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Associations of Adiposity Phenotypes with Incident Frailty among Older Chinese Adults: A Longitudinal Analysis of CHARLS 2011–2020

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Abstract

Background

Adiposity is heterogeneous with respect to metabolic status, muscle function, and inflammation, but it is unclear whether these phenotypes differ in their associations with incident frailty. We compared metabolic, possible sarcopenic, and inflammatory adiposity phenotypes in older Chinese adults.

Methods

We analyzed 5,339 CHARLS participants aged ≥ 60 years who were non-frail in 2011 and had at least one follow-up frailty assessment. Fifty outcome-assisted multiple imputations completed baseline components; frailty index (FI) were not imputed. Cox models used covariate stratification or time-varying exposure coefficients when indicated by proportional-hazards diagnostics. Sensitivity analyses examined baseline deficit burden, FI construction, event timing and follow-up participation.

Results

During 35,407 person-years, 1,912 incident frailty events occurred (54.0 per 1000 person-years). Overall adiposity was associated with frailty (HR 1.25, 95% CI 1.11–1.42). Possible sarcopenic adiposity (PSA) versus non-sarcopenic non-adiposity had HRs of 2.44 (1.79–3.32), 2.08 (1.73–2.51), 1.80 (1.44–2.25) and 1.68 (1.27–2.24) at 2, 4, 7 and 9 years, respectively. Within adiposity, PSA versus non-sarcopenic adiposity had HRs of 1.41 (1.21–1.65) and 1.32 (1.08–1.62) at 7 and 9 years. Linear baseline-FI adjustment with time-varying FI effects yielded corresponding within-adiposity HRs of 1.34 (1.15–1.57) and 1.28 (1.05–1.56), and spline adjustment was concordant. The 34-item harmonized FI gave full-cohort and within-adiposity HRs of 1.85 (1.49–2.29) and 1.40 (1.21–1.61) when ≥ 30 items were required. The within-adiposity metabolic contrast was sensitive to the abnormality threshold, and the inflammatory contrast was imprecise.

Conclusions

Possible-sarcopenia indicators differentiated observed frailty risk among older adults with adiposity. The findings support further evaluation of grip strength and chair-stand performance alongside anthropometry; shared functional content and the observational design limit causal interpretation.

1. Background

Frailty is associated with falls, disability, hospitalization, and mortality.[1–3] China's 2020 census counted more than 264 million adults aged 60 years or older, representing 18.7% of the population.[4] This demographic burden increases the need to identify potentially modifiable factors associated with frailty while distinguishing association from causation.[5, 6]

Adiposity is a potentially modifiable correlate of frailty, but body mass index (BMI) alone cannot distinguish fat distribution or muscle composition.[7–9] We therefore defined adiposity using BMI, waist circumference, or waist-to-height ratio to capture general and central adiposity.[9, 10] People with similar adiposity may nevertheless differ in metabolic health, muscle function, and inflammatory status.[11–13]

Metabolic, possible sarcopenic, and inflammatory adiposity phenotypes therefore represent distinct dimensions of this heterogeneity.[11, 13, 14] However, these phenotype frameworks have rarely been compared within the same longitudinal cohort using a common frailty outcome. Because CHARLS did not measure muscle mass, possible sarcopenic adiposity denotes adiposity accompanied by possible sarcopenia indicators (low grip strength or poor chair-stand performance) and is not equivalent to sarcopenic adiposity. Similarly, the inflammatory phenotype was defined by a single high-sensitivity C-reactive protein (hsCRP) measurement and should not be interpreted as proven chronic inflammation. We compared the three phenotype frameworks in one longitudinal cohort under a common frailty outcome and covariate framework, and examined whether they further differentiated frailty risk among participants with adiposity.

2. Methods

2.1 Participants and procedures

To compare the association between adiposity-related phenotypes and incident frailty within the same cohort using a common frailty outcome, this study used data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey of Chinese adults aged 45 years or older.[15] CHARLS used a multistage, stratified, probability-proportional-to-size sampling design across 28 provinces, 150 counties, and approximately 450 communities. The 2011 baseline survey recruited 17,705 individuals, with follow-up surveys in 2013, 2015, 2018, and 2020. Among 7,701 participants aged 60 years or older, 7,477 had an evaluable baseline frailty index. We excluded 1,745 with baseline frailty; 5,732 were baseline non-frail, of whom 393 had no follow-up FI and 5,339 entered the primary analysis (5,133 for the hsCRP-defined inflammatory phenotype). (Fig. 1) The 393 participants without follow-up FI were retained for the loss-to-follow-up comparison and participation-weight model. Ethical approval was obtained from the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided written informed consent.

2.2 Exposure: general or central adiposity and adiposity-related phenotypes

2.2.1 General or central adiposity

Participants were first classified as non-adiposity and adiposity. We operationally defined general or central adiposity as BMI ≥ 28 kg/m^2, waist circumference (WC) ≥ 90 cm in men or ≥ 85 cm in women,[16] or waist-to-height ratio (WHtR) ≥ 0.50.[17] The BMI and WC thresholds follow Chinese criteria; the uniform WHtR threshold and combination requiring any of the three criteria were study choices. BMI was weight (kg) divided by height squared (m^2), and WHtR was WC (cm) divided by height (cm). The criteria could overlap. Seven

nonempty, mutually exclusive combinations were summarized within each completed dataset; counts and percentages were averaged separately across the 50 datasets, with imputation ranges in **Additional file 1**.

2.2.2 Adiposity-related phenotype definitions

To characterize adiposity-related heterogeneity, participants were further categorized according to metabolic status, sarcopenic status, and inflammatory status. The three phenotype frameworks were evaluated separately and were not mutually exclusive across frameworks. Participants meeting criteria in more than one framework contributed to each relevant analysis. The four categories within each framework were mutually exclusive, but MUA, PSA and IA could coexist in the same participant. Participants with an unavailable inflammatory classification did not contribute to that framework. Before imputation, phenotypes that could not be determined from the observed components were coded as missing. In each completed dataset, phenotypes were derived from the imputed baseline component variables. All adiposity and phenotype exposures were defined at baseline.

Metabolic adiposity phenotypes

Metabolic health status was determined based on the presence of metabolic abnormalities according to the modified Adult Treatment Panel III (ATP III) criteria for metabolic syndrome, including hypertension, diabetes, related medication use, and dyslipidemia, derived from questionnaire responses, physical measurements, and laboratory tests.[18] To avoid overlap with the definition of adiposity, the abdominal obesity component of the ATP criteria was omitted. Participants were classified as metabolically unhealthy if they met at least two of the following criteria: (1) Elevated triglyceride levels of ≥ 1.7 mmol/L; (2) Reduced HDL-C levels, defined as < 1.03 mmol/L in men or < 1.3 mmol/L in women; (3) High blood pressure, either a systolic pressure of ≥ 130 mmHg, a diastolic pressure of ≥ 85 mmHg, or the use of antihypertensive medication; (4) High fasting blood glucose levels of ≥ 5.6 mmol/L or the use of antidiabetic medications. The blood-pressure flags included Chinese or Western antihypertensive medicines; glucose-lowering flags included Chinese or Western medicines or insulin. Lipid-lowering medication and self-reported diagnoses alone did not enter the implemented classification. Medication flags were not imputed, and missing flags did not establish treatment. Zero or one abnormality defined metabolically healthy status, which did not mean that all biomarkers were normal. This study-specific classification was not a diagnosis of metabolic syndrome.

Participants were categorized as metabolically healthy non-adiposity (MHNA), metabolically healthy adiposity (MHA), metabolically unhealthy non-adiposity (MUNA), or metabolically unhealthy adiposity (MUA).

Sarcopenic adiposity phenotypes

Because CHARLS did not measure muscle mass, possible sarcopenia was defined according to the Asian Working Group for Sarcopenia (AWGS) 2019 concept.[19] It was identified by "low handgrip strength" (maximum power of handgrip strength < 28 kg for men or < 18 kg for women), or "poor physical performance" (five-time chair stand test duration ≥ 12 seconds). Handgrip strength was measured with a dynamometer twice per hand, alternating hands; the maximum available valid value across four trials was used. Values coded 0, 993 or 999, or > 100 kg, were treated as missing. For chair-stand test, participants stood from a stool and sat down five times as quickly as possible with their arms crossed over the chest. A completed timed test was accepted when no arm assistance was recorded. Tried-but-unable or recorded incomplete attempts

were assigned 13 seconds and classified as poor performance; refusal and other untimed tests remained missing for component imputation. Possible sarcopenic adiposity (PSA) was adiposity accompanied by these possible sarcopenia indicators, without a muscle-mass criterion.

Participants were classified into four sarcopenic adiposity phenotypes: (1) Non-sarcopenic non-adiposity (NSNA). (2) Non-sarcopenic adiposity (NSA). (3) Possible sarcopenic non-adiposity (PSNA). (4) Possible sarcopenic adiposity (PSA).

Inflammatory adiposity phenotypes

The hsCRP phenotype was based on a single baseline blood measurement. Among eligible participants, elevated hsCRP was defined as 3 to < 10 mg/L and the comparison category as 0 < hsCRP < 3 mg/L. Participants with an observed baseline hsCRP ≥ 10 mg/L were flagged before imputation and excluded from the hsCRP phenotype analyses, including those with a value exactly equal to 10 mg/L. This eligibility decision was retained in all completed datasets. Participants with originally missing hsCRP and no observed ≥ 10 mg/L value were classified using their imputed hsCRP values.[20] These concentration categories do not establish the absence of inflammation or persistent inflammatory disease. Baseline hsCRP was assayed from stored venous plasma using an immunoturbidimetric method at the Youanmen Center for Clinical Laboratory of Capital Medical University. The CHARLS baseline blood-data guide reports within-assay and between-assay coefficients of variation of < 1.3% and < 5.7%, respectively, and a reported detection range of 0.1–20 mg/L.

Combining adiposity and hsCRP status yielded four mutually exclusive categories within this framework: (1) non-adiposity with hsCRP < 3 mg/L (NINA). (2) adiposity with hsCRP < 3 mg/L (NIA). (3) non-adiposity with hsCRP 3–<10 mg/L (INA). (4) adiposity with hsCRP 3–<10 mg/L (IA). All classified hsCRP values were positive. The labels indicate hsCRP concentration categories, rather than clinical diagnoses of inflammatory or non-inflammatory states.

2.2.3 Adiposity-specific analyses

To further investigate heterogeneity among participants with adiposity, adiposity-specific analyses were conducted in MHA vs MUA, NSA vs PSA, and NIA vs IA. The phenotype frameworks were evaluated separately and could overlap across participants. PSA versus NSNA compares both adiposity and possible-sarcopenia status; PSA versus NSA compares possible-sarcopenia status among participants with adiposity. These contrasts do not establish synergy, phenotype-specific mechanisms or superiority over PSNA.

2.3 Outcome: frailty

Frailty was assessed using a deficit-accumulation frailty index (FI).[2, 21, 22] The standard FI comprised activities of daily living (6 items), instrumental activities of daily living (6 items), physical limitations (9 items), chronic diseases (14 items), mental health (7 items), and subjective health items (2 items) (**Additional file 2**). The CHARLS coding algorithms were informed by previous applications.[5, 23] The available items varied by wave (43 in 2011, 44 in 2013–2018, and 35 in 2020) and the primary FI required at least 30 observed items. FI was calculated as the sum of observed deficit scores divided by the number of observed items at that wave, giving a value from 0 to 1, and frailty was defined as FI ≥ 0.25.[5, 23–25] The specific differences across

waves are detailed in **Additional file 2**. For sensitivity analyses, we constructed an exposure-related FI excluding nine items related to the metabolic-unhealthiness and possible-sarcopenia definitions, a PSA-specific FI excluding six physical-function items conceptually related to the possible-sarcopenia definition and a 34-item harmonized FI using items available in all waves, requiring at least 28 items with a stricter 30-item check. The overlap-reduced and PSA-specific FI required at least 30 observed items; each sensitivity reselected baseline non-frailty and derived follow-up events using its corresponding FI version. Version-specific item availability, score denominators and cohort flows are reported in **Additional file 2**.

The primary outcome was first incident frailty, defined as the first follow-up assessment with FI ≥ 0.25. Participants entered follow-up at the 2011 baseline and were assessed in 2013, 2015, 2018, and 2020, corresponding to 2, 4, 7, and 9 years after baseline. Event time was assigned to the first wave meeting the frailty threshold. Participants without incident frailty were censored at their last available FI assessment. A requirement for FI ≥ 0.25 at least twice was examined only as a sensitivity analysis.

2.4 Covariates

Covariates were chosen from previous studies[5, 26–28] and included: (1) demographic variables, including age group (60–64, 65–79 or ≥ 80), sex (male or female). (2) socioeconomic characteristics, including educational level (illiterate, middle school and high school, primary school and below, technical school and above), residence (rural or urban), marital status (currently unmarried or married), and medical insurance (no medical insurance-NMI, urban employee medical insurance-UEMI, urban resident medical insurance-URMI, urban and rural resident medical insurance-URRMI, new cooperative medical insurance-NCMI, others, and multiple). (3) health-related behaviors, including smoking status (never, current or former), alcohol consumption (never, current or former), and physical activity (insufficiently active or sufficiently active, see the detailed assessment methods in **Additional file 3**). Physical-activity coding was adapted from previous CHARLS applications.[5, 26] Physical activity was assessed using CHARLS items mapped to the International Physical Activity Questionnaire framework, and the main analysis used the sufficiently active versus insufficiently active classification, with detailed scoring in **Additional file 3**.

2.5 Statistical analysis

Missing baseline components were addressed with MICE in 7,701 participants aged ≥ 60 years, using 50 imputations, 20 iterations and seed 20260816.[29] The variable-level patterns and imputation diagnostics are reported in **Additional file 4** and **5**. Under a missing-at-random assumption conditional on observed predictors, outcome-assisted multiple imputation by chained equations generated 50 completed datasets. The event indicator, follow-up time, Nelson-Aalen cumulative hazard and a follow-up observation indicator were included as auxiliary predictors but were not imputed;[30] the FI was not imputed. HsCRP was imputed by predictive mean matching on its original mg/L scale, without logarithmic transformation. Observed values ≥ 10 mg/L were masked before imputation, and the corresponding fixed eligibility flag was neither imputed nor used as a predictor. The observed donor values and all filled values in the retained 50-imputation object ranged from 0.01 to 9.97 mg/L. When phenotypes were derived in each completed dataset, hsCRP was reset to missing for flagged participants, who remained ineligible for the hsCRP framework regardless of their filled value. No additional post-imputation ≥ 10 mg/L exclusion changed the eligible sample. Adiposity and phenotype variables were recalculated passively from completed component variables, and model estimates

were combined using Rubin's rules.[31] For the 393 participants without follow-up FI, event, time and cumulative-hazard auxiliaries were set to zero alongside a zero follow-up-observation indicator; these computational encodings were not observed negative outcomes. Ordinary MICE did not implement compatibility with time-varying coefficients, splines or interactions.[32] The variable-level inclusion status is listed in **Additional file 4**.

The proportional-hazards (PH) assumption was screened in each imputed dataset using whole-term scaled Schoenfeld-residual tests with rank-transformed time. $P < 0.05$ in at least 50% of available imputation diagnostics triggered a common model specification across all 50 datasets. Violating covariates were used for stratification, and a violating exposure was modelled with exposure×log(1 + t), using current risk-set time t in years in survival::coxph tt(). Time-specific HRs at 2, 4, 7 and 9 years incorporated main-effect/time-interaction covariance. The PH-adapted Cox estimates used normal Wald intervals after Rubin pooling. “PH-robust” refers to these adaptations, not to sandwich or survey-design standard errors. The common final specification was fitted in every imputation before pooling.

The primary analysis used PH-adapted Cox models. To assess the robustness of the PSA-related findings, we conducted several sensitivity analyses including the second positive visit of two-observation frailty definition, exclusion of early events in 2013, alternative physical-activity adjustment, separate prefrailty and frailty outcomes, excluding exposure-related FI items, complete cases, common sample, jointly modelled dimensions, separate BMI/WC/WHtR adiposity definitions, possible-sarcopenia-specific FI, adjustment for baseline continuous FI, harmonized FI, interval-observed outcomes, inverse-probability weighting for follow-up participation, and the ≥ 3 metabolic-abnormality definition. In sensitivity analysis 11, baseline FI was modelled as a continuous linear term and interacted with log(1 + t) to address its time-varying effect; the sarcopenic-phenotype indicators were also interacted with log(1 + t), and exact FI values were not used as strata. A four-knot restricted cubic-spline FI specification was examined as a functional-form check. Restricted cubic splines (RCS) for continuous adiposity-related exposures, subgroup analyses, multidimensional interactions, and geographic descriptions were treated as exploratory. RCS minima were evaluated only after calculating cohort-specific BH-adjusted q values, requiring both nonlinear $P < 0.05$ and nonlinear $q < 0.05$.

For the separate-endpoint sensitivity analysis, participants with baseline FI ≤ 0.10 and at least one follow-up FI were included. Prefrailty was the first recorded follow-up FI > 0.10 and < 0.25, and frailty was the first recorded FI ≥ 0.25. Separate Cox models used each endpoint's own first observed event wave (2, 4, 7, or 9 years), with participants who did not meet that endpoint censored at their last available FI assessment. The same participant could meet both endpoints at different waves, including prefrailty after a recorded frailty wave. Death was not modeled as a competing event in these two analyses; participants without a later FI after death or loss to follow-up were censored at their last observed FI.

Common-sample joint-dimension Cox models included binary indicators for adiposity, metabolic unhealthiness, possible sarcopenia, and inflammation in the full cohort; the adiposity-restricted model included the latter three indicators. These main-effect models adjusted for age group, sex, education, residence, marital status, medical insurance, smoking, drinking, and physical activity, with PH concerns handled as in the Cox analyses. The full-cohort possible-sarcopenia coefficient covers participants with and

without adiposity. Within the adiposity-restricted cohort, this coefficient compares PSA with NSA while adjusting for the other dimensions.

The interval-observation sensitivity fitted a grouped-time proportional-hazards likelihood with separate baseline hazards over 0–2, 2–4, 4–7 and 7–9 years. An event contributed S(L) − S(R), where L was the last observed non-frail visit before the first positive visit R; censoring contributed S(C) at the last evaluable FI time. Missing intermediate visits were spanned rather than coded as negative, and the 2-, 2-, 3- and 2-year interval lengths entered cumulative hazard explicitly. The exponentiated common exposure coefficient summarizes association across follow-up under this model.

Follow-up participation weights addressed having at least one observed follow-up FI.[33] The baseline non-frail source contained 5,732 participants; the common participation model additionally required all baseline covariates and three phenotype classifications, leaving 5,506 eligible participants (5,133 responders and 373 nonresponders). The 226 exclusions comprised 206 responders and 20 nonresponders with observed baseline hsCRP ≥ 10 mg/L. Models used age group, sex, baseline FI, education, residence, marriage, insurance, smoking, drinking, activity, adiposity and phenotype groups. Within-adiposity eligibility was applied before fitting its participation model. Stabilized responder weights were truncated at each imputation's 1st and 99th percentiles. Weighted responders were compared with the eligible baseline target using absolute standardized mean differences (SMDs). These weights did not directly address subsequent dropout or intermittent missingness.

RCS used the Hmisc spline basis with four common knots at the medians of imputation-specific 5th, 35th, 65th and 95th percentiles, a pooled-median reference, and a 1st–99th percentile display range.[34] Overall and nonlinear Wald tests used Rubin-pooled coefficients and covariance matrices, including relevant time interactions. Benjamini–Hochberg (BH) adjustment was applied separately to overall and nonlinear RCS tests within each cohort (10 and eight tests, respectively).[35] Subgroup interaction contrasts were corrected within each of four full-cohort phenotype families, including their reported time points; restricted-cohort multidimensional contrasts shared one family. PH screens and primary/sensitivity effect tests were outside these families. Here q means BH-adjusted P. All testing families are reported in **Additional file 6**.

Death fields were assembled from Harmonized CHARLS regular-wave, End of Life and available exit records. Partial dates used explicit calendar conventions; undated deaths were assigned midpoint, lower-bound-plus-one-day or upper-bound dates within their available intervals. Conflicting dates and deaths incompatible with later FI observations were excluded. Observed frailty on or before the assigned death date took precedence, and earlier death was competing. Cause-specific Cox and Fine–Gray subdistribution models were fitted with PH adaptations where indicated.[36]

Analyses were conducted using R version 4.6.1 in RStudio. Primary, secondary, and exploratory analyses were distinguished before interpretation. Two-sided $P < 0.05$ was used for primary and sensitivity analyses; exploratory P values and confidence intervals were interpreted without treating non-significance as evidence of equivalence or biological independence. The analyses did not incorporate CHARLS sampling weights, official sampling strata, or household/community clustering. Proportions therefore describe the analytic sample and are not nationally weighted prevalence estimates. Participation weights cannot substitute for sampling weights.

3. Results

3.1 Baseline characteristics and distribution of adiposity phenotypes

The final analytic cohort included 5,339 baseline non-frail participants; 1,912 developed frailty over 35,407 person-years (54.0 events per 1000 person-years). Across the 50 imputed datasets, the mean age was 67.6 years and 46.9% were women. Table 1 reports baseline characteristics for the final analysis cohort rather than the broader baseline-FI sample.

Table 1
Baseline characteristics of CHARLS participants stratified by observed incident frailty status after outcome-assisted MICE.

Characteristic	Primary cohort			hsCRP-eligible cohort		
	Total (n = 5339) n (%)	No observed incident frailty (n = 3427) n (%)	Incident frailty (n = 1912) n (%)	Total (n = 5133) n (%)	No observed incident frailty (n = 3302) n (%)	Incident frailty (n = 1831) n (%)
Age years	67.55 (6.41)	66.94 (6.06)	68.65 (6.85)	67.52 (6.40)	66.91 (6.05)	68.63 (6.85)
Baseline FI	0.135 (0.058)	0.119 (0.055)	0.164 (0.053)	0.135 (0.058)	0.118 (0.055)	0.164 (0.054)
BMI kg/m²	22.97 (4.00)	22.90 (3.89)	23.10 (4.19)	22.95 (3.99)	22.91 (3.90)	23.04 (4.16)
Waist cm	85.16 (10.72)	84.86 (10.52)	85.72 (11.05)	85.09 (10.70)	84.81 (10.53)	85.61 (10.96)
Waist to height ratio	0.543 (0.071)	0.537 (0.069)	0.554 (0.075)	0.543 (0.071)	0.537 (0.069)	0.553 (0.075)
Maximum grip strength kg	30.59 (9.63)	31.96 (9.56)	28.14 (9.25)	30.62 (9.62)	32.01 (9.54)	28.10 (9.25)
Chair stand time s	11.39 (4.34)	10.78 (3.77)	12.49 (5.01)	11.38 (4.35)	10.76 (3.77)	12.50 (5.04)
Triglycerides mmol/L	1.46 (1.15)	1.44 (1.16)	1.49 (1.14)	1.46 (1.16)	1.44 (1.17)	1.49 (1.15)
HDL-C mmol/L	1.34 (0.40)	1.33 (0.40)	1.35 (0.41)	1.34 (0.41)	1.33 (0.40)	1.35 (0.41)
Systolic BP mmHg	134.53 (22.46)	133.13 (21.78)	137.05 (23.43)	134.35 (22.38)	132.86 (21.69)	137.04 (23.33)
Diastolic BP mmHg	74.79 (11.70)	74.45 (11.56)	75.41 (11.93)	74.75 (11.70)	74.34 (11.57)	75.50 (11.88)
Fasting glucose mmol/L	6.17 (1.91)	6.12 (1.88)	6.27 (1.97)	6.16 (1.89)	6.11 (1.87)	6.25 (1.94)
hsCRP mg/L	1.72 (1.77)	1.66 (1.71)	1.83 (1.87)	1.72 (1.77)	1.66 (1.71)	1.83 (1.87)
Sex						
Female	2504 (46.9)	1424 (41.6)	1080 (56.5)	2414 (47)	1375 (41.6)	1039 (56.7)
Male	2835 (53.1)	2003 (58.4)	832 (43.5)	2719 (53)	1927 (58.4)	792 (43.3)

Characteristic	Primary cohort			hsCRP-eligible cohort		
	Total (n = 5339) n (%)	No observed incident frailty (n = 3427) n (%)	Incident frailty (n = 1912) n (%)	Total (n = 5133) n (%)	No observed incident frailty (n = 3302) n (%)	Incident frailty (n = 1831) n (%)
Age group						
60–64	2198 (41.2)	1523 (44.4)	675 (35.3)	2122 (41.3)	1476 (44.7)	646 (35.3)
65–79	2838 (53.2)	1761 (51.4)	1077 (56.3)	2725 (53.1)	1691 (51.2)	1034 (56.5)
≥80	303 (5.7)	143 (4.2)	160 (8.4)	286 (5.6)	135 (4.1)	151 (8.2)
Educational level						
Illiterate	1754 (32.9)	958 (28)	796 (41.6)	1682 (32.8)	921 (27.9)	761 (41.6)
Primary school and below	2458 (46)	1604 (46.8)	854 (44.7)	2358 (45.9)	1537 (46.5)	821 (44.8)
Middle school and high school	814 (15.2)	621 (18.1)	193 (10.1)	784 (15.3)	604 (18.3)	180 (9.8)
Technical school and above	313 (5.9)	244 (7.1)	69 (3.6)	309 (6)	240 (7.3)	69 (3.8)
Marriage						
Currently unmarried	1022 (19.1)	586 (17.1)	436 (22.8)	980 (19.1)	561 (17)	419 (22.9)
Married	4317 (80.9)	2841 (82.9)	1476 (77.2)	4153 (80.9)	2741 (83)	1412 (77.1)
Residence						
Rural	3221 (60.3)	1942 (56.7)	1279 (66.9)	3088 (60.2)	1863 (56.4)	1225 (66.9)
Urban	2118 (39.7)	1485 (43.3)	633 (33.1)	2045 (39.8)	1439 (43.6)	606 (33.1)
Medical insurance						
NMI*	345 (6.5)	210 (6.1)	135 (7.1)	334 (6.5)	206 (6.2)	128 (7)
UEMI*	648 (12.1)	499 (14.6)	149 (7.8)	624 (12.2)	485 (14.7)	139 (7.6)
URMI*	213 (4)	141 (4.1)	72 (3.8)	205 (4)	134 (4.1)	71 (3.9)

Characteristic	Primary cohort			hsCRP-eligible cohort		
	Total (n = 5339) n (%)	No observed incident frailty (n = 3427) n (%)	Incident frailty (n = 1912) n (%)	Total (n = 5133) n (%)	No observed incident frailty (n = 3302) n (%)	Incident frailty (n = 1831) n (%)
URRMI*	68 (1.3)	47 (1.4)	21 (1.1)	60 (1.2)	43 (1.3)	17 (0.9)
NCMI*	3757 (70.4)	2314 (67.5)	1443 (75.5)	3606 (70.3)	2222 (67.3)	1384 (75.6)
Others	240 (4.5)	168 (4.9)	72 (3.8)	238 (4.6)	166 (5)	72 (3.9)
Multiple	68 (1.3)	48 (1.4)	20 (1)	66 (1.3)	46 (1.4)	20 (1.1)
Smoking						
Never	3015 (56.5)	1829 (53.4)	1186 (62)	2907 (56.6)	1770 (53.6)	1137 (62.1)
Current or former	2324 (43.5)	1598 (46.6)	726 (38)	2226 (43.4)	1532 (46.4)	694 (37.9)
Drinking						
Never	3583 (67.1)	2175 (63.5)	1408 (73.6)	3448 (67.2)	2099 (63.6)	1349 (73.7)
Current or former	1756 (32.9)	1252 (36.5)	504 (26.4)	1685 (32.8)	1203 (36.4)	482 (26.3)
Physical activity						
Insufficiently active	1089 (20.4)	678 (19.8)	411 (21.5)	1036 (20.2)	646 (19.6)	390 (21.3)
Sufficiently active	4250 (79.6)	2749 (80.2)	1501 (78.5)	4097 (79.8)	2656 (80.4)	1441 (78.7)
Adiposity						
Non-adiposity	1383 (25.9)	974 (28.4)	408 (21.3)	—	—	—
Adiposity	3956 (74.1)	2452 (71.6)	1504 (78.7)	—	—	—
Metabolic phenotypes						
MHNA*	879 (16.5)	639 (18.6)	240 (12.5)	—	—	—
MHA*	1401 (26.2)	889 (25.9)	512 (26.8)	—	—	—

Characteristic	Primary cohort			hsCRP-eligible cohort		
	Total (n = 5339) n (%)	No observed incident frailty (n = 3427) n (%)	Incident frailty (n = 1912) n (%)	Total (n = 5133) n (%)	No observed incident frailty (n = 3302) n (%)	Incident frailty (n = 1831) n (%)
MUNA*	504 (9.4)	335 (9.8)	168 (8.8)	—	—	—
MUA*	2555 (47.9)	1564 (45.6)	992 (51.9)	—	—	—
Sarcopenic phenotypes						
NSNA*	837 (15.7)	637 (18.6)	200 (10.5)	—	—	—
NSA*	2244 (42)	1553 (45.3)	691 (36.1)	—	—	—
PSNA*	546 (10.2)	338 (9.9)	208 (10.9)	—	—	—
PSA*	1713 (32.1)	900 (26.3)	813 (42.5)	—	—	—
Inflammatory phenotypes						
NINA*	—	—	—	1172 (22.8)	837 (25.4)	335 (18.3)
NIA*	—	—	—	3149 (61.3)	1976 (59.8)	1173 (64)
INA*	—	—	—	165 (3.2)	108 (3.3)	57 (3.1)
IA*	—	—	—	648 (12.6)	381 (11.5)	267 (14.6)

Characteristic	Primary cohort			hsCRP-eligible cohort		
	Total (n = 5339) n (%)	No observed incident frailty (n = 3427) n (%)	Incident frailty (n = 1912) n (%)	Total (n = 5133) n (%)	No observed incident frailty (n = 3302) n (%)	Incident frailty (n = 1831) n (%)
Non-medical insurance (NMI); Urban employee medical insurance (UEMI); Urban resident medical insurance (URMI); Urban and rural resident medical insurance (URRMI); New cooperative medical insurance (NCMI); Metabolically healthy non-adiposity (MHNA); Metabolically healthy adiposity (MHA); Metabolically unhealthy non-adiposity (MUNA); Metabolically unhealthy adiposity (MUA); Non-sarcopenic non-adiposity (NSNA); Non-sarcopenic adiposity (NSA); Possible sarcopenic non-adiposity (PSNA); Possible sarcopenic adiposity (PSA); Non-adiposity with hsCRP < 3 mg/L (NINA); Adiposity with hsCRP < 3 mg/L (NIA); Non-adiposity with hsCRP 3–<10 mg/L (INA); Adiposity with hsCRP 3–<10 mg/L (IA). Values are pooled summaries across 50 imputed datasets; counts and percentages are averaged across imputations before rounding. Primary cohort uses 5339 participants (3427 non-frail and 1912 frail) and hsCRP-eligible cohort independently uses 5133 participants (3302 non-frail and 1831 frail) with no missing inflammatory phenotype. Non-frail/frail refers to follow-up outcome, since all participants were non-frail at baseline. No observed incident frailty denotes no event before the last evaluable FI, not verified non-frailty in 2020. Inflammatory phenotype rows are intentionally blank in primary cohort; adiposity, metabolic and sarcopenic phenotype rows are intentionally blank in hsCRP-eligible cohort. Percentages use the corresponding panel and outcome-group denominator. Baseline significance tests are omitted. Continuous summaries are mean (SD), with FI and WHtR shown to three decimals.						

Across the 50 completed datasets, a mean of 3,956.40 participants (range 3,919–3,995; 74.10% of the 5,339-person primary cohort) met the operational adiposity definition. Of these, 1,738.84 (1,701–1,768) met only the WHtR criterion, corresponding to a mean of 43.95% of participants with adiposity and 32.57% of the primary cohort. WHtR was positive in 99.67% of those classified as having adiposity. The seven criterion intersections are reported in **Additional file 1**; these percentages describe the selected, unweighted analytic sample rather than population obesity prevalence.

The 393 baseline non-frail participants without follow-up FI were older than included participants (mean 71.0 versus 67.6 years) and had a higher mean baseline FI (0.145 versus 0.135). The descriptive comparison used 393 versus 5,339 participants for the general, metabolic and muscle-function frameworks, and 373 versus 5,133 for the hsCRP framework. Participation-weight eligibility was separately restricted to the common predictor-complete target described above (**Additional file 7**).

Baseline characteristics differed across adiposity phenotype groups. Participants with MUA, PSA, or IA tended to be older and were more often female, currently unmarried, or physically inactive than their corresponding reference groups. PSA also co-occurred with lower educational attainment and lower physical activity, while IA co-occurred with indicators of socioeconomic disadvantage (**Additional file 8**). These descriptive differences were not adjusted comparisons and should not be interpreted as independent phenotype effects.

The common sample with all three dimensions and required model variables available included 5,133 participants. Within its adiposity subset (mean 3,796.24; range 3,761–3,833), 213.96 participants (196–230) had MUA, PSA and IA concurrently, corresponding to a mean of 5.64% of this subset. The eight mutually

exclusive patterns, including participants negative for all three dimensions, are descriptive counts (**Additional file 1**).

(Table 1 **at the end of the document should be placed here.)**

Geographic descriptions are presented in **Additional file 9** as exploratory data displays. They were not used to make inferences about provincial differences because design-adjusted provincial uncertainty was not estimated.

3.2 Overall association between adiposity and incident frailty

After full adjustment and PH-robust model selection, overall adiposity was associated with incident frailty (HR 1.25, 95% CI 1.11–1.42, P < 0.001). (Fig. 2, Table 2; full table was presented in **Additional file 10**) The final model stratified by medical insurance. The grouped-time PH estimate was 1.25 (95% CI 1.11–1.42), and the stabilized-IPW estimate was 1.26 (95% CI 1.12–1.43). (**Additional file 11**, sensitivity analysis 13 and 14)

Table 2
Association of adiposity-related phenotypes with incident frailty among CHARLS cohorts: PH-robust Cox regression results.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
General or central adiposity	Adiposity model total	—	1912/5339	35407	54.00	—	—
	Non-adiposity	Reference	408 (397–426) / 1383 (1344–1420)	9349 (9078–9578)	43.65 (41.93–45.16)	1.00 (reference)	—
	Adiposity	Overall	1504 (1486–1515) / 3956 (3919–3995)	26058 (25829–26329)	57.71 (57.19–58.42)	1.25 (1.11–1.42)	< 0.001
Metabolic phenotype	Metabolic group model total	—	1912/5339	35407	54.00	—	—
	MHNA	Reference	240 (228–253) / 879 (852–911)	6007 (5807–6211)	39.94 (37.63–42.26)	1.00 (reference)	—
	MHA	Overall	512 (490–533) / 1401 (1358–1448)	9454 (9132–9732)	54.17 (52.25–56.56)	1.27 (1.08–1.50)	0.005
	MUNA	Overall	168 (155–184) / 504 (484–530)	3341 (3176–3511)	50.35 (45.53–54.30)	1.20 (0.95–1.53)	0.125
	MUA	Overall	992 (968–1021) / 2555	16604 (16315–16907)	59.73 (58.65–61.05)	1.40 (1.19–1.65)	< 0.001

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
			(2513–2607)				
Sarcopenic phenotype	Sarcopenic group model total	—	1912/5339	35407	54.00	—	—
	NSNA	Reference	200 (185–214) / 837 (808–874)	6115 (5914–6366)	32.74 (30.65–34.40)	1.00 (reference)	—
	NSA	2	691 (664–714) / 2244 (2196–2279)	15799 (15464–16074)	43.75 (42.15–44.95)	1.34 (0.98–1.84)	0.070
	NSA	4	691 (664–714) / 2244 (2196–2279)	15799 (15464–16074)	43.75 (42.15–44.95)	1.33 (1.10–1.60)	0.003
	NSA	7	691 (664–714) / 2244 (2196–2279)	15799 (15464–16074)	43.75 (42.15–44.95)	1.31 (1.06–1.63)	0.013
	NSA	9	691 (664–714) / 2244 (2196–2279)	15799 (15464–16074)	43.75 (42.15–44.95)	1.31 (0.99–1.72)	0.056
	PSNA	2	208 (194–219) / 546 (526–564)	3234 (3073–3366)	64.29 (61.06–67.56)	2.48 (1.76–3.51)	< 0.001
	PSNA	4	208 (194–219) / 546 (526–564)	3234 (3073–3366)	64.29 (61.06–67.56)	1.79 (1.43–2.23)	< 0.001

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
	PSNA	7	208 (194–219) / 546 (526–564)	3234 (3073–3366)	64.29 (61.06–67.56)	1.32 (0.97–1.81)	0.081
	PSNA	9	208 (194–219) / 546 (526–564)	3234 (3073–3366)	64.29 (61.06–67.56)	1.14 (0.77–1.70)	0.508
	PSA	2	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	2.44 (1.79–3.32)	< 0.001
	PSA	4	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	2.08 (1.73–2.51)	< 0.001
	PSA	7	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.80 (1.44–2.25)	< 0.001
	PSA	9	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.68 (1.27–2.24)	< 0.001
Inflammatory phenotype	Inflammatory group model total	—	1831/5133	34200	53.54	—	—
	NINA	Reference	335 (324–352) / 1172 (1140–1200)	8059 (7837–8241)	41.55 (40.02–44.15)	1.00 (reference)	—

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
	NIA	Overall	1173 (1150–1205) / 3149 (3111–3202)	21002 (20736–21435)	55.84 (54.77–57.02)	1.29 (1.13–1.48)	< 0.001
	INA	Overall	57 (46–65) / 165 (150–180)	1042 (943–1163)	54.38 (46.32–61.57)	1.36 (0.98–1.88)	0.065
	IA	Overall	267 (240–290) / 648 (599–683)	4097 (3739–4314)	65.13 (61.14–69.63)	1.46 (1.22–1.76)	< 0.001
Adiposity-restricted cohort							
Metabolic phenotype	Metabolic group model total	—	1504 (1486–1515) / 3956 (3919–3995)	26058 (25829–26329)	57.71 (57.19–58.42)	—	—
	MHA	Reference	512 (490–533) / 1401 (1358–1448)	9454 (9132–9732)	54.17 (52.25–56.56)	1.00 (reference)	—
	MUA	Overall	992 (968–1021) / 2555 (2513–2607)	16604 (16315–16907)	59.73 (58.65–61.05)	1.10 (0.98–1.25)	0.113

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
Sarcopenic phenotype	Sarcopenic group model total	—	1504 (1486–1515) / 3956 (3919–3995)	26058 (25829–26329)	57.71 (57.19–58.42)	—	—
	NSA	Reference	691 (664–714) / 2244 (2196–2279)	15799 (15464–16074)	43.75 (42.15–44.95)	1.00 (reference)	—
	PSA	2	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.85 (1.50–2.30)	< 0.001
	PSA	4	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.61 (1.41–1.82)	< 0.001
	PSA	7	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.41 (1.21–1.65)	< 0.001
	PSA	9	813 (791–842) / 1713 (1674–1755)	10259 (9980–10538)	79.22 (77.46–81.76)	1.32 (1.08–1.62)	0.006
Inflammatory phenotype	Inflammatory group model total	—	1440 (1422–1450) / 3796	25099 (24883–25356)	57.36 (56.81–57.98)	—	—

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Exposure	Level	Time at HR evaluation, years	Events / N mean (min-max) / mean (min-max)	Person-years mean (min-max)	Crude rate per 1000 person-years mean (min-max)	HR (95% CI)	P
Full cohort							
			(3761–3833)				
	NIA	Reference	1173 (1150–1205) / 3149 (3111–3202)	21002 (20736–21435)	55.84 (54.77–57.02)	1.00 (reference)	—
	IA	Overall	267 (240–290) / 648 (599–683)	4097 (3739–4314)	65.13 (61.14–69.63)	1.14 (0.98–1.33)	0.097

Outcome: risk of frailty. Fully adjusted estimates account for proportional-hazards violations using covariate stratification or exposure-by-log(1 + time) interactions. Time-specific estimates are shown when the exposure violated the proportional-hazards assumption. In extended Cox models, baseline phenotype indicators were interacted with log(1 + t) through survival::coxph() using tt=function(x,t,...) x*log1p(t), where t denotes current risk-set event time in years since baseline. Time-specific hazard ratios were calculated as HR(t) = exp{β + γlog(1 + t)}, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients.

Conventional Cox estimates before proportional-hazards-robust model adaptation are shown in **Additional file 12** as supporting results. Final PH-robust estimates for all phenotype frameworks, including cohort-specific participant counts, events, person-years, and crude incidence rates, are provided in Table 2. The subsequent sections describe the comparisons without ranking phenotype frameworks by HR magnitude.

Sensitivity analyses reassessed proportional-hazards violations within each analysis. Their model-selection diagnostics and estimates are reported in **Additional file 11**.

(Table 2 **at the end of the document should be placed here.)**

Table 3
Sensitivity analyses of possible sarcopenic adiposity and incident frailty.

Analysis, follow-up time	Full cohort PSA vs NSNA HR (95% CI)	Adiposity-restricted PSA vs NSA HR (95% CI)
Primary, 7 years	1.80 (1.44–2.25)	1.41 (1.21–1.65)
Primary, 9 years	1.68 (1.27–2.24)	1.32 (1.08–1.62)
Sensitivity analysis 1: two observed frailty assessment, 7 years	2.32 (1.74–3.08)	1.46 (1.21–1.75)
Sensitivity analysis 1: two observed frailty assessment, 9 years	2.01 (1.37–2.96)	1.27 (0.97–1.65)
Sensitivity analysis 2: selection on observed non-frailty in 2013, overall	1.89 (1.52–2.35)	1.48 (1.28–1.73)
Sensitivity analysis 3: three-level physical activity covariate assessment, 7 years	1.79 (1.43–2.24)	1.41 (1.20–1.64)
Sensitivity analysis 3: three-level physical activity covariate assessment, 9 years	1.67 (1.26–2.22)	1.32 (1.08–1.61)
Sensitivity analysis 4a: first observed prefrailty endpoint, overall	1.22 (0.99–1.51)	1.20 (1.01–1.43)
Sensitivity analysis 4b: first observed frailty endpoint, overall	2.09 (1.33–3.27)	1.82 (1.29–2.56)
Sensitivity analysis 5: excluding exposure-related items from frailty index, overall	1.82 (1.46–2.26)	1.50 (1.30–1.72)
Sensitivity analysis 6: complete case analysis, overall	1.78 (1.36–2.34)	1.22 (1.01–1.48)
Sensitivity analysis 7: common sample assessment, 7 years	1.79 (1.43–2.24)	1.40 (1.19–1.64)
Sensitivity analysis 7: common sample assessment, 9 years	1.65 (1.24–2.19)	1.30 (1.06–1.60)
Sensitivity analysis 9: alternative adiposity definition assessment by BMI, 7 years	1.62 (1.17–2.24)	–
Sensitivity analysis 9: alternative adiposity definition assessment by BMI, 9 years	1.46 (0.97–2.22)	–
Sensitivity analysis 9: alternative adiposity definition assessment by BMI, overall	–	1.44 (1.03–2.01)
Sensitivity analysis 9: alternative adiposity definition assessment by waist, 7 years	1.87 (1.53–2.27)	1.39 (1.14–1.70)
Sensitivity analysis 9: alternative adiposity definition assessment by waist, 9 years	1.79 (1.39–2.29)	1.27 (0.98–1.64)
Sensitivity analysis 9: alternative adiposity definition assessment by WHtR, 7 years	1.82 (1.45–2.27)	1.41 (1.21–1.65)

Analysis, follow-up time	Full cohort PSA vs NSNA HR (95% CI)	Adiposity-restricted PSA vs NSA HR (95% CI)
Sensitivity analysis 9: alternative adiposity definition assessment by WHtR, 9 years	1.70 (1.28–2.25)	1.33 (1.09–1.62)
Sensitivity analysis 10: excluding sarcopenic phenotype specific overlap FI items assessment, 7 years	1.95 (1.53–2.48)	–
Sensitivity analysis 10: excluding sarcopenic phenotype specific overlap FI items assessment, 9 years	1.91 (1.41–2.60)	–
Sensitivity analysis 10: excluding sarcopenic phenotype specific overlap FI items assessment, overall	–	1.53 (1.33–1.75)
Sensitivity analysis 11a: linear continuous baseline FI adjustment, 7 years	1.60 (1.28-2.00)	1.34 (1.15–1.57)
Sensitivity analysis 11a: linear continuous baseline FI adjustment, 9 years	1.54 (1.16–2.04)	1.28 (1.05–1.56)
Sensitivity analysis 11b: four-knot RCS continuous baseline FI adjustment, 7 years	1.60 (1.28-2.00)	1.34 (1.15–1.57)
Sensitivity analysis 11b: four-knot RCS continuous baseline FI adjustment, 9 years	1.54 (1.16–2.04)	1.28 (1.05–1.56)
Sensitivity analysis 12a: assessment with FI defined by at least 28 items of 34 harmonized items across five waves, 7 years	1.93 (1.49–2.50)	–
Sensitivity analysis 12a: assessment with FI defined by at least 28 items of 34 harmonized items across five waves, 9 years	1.96 (1.41–2.73)	–
Sensitivity analysis 12a: assessment with FI defined by at least 28 items of 34 harmonized items across five waves, overall	–	1.43 (1.25–1.65)
Sensitivity analysis 12b: assessment with FI defined by stricter conditions as at least 30 items of 34 harmonized items across five waves, overall	1.85 (1.49–2.29)	1.40 (1.21–1.61)
Sensitivity analysis 13: grouped-time proportional-hazards likelihood, overall	2.01 (1.68–2.41)	1.57 (1.39–1.77)
Sensitivity analysis 14: inverse-probability-weighted analyses of follow-up participation, 7 years	1.79 (1.43–2.25)	1.40 (1.19–1.65)
Sensitivity analysis 14: inverse-probability-weighted analyses of follow-up participation, 9 years	1.65 (1.24–2.20)	1.30 (1.06–1.61)
Cause-specific mortality sensitivity: midpoint, 7 years	1.78 (1.42–2.23)	1.38 (1.18–1.62)
Cause-specific mortality sensitivity: midpoint, 9 years	1.66 (1.25–2.21)	1.29 (1.06–1.58)
Cause-specific mortality sensitivity: lower bound, 7 years	1.79 (1.43–2.25)	1.39 (1.19–1.63)
Cause-specific mortality sensitivity: lower bound, 9 years	1.67 (1.26–2.23)	1.30 (1.07–1.59)

Analysis, follow-up time	Full cohort PSA vs NSNA HR (95% CI)	Adiposity-restricted PSA vs NSA HR (95% CI)
Cause-specific mortality sensitivity: upper bound, 7 years	1.78 (1.42–2.23)	1.38 (1.18–1.62)
Cause-specific mortality sensitivity: upper bound, 9 years	1.66 (1.24–2.21)	1.29 (1.06–1.59)
Fine-Gray mortality sensitivity: midpoint, 7 years (sHR)	1.78 (1.42–2.23)	1.36 (1.16–1.59)
Fine-Gray mortality sensitivity: midpoint, 9 years (sHR)	1.66 (1.24–2.22)	1.26 (1.03–1.55)
Fine-Gray mortality sensitivity: lower bound, 7 years (sHR)	1.78 (1.42–2.23)	1.36 (1.16–1.59)
Fine-Gray mortality sensitivity: lower bound, 9 years (sHR)	1.67 (1.25–2.22)	1.27 (1.03–1.55)
Fine-Gray mortality sensitivity: upper bound, 7 years (sHR)	1.78 (1.42–2.23)	1.35 (1.16–1.58)
Fine-Gray mortality sensitivity: upper bound, 9 years (sHR)	1.66 (1.24–2.22)	1.26 (1.03–1.54)

"–" indicates that the model did not report results in this time-point-specific format, rather than indicating no association or an inability to estimate the effect. Follow-up time is in years for time-specific HRs; Overall denotes a common coefficient in a Cox model. Time-specific hazard ratios were calculated as $HR(t) = \exp\{\beta + \gamma \log(1 + t)\}$, with confidence intervals incorporating the covariance between the main-effect and time-interaction coefficients. For analysis 11, spline knots correspond to the 5th, 35th, 65th and 95th percentiles in completed dataset 1 and remain fixed in all 50 imputations. Four-knot restricted cubic-spline FI models produced nearly identical estimates, with no clear evidence of FI nonlinearity in the full or adiposity-restricted cohort (joint Wald P = 0.472 and P = 0.576, respectively). HRs, sHRs, and confidence intervals are model estimates, pooled across imputations for MICE analyses. The complete tables are provided in **Additional files 11** and **19**.

3.3 Metabolic adiposity phenotypes and incident frailty

Compared with MHNA, MHA (HR 1.27, 95% CI 1.08–1.50, P = 0.005) and MUA (HR 1.40, 95% CI 1.19–1.65, P < 0.001) were associated with incident frailty, whereas MUNA was not clearly associated (HR 1.20, 95% CI 0.95–1.53, P = 0.125) (Table 2, Fig. 2).

Within the adiposity-restricted cohort, the MUA versus MHA estimate was 1.10 (95% CI 0.98–1.25, P = 0.113) (Table 2, Fig. 3). This imprecise estimate does not provide clear evidence that metabolic unhealthiness further differentiated frailty incidence among participants already classified as having adiposity.

With metabolic unhealthiness defined as ≥ 3 abnormalities, MHA and MUA versus MHNA had full-cohort HRs of 1.24 (95% CI 1.09–1.42) and 1.43 (1.23–1.66), respectively; MUNA had HR 1.34 (0.93–1.94). Within adiposity, MUA versus MHA had HR 1.15 (1.02–1.30, P = 0.027), compared with 1.10 (0.98–1.25, P = 0.113) under the primary definition. These results indicate definition sensitivity, not a formal difference between HRs (**Additional file 13**).

3.4 Sarcopenic adiposity phenotypes and incident frailty

In the full cohort, PSA versus NSNA had HRs of 2.44 (95% CI 1.79–3.32), 2.08 (1.73–2.51), 1.80 (1.44–2.25) and 1.68 (1.27–2.24) at 2, 4, 7 and 9 years, respectively. Within adiposity, PSA versus NSA had corresponding HRs of 1.82 (1.50–2.30), 1.61 (1.41–1.82), 1.41 (1.21–1.65) and 1.32 (1.08–1.62). PSNA versus NSNA attenuated from 2.48 (1.76–3.51) at 2 years to 1.14 (0.77–1.70) at 9 years (Table 2, **Additional file 10**).

With the PSA-specific FI, full-cohort PSA HRs were 1.95 (95% CI 1.53–2.48) at 7 years and 1.91 (1.41–2.60) at 9 years; the within-adiposity estimate was an overall HR of 1.53 (1.33–1.75). Linear baseline-FI adjustment with FI-by-log-time effects yielded full-cohort HRs of 1.60 (1.28–2.00) and 1.54 (1.16–2.04), and within-adiposity HRs of 1.34 (1.15–1.57) and 1.28 (1.05–1.56), at 7 and 9 years. Four-knot spline FI adjustment was concordant (nonlinearity P = 0.472 and 0.576). (Table 3, **Additional file 11**)

3.5 Inflammatory adiposity phenotypes and incident frailty

Compared with NINA, NIA (HR 1.29, 95% CI 1.13–1.48, P < 0.001) and IA (HR 1.46, 95% CI 1.22–1.76, P < 0.001) were associated with incident frailty; the INA estimate was imprecise (HR 1.36, 95% CI 0.98–1.88, P = 0.065). Within the adiposity-restricted cohort, IA versus NIA was not clearly associated (HR 1.14, 95% CI 0.98–1.33, P = 0.097).

3.6 Potential nonlinear relationships between adiposity-related variables and the risks of frailty

Restricted cubic spline analyses were exploratory. In the full cohort, BMI and chair-stand time retained evidence of nonlinearity after BH adjustment, whereas WHtR was nominally nonlinear before adjustment but not after BH correction (P = 0.044; q = 0.148) (Fig. 4, **Additional file 14**). Estimated minima were data-driven and should not be interpreted as clinical thresholds; complete multiplicity-adjusted results are reported in **Additional file 14**.

BMI and chair-stand duration showed nonlinearity after BH adjustment. WHtR was nominally nonlinear but did not meet the adjusted criterion. Bootstrap minimum estimates and conditional intervals are reported with their success rates in **Additional file 15** and **16**.

3.7 Subgroup and interaction analyses

No reported subgroup or multidimensional interaction contrast was statistically clear after the implemented BH adjustment. The minimum adjusted P across all full-cohort subgroup families was 0.415; the minimum within the sarcopenic family was 0.861. The restricted-cohort multidimensional-interaction minimum was 0.996. In the three-dimension model, the seven-year MUA×PSA interaction was 0.94 (95% CI 0.65–1.37), PSA×IA was 1.14 (0.49–2.61), and the three-way term was 0.79 (0.28–2.21). These time-specific contrasts had wide confidence intervals (**Additional file 17** and **18**).

3.8 Sensitivity analyses

Sensitivity analyses addressed outcome confirmation, early-event selection, physical activity, separate endpoints, FI construction, complete cases, phenotype sample comparability, alternative adiposity definitions, baseline FI, interval-observed outcomes and follow-up participation. (Table 3, **Additional file 11**)

For frailty confirmed at any two observed visits, with time assigned to the second positive visit, full-cohort PSA HRs were 2.32 (95% CI 1.74–3.08) at 7 years and 2.01 (95% CI 1.37–2.96) at 9 years. Restricting to participants with observed non-frailty in 2013, while retaining time since 2011, yielded HR 1.89 (1.52–2.35). The selection retained only observed non-frailty in 2013; follow-up time remained measured from 2011.

Among participants with baseline FI ≤ 0.10, the separate first-observed prefrailty estimate for PSA was imprecise in the full cohort (HR 1.22, 95% CI 0.99–1.51, P = 0.060) and modestly positive in the adiposity-restricted cohort (HR 1.20, 95% CI 1.01–1.43, P = 0.041). The corresponding first-observed frailty HRs were 2.09 (1.33–3.27, P = 0.001) and 1.82 (1.29–2.56, P < 0.001). The two endpoints could occur in the same participant. With the 34-item harmonized FI requiring at least 28 observed items, full-cohort PSA HRs were 1.93 (95% CI 1.49–2.50) at 7 years and 1.96 (95% CI 1.41–2.73) at 9 years; the within-adiposity overall HR was 1.43 (1.25–1.65). Requiring ≥ 30 items yielded overall HRs of 1.85 (1.49–2.29) in full cohort and 1.40 (1.21–1.61) in adiposity-restricted cohort.

The grouped-time model estimated an HR of 2.01 (95% CI 1.68–2.41) for PSA versus NSNA and 1.57 (1.39–1.77) for PSA versus NSA. Participation-weighted full-cohort PSA HRs were 1.79 (1.43–2.25) at 7 years and 1.65 (1.24–2.20) at 9 years. Median maximum absolute SMDs after weighting were 0.0019 (range 0.0012–0.0029) and 0.0022 (0.0012–0.0041) in the full and adiposity-restricted targets, respectively; every measured covariate was below 0.10 in all 50 imputations.

Under separate BMI, waist-circumference, and WHtR definitions, full-cohort PSA HRs at 7 years were 1.62, 1.87, and 1.82, respectively; the corresponding 9-year estimates were 1.46, 1.79, and 1.70. In the adiposity-restricted analyses, the BMI-based definition yielded an overall HR of 1.44 (95% CI 1.03–2.01). The waist-circumference-based estimates were 1.39 (1.14–1.70) at 7 years and 1.27 (0.98–1.64) at 9 years; the corresponding WHtR-based estimates were 1.41 (1.21–1.65) and 1.33 (1.09–1.62). In the full-cohort joint-dimension model, possible sarcopenia across both adiposity states had mutually adjusted HRs of 1.37 (95% CI 1.18–1.58, P < 0.001) at 7 years and 1.25 (1.04–1.51, P = 0.017) at 9 years. Within the adiposity-restricted cohort, the corresponding PSA versus NSA HRs were 1.40 (1.20–1.65, P < 0.001) and 1.31 (1.06–1.61, P = 0.011). The full joint-dimension results are reported in the joint-model appendix of **Additional file 11**.

3.9 Competing-risk analyses

Competing-risk analyses excluded one conflicting/unusable death record, leaving 5,338 participants, 1,911 frailty events, 536 competing deaths and 2,891 censored participants. Counts were stable across the three death-date assignments. Complete PSA estimates, model counts and death-date/event-ordering rules are reported in **Additional file 19**.

Under midpoint assignment in the full cohort, PSA cause-specific HRs were 1.78 (95% CI 1.42–2.23) at seven years and 1.66 (1.25–2.21) at nine years. Corresponding subdistribution HRs were 1.78 (1.42–2.23) and 1.66 (1.24–2.22).

4. Discussion

4.1 Principal findings

Among 5,339 baseline non-frail older adults, 1,912 incident frailty events occurred. Overall adiposity was associated with frailty, and possible-sarcopenia indicators further differentiated risk within adiposity. The PSA-versus-NSA association attenuated over follow-up but remained positive at 7 and 9 years, including linear and spline baseline-FI adjustment. The PSA-specific and harmonized FIs supported this pattern. The metabolic contrast within adiposity depended on its abnormality threshold, and the inflammatory contrast had greater uncertainty.

4.2 Heterogeneity of adiposity-related frailty risk

Longitudinal studies have linked BMI and waist circumference with frailty or prefrailty.[7, 10] A study of prevalent frailty also examined BMI and abdominal adiposity.[37] Mortality analyses in general populations and in frail older women address different outcomes from first incident frailty.[38, 39] Our use of general or central adiposity therefore extends the anthropometric definition, while the phenotype frameworks distinguish metabolic status, muscle function and a baseline inflammatory marker.

The three frameworks describe metabolic status, muscle function and a baseline inflammatory marker in the same cohort. Their distinct reference categories answer different questions; common-sample and joint-dimension analyses provide complementary comparisons.

Baseline phenotype classification preceded the recorded follow-up frailty wave, but this temporal ordering did not eliminate reverse causation. Early functional decline could simultaneously reduce grip strength, slow chair-stand performance, and increase baseline FI before frailty crossed the 0.25 threshold.

Our positive MHA association differs from the absence of accelerated FI progression for metabolically healthy overweight/obesity in the CHARLS/English Longitudinal Study of Ageing (ELSA) study by He et al.[11] That study included adults aged ≥ 50 years, used BMI-defined overweight/obesity and modelled change in a 32-item FI; ours included baseline non-frail adults aged ≥ 60 years, used BMI/WC/WHtR adiposity and modelled first FI ≥ 0.25. Although both primary metabolic definitions required ≥ 2 abnormalities, He et al. also used glycated haemoglobin (HbA1c) and lipid-lowering treatment criteria, which our classification did not include. These differences could contribute to the discrepancy, but were not tested in harmonized models. The MUA-versus-MHA contrast within adiposity was also sensitive to the ≥ 2 versus ≥ 3 threshold (Section 3.3). Evidence on metabolic-health transitions and cardiovascular events concerns a different endpoint; our exposures were classified only at baseline.[40]

IA and NIA were associated with frailty relative to NINA, while the within-adiposity IA-versus-NIA estimate was imprecise. Prior work links inflammation to ageing and frailty,[41–43] but this study's single hsCRP measurement could not establish a persistent inflammatory state.

4.3 Interpretation of possible sarcopenic adiposity

Yao et al. reported an association between sarcopenic obesity and frailty in a systematic review of adults aged ≥ 60 years.[14] Their studies used varied sarcopenia and obesity criteria and frailty instruments; the pooled odds ratio for sarcopenic obesity versus neither condition was 3.76 (95% CI 2.62–5.39). Our PSA definition used low grip strength or poor chair-stand performance without muscle-mass measurement, and our endpoint was first incident FI-defined frailty. These construct and estimand differences preclude directly

comparing the pooled odds ratio with our time-specific HRs. Our contribution is the longitudinal comparison of possible-sarcopenia indicators within operational adiposity.

The PSA-specific FI reduced overlap with six self-reported functional items. Its positive PSA association, together with the baseline-FI-adjusted results, supports examining muscle function within adiposity, while remaining shared content and early functional decline could contribute to the association.

Insulin resistance involves altered insulin action in skeletal muscle, liver and adipose tissue,[44] and prospective evidence has linked insulin resistance and inflammation with frailty.[13] In our cohort, baseline functional impairment, early disease processes, and shared functional content in exposure and outcome measures could also contribute to the observed associations.

4.4 Exploratory nonlinear associations

BMI and chair-stand duration showed evidence of nonlinearity after BH correction, whereas WHtR did not. The estimated minimum for restricted-cohort chair-stand duration at 9 years appeared in only 107 of 200 bootstrap resamples. Its conditional interval and the data-driven BMI minimum require external evaluation before any clinical threshold is considered.

4.5 Separate prefrailty and frailty endpoints

Studies of frailty-state transitions describe changes between states.[45] Our separate-endpoint models instead selected baseline FI ≤ 0.10 and allowed the same participant to reach first observed prefrailty and first observed frailty. The modest prefrailty estimate and larger frailty estimate therefore describe different first-observation endpoints; they do not identify direct transition intensities.

4.6 Interaction analyses

No interaction contrast was statistically clear after BH adjustment. Confidence intervals spanned interaction HRs below and above 1, and sparse phenotype combinations limited precision. These results leave effect modification unresolved (**Additional file 17** and **18**).

4.7 Implications for future research and clinical practice

The findings motivate studies of functional assessment alongside anthropometry in older adults with adiposity. External replication, formal tests of incremental prediction and intervention studies would clarify whether these associations can improve clinical decisions.

5. Limitations

Several limitations affect interpretation. The observational design, baseline functional impairment and shared content between muscle-function indicators and FI leave reverse causation and residual confounding possible. Broad age categories, especially 65–79 years, may leave age-related confounding. Safety-related non-tests and refusals remained missing and were imputed alongside other component missingness, so their informative nature may affect muscle-function classification. FI item availability varied across waves; harmonized-FI analyses address only part of that measurement difference. Baseline-FI models depend on their specified functional and time-varying forms, and the chosen log-time forms were not verified by residual

retesting. Events were interval-observed, and grouped-time analyses rely on proportional-effect and observation assumptions. Participation weights addressed having any follow-up FI, rather than subsequent dropout, intermittent missingness or mortality. Missingness was substantial; missing at random (MAR) remains an assumption, and ordinary MICE did not ensure compatibility with time-varying coefficients, splines or interactions. A single hsCRP measurement may misclassify inflammatory status. Models did not use survey weights or household/community design adjustment. Multiple testing, sparse interaction cells and conditional bootstrap intervals limit exploratory conclusions.

6. Conclusions

Adiposity and possible-sarcopenia indicators were associated with incident frailty. Within adiposity, the PSA association attenuated over time and remained positive after continuous baseline-FI adjustment. These findings support further evaluation of muscle function alongside anthropometry, with interpretation limited by shared functional content and the observational design.

Abbreviations

Body mass index (BMI); The China Health and Retirement Longitudinal Study (CHARLS); Waist circumference (WC); Waist-to-height ratio (WHtR); High density lipoprotein cholesterol (HDL-C); High-sensitivity C-reactive protein (hsCRP); Frailty index (FI); Metabolically healthy non-adiposity (MHNA); Metabolically healthy adiposity (MHA); Metabolically unhealthy non-adiposity (MUNA); Metabolically unhealthy adiposity (MUA); Non-sarcopenic non-adiposity (NSNA); Non-sarcopenic adiposity (NSA); Possible sarcopenic non-adiposity (PSNA); Possible sarcopenic adiposity (PSA); Non-adiposity with hsCRP <3 mg/L (NINA); Adiposity with hsCRP <3 mg/L (NIA); Non-adiposity with hsCRP 3–<10 mg/L (INA); Adiposity with hsCRP 3–<10 mg/L (IA); No medical insurance (NMI); Urban employee medical insurance (UEMI); Urban resident medical insurance (URMI); Urban and rural resident medical insurance (URRMI); New cooperative medical insurance (NCMI); Hazard ratio (HR); Confidence interval (CI); Restricted cubic spline (RCS); Multiple imputation by chained equations (MICE); Multiple imputation (MI); Proportional hazards (PH); Inverse probability weighting (IPW); Benjamini–Hochberg (BH); False discovery rate (FDR); Asian Working Group for Sarcopenia (AWGS); Adult Treatment Panel III (ATP III); International Physical Activity Questionnaire (IPAQ); Missing at random (MAR); Activities of daily living (ADL); Instrumental activities of daily living (IADL); Metabolic equivalent of task (MET); Blood pressure (BP); Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Fasting blood glucose (FBG); Triglycerides (TG); Standard deviation (SD); Standard error (SE); Standardized mean difference (SMD); Effective sample size (ESS); Predictive mean matching (PMM); Classification and regression trees (CART); Person-years (PY); Not estimable (NE); Subdistribution hazard ratio (sHR); Other medical insurance (OthersMI); English Longitudinal Study of Ageing (ELSA); Glycated haemoglobin (HbA1c); Chair-stand test (CST).

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The database supporting the conclusions of this article is available in the CHARLS repository, https://charls.charlsdata.com/pages/data/111/zh-cn.html.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

PQ was responsible for the primary data processing, statistical analyses, implementation of study details, and manuscript drafting. ZZ contributed to statistical analyses and code debugging. HQ was responsible for the statistical analysis of the complete-case data. JS and MG contributed to data processing and table formatting. MD conducted exploratory analyses. JM was responsible for study design and critical revision of the manuscript. All authors read and approved the final manuscript.

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Figures

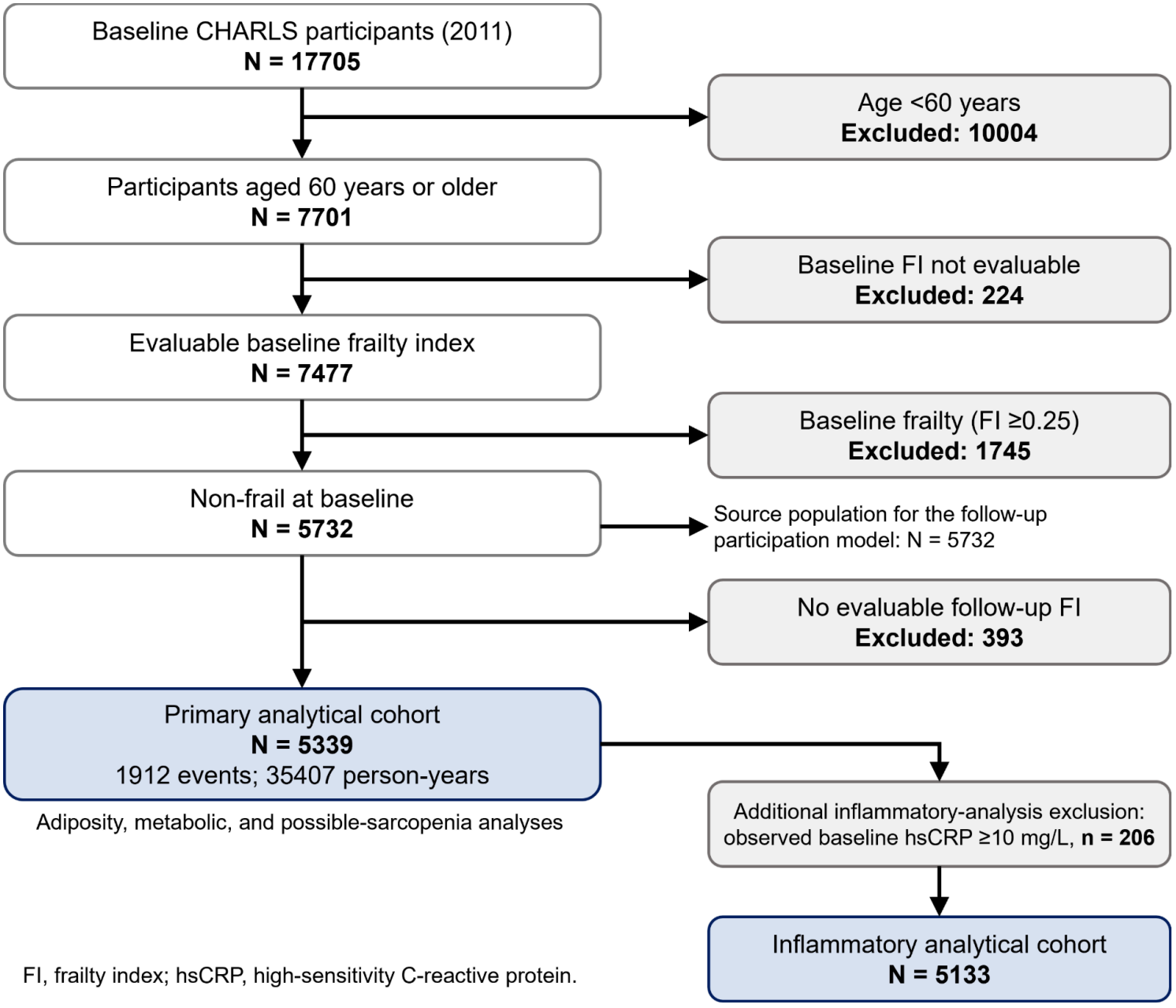

Figure 1

Flowchart of participant selection and analytical cohorts. The hsCRP exclusion flag was determined from observed baseline values before imputation. The 206 exclusions are those flagged participants who otherwise met primary-cohort eligibility. This count was fixed across all 50 completed datasets; participants with originally missing hsCRP were classified from their completed values. Metabolic, muscle-function and hsCRP phenotype labels denote separate analyses; participants may contribute to more than one framework. Their participant counts should not be added across frameworks.

Group	Events / N	HR (95% CI)
General or central adiposity	**1912/5339**	
*Adiposity vs Non-adiposity****	*1504/3956 (1486-1515/3919-3995)*	*1.25 (1.11-1.42)*
Metabolic phenotype	**1912/5339**	
*MHA vs MHNA***	*512/1401 (490-533/1358-1448)*	*1.27 (1.08-1.50)*
MUNA vs MHNA	*168/504 (155-184/484-530)*	*1.20 (0.95-1.53)*
*MUA vs MHNA****	*992/2555 (968-1021/2513-2607)*	*1.40 (1.19-1.65)*
Sarcopenic phenotype	**1912/5339**	
NSA vs NSNA, 2 years	*691/2244 (664-714/2196-2279)*	*1.34 (0.98-1.84)*
*NSA vs NSNA, 4 years***	*691/2244 (664-714/2196-2279)*	*1.33 (1.10-1.60)*
*NSA vs NSNA, 7 years**	*691/2244 (664-714/2196-2279)*	*1.31 (1.06-1.63)*
NSA vs NSNA, 9 years	*691/2244 (664-714/2196-2279)*	*1.31 (0.99-1.72)*
*PSNA vs NSNA, 2 years****	*208/546 (194-219/526-564)*	*2.48 (1.76-3.51)*
*PSNA vs NSNA, 4 years****	*208/546 (194-219/526-564)*	*1.79 (1.43-2.23)*
PSNA vs NSNA, 7 years	*208/546 (194-219/526-564)*	*1.32 (0.97-1.81)*
PSNA vs NSNA, 9 years	*208/546 (194-219/526-564)*	*1.14 (0.77-1.70)*
*PSA vs NSNA, 2 years****	*813/1713 (791-842/1674-1755)*	*2.44 (1.79-3.32)*
*PSA vs NSNA, 4 years****	*813/1713 (791-842/1674-1755)*	*2.08 (1.73-2.51)*
*PSA vs NSNA, 7 years****	*813/1713 (791-842/1674-1755)*	*1.80 (1.44-2.25)*
*PSA vs NSNA, 9 years****	*813/1713 (791-842/1674-1755)*	*1.68 (1.27-2.24)*
Inflammatory phenotype	**1831/5133**	
*NIA vs NINA****	*1173/3149 (1150-1205/3111-3202)*	*1.29 (1.13-1.48)*
INA vs NINA	*57/165 (46-65/150-180)*	*1.36 (0.98-1.88)*
*IA vs NINA****	*267/648 (240-290/599-683)*	*1.46 (1.22-1.76)*

PH-robust Cox; time-varying effects at 2, 4, 7 and 9 years.
Events/N: mean (min-max) across 50 imputations; exact if invariant.
****P<0.001, **P<0.01, *P<0.05*

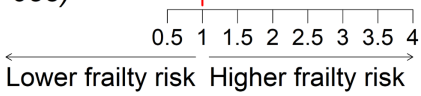

Figure 2

Associations of adiposity-related phenotypes with first incident frailty among 5,339 CHARLS participants after multiple imputation. Estimates are from fully adjusted PH-robust Cox models and time-specific HRs are shown when the exposure violated the proportional-hazards assumption. Model covariates and PH handling are defined in the statistical analysis section.

Group	Events / N	HR (95% CI)
Metabolic phenotype	**1504/3956 (1486-1515/3919-3995)**	
MUA vs MHA	*992/2555 (968-1021/2513-2607)*	*1.10 (0.98-1.25)*
Sarcopenic phenotype	**1504/3956 (1486-1515/3919-3995)**	
*PSA vs NSA, 2 years****	*813/1713 (791-842/1674-1755)*	*1.85 (1.50-2.30)*
*PSA vs NSA, 4 years****	*813/1713 (791-842/1674-1755)*	*1.61 (1.41-1.82)*
*PSA vs NSA, 7 years****	*813/1713 (791-842/1674-1755)*	*1.41 (1.21-1.65)*
*PSA vs NSA, 9 years***	*813/1713 (791-842/1674-1755)*	*1.32 (1.08-1.62)*
Inflammatory phenotype	**1440/3796 (1422-1450/3761-3833)**	
IA vs NIA	*267/648 (240-290/599-683)*	*1.14 (0.98-1.33)*

PH-robust Cox; time-varying effects at 2, 4, 7 and 9 years.
Events/N: mean (min-max) across 50 imputations; exact if invariant.
****P<0.001, **P<0.01, *P<0.05*

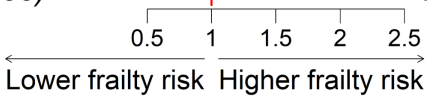

Figure 3

Associations of adiposity-related phenotypes with first incident frailty among adiposity-restricted CHARLS participants after multiple imputation. Estimates are from fully adjusted PH-robust Cox models and time-specific HRs are shown when the exposure violated the proportional-hazards assumption. Model covariates and PH handling are defined in the statistical analysis section.

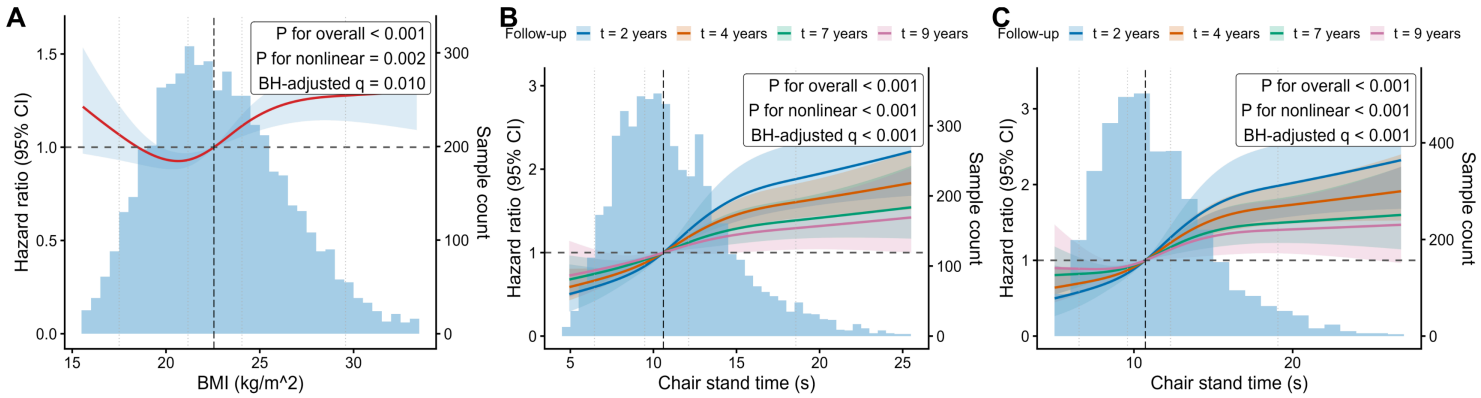

Figure 4

Restricted cubic spline associations of two continuous adiposity-related measures with first incident frailty. Panels A and B show the results from the full cohort, whereas Panel C shows the results from the adiposity-restricted cohort. Panels show (A) body mass index, (B) chair stand time in full cohort, and (C) chair stand time in adiposity-restricted cohort. Four knots were fixed across imputations at the medians of the imputation-specific 5th, 35th, 65th and 95th percentiles. The reference was the median of imputation-specific medians. Models used all eligible observations; display limits were the corresponding pooled 1st and 99th percentiles. Histograms show exposure distributions in completed dataset 1. Chair stand time is shown at 2, 4, 7, and 9 years because its spline basis violated the proportional-hazards assumption. Each panel reports the pooled overall P value, nonlinear P value and BH-adjusted q value for the nonlinear test. BH adjustment is applied separately within each cohort and test family before plotting. Estimated minima are explored only if both the nonlinear P value and its BH-adjusted q value are <0.05, and an interior slope reversal is identifiable. Reference-value and HR=1 lines are retained; bootstrap minimum estimates are reported in the supplementary captions.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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