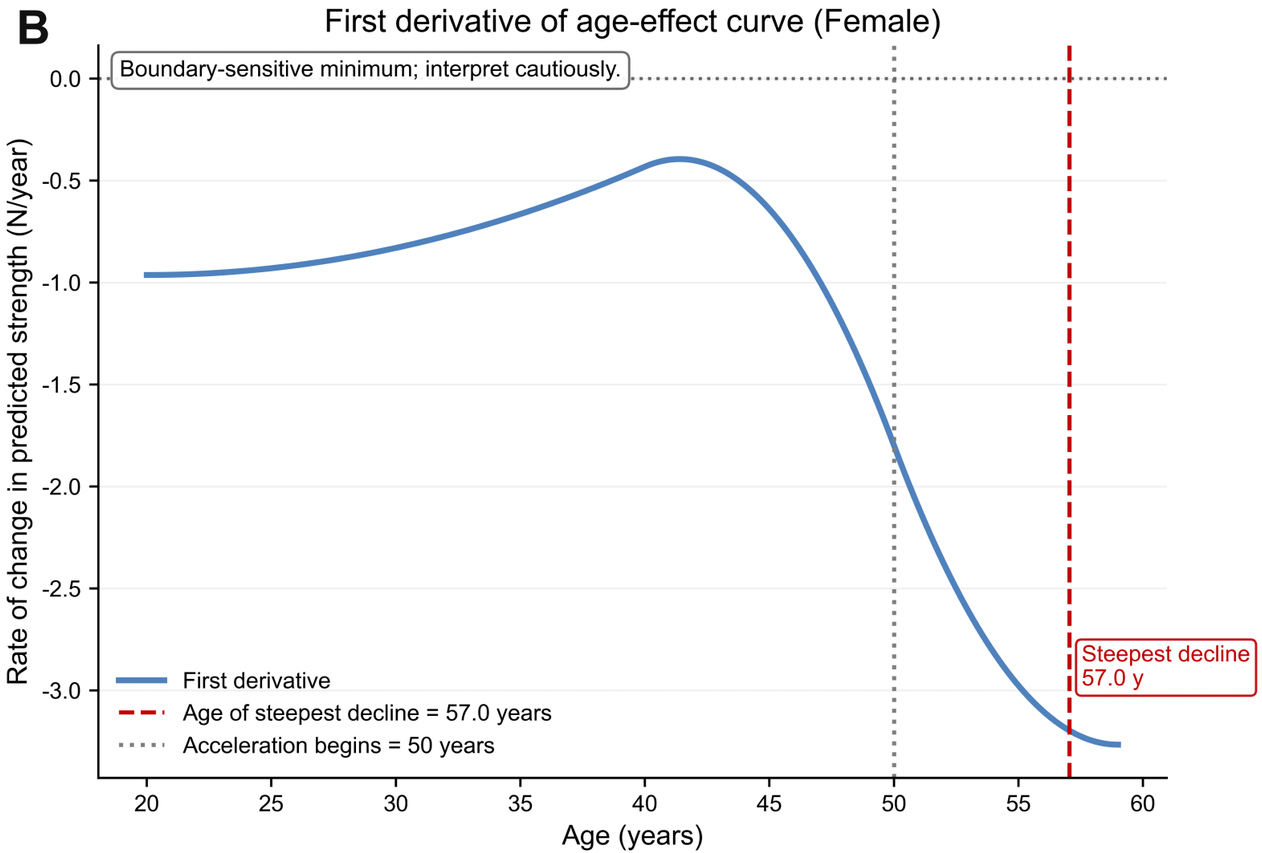



# Panel of Piecewise Regression Plots



# Panel of First-derivative Curves



## Supplementary Files

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