Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Transitions between diabetes and frailty and their joint association with mortality in older Chinese adults: a five-state multi-state Markov analysis of the CHARLS cohort

Tianrui Cun

cuntianrui@cxtc.edu.cn

Chuxiong Normal University

Aidi Xu

Chuxiong City People's Hospital

Research Article

Keywords: diabetes mellitus, frailty, multi-state model, mortality, cohort studies, China

Posted Date: November 12th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11113516/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Transitions between diabetes and frailty and their joint association with mortality in older Chinese adults: a five-state multi-state Markov analysis of the CHARLS cohort

Tianrui Cun,[1,*] Aidi Xu,[2]

1 School of Computer and Intelligent Technology, Chuxiong Normal University, Chuxiong 675000, China;

2 First Department of Internal Medicine, Chuxiong City People's Hospital, Chuxiong 675000, China

* Corresponding author: Tianrui Cun. Email: cuntianrui@cxtc.edu.cn

Abstract

Background. Diabetes and frailty frequently co-occur in older adults, but their joint contribution to mortality, and the transitions between the two conditions, remain poorly characterised in Chinese populations.

Methods. We analysed five waves (2011–2020) of the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative cohort of community-dwelling adults aged ≥45 years (n = 16,658). A five-state Markov multi-state model (S0 neither condition; S1 diabetes only; S2 frailty only; S3 both; S4 death) was fitted to panel data with multiple imputation (m = 50). Death intensities were compared across states, additive interaction was quantified with the relative excess risk due to interaction (RERI), and transitions between the two conditions were summarised as transition intensity ratios (TIRs). Fifteen sensitivity analyses were pre-specified; two further analyses restricted the cohort to participants free of both conditions at baseline and reversed the assumed order of within-interval changes.

Results. Over nine years 2,417 participants (14.5%) died. Death intensity was highest with frailty alone (≈0.16 per person-year) versus neither condition (≈0.07); diabetes alone added little, and additive interaction was unclear (RERI −0.15, 95% CI −1.70 to 1.39). Both transition ratios were below 1 (TIR diabetes→frailty 0.22, 95% CI 0.18–0.29; TIR frailty→diabetes 0.65, 95% CI 0.49–

0.85). Restricting to the 14,061 participants free of both conditions at baseline left the first ratio essentially unchanged (0.248, 95% CI 0.191–0.305) but reduced the second to 0.099 (95% CI 0.056–0.141), indicating that this direction is shaped by the prevalent-case design.

Conclusions. Frailty carries the dominant mortality burden in this cohort and diabetes adds little beyond it, with no clear evidence of additive interaction. Transition ratios between the two conditions are not interpretable as causal acceleration; they describe associations conditional on the baseline state. Early frailty detection and shared risk-factor reduction should be prioritised.

Keywords: diabetes mellitus; frailty; multi-state model; mortality; cohort studies; China

Key points

• In 16,658 Chinese adults aged ≥45 years, prevalent diabetes was associated with a lower relative rate of new frailty (TIR 0.22), and frailty was associated with a lower relative rate of new diabetes (TIR 0.65).

• Co-occurring diabetes and frailty showed no clear evidence of additive mortality interaction (RERI = −0.15, 95% CI −1.70 to 1.39); the estimate changed sign across structural scenarios.

• The direction of the diabetes→frailty ratio was robust across 14 feasible sensitivity scenarios, including biochemical diabetes detection, diagnosis-year backfill, and inverse-probability-of-censoring weights; the frailty→diabetes direction was not robust.

Background

Diabetes and frailty are among the most common syndromes of ageing and frequently co-occur: diabetes is associated with accelerated sarcopenia and functional decline, while frailty predicts incident diabetes and worse glycaemic control [1-5]. Understanding whether diabetes promotes frailty—or whether clustering reflects shared risk factors, reverse causation, or survivor selection—is essential for prevention.

Most prior research treats diabetes and frailty as a static exposure–outcome pair, which cannot capture how the two conditions evolve jointly over time: a person may develop diabetes then frailty, frailty then diabetes, or both, and each state alters future transition risks. Multi-state models can disentangle these bidirectional dynamics while accounting for interval censoring and competing death.[6, 7] Applications to diabetes–frailty co-evolution remain scarce, especially in China where both burdens are rising fastest.

A second unresolved question is whether diabetes and frailty act synergistically on mortality. Additive interaction on the risk-difference scale, quantified by the relative excess risk due to interaction (RERI), indicates whether integrated management could yield disproportionate survival gains.[8] Using five waves of CHARLS data (2011–2020), we fitted a five-state Markov multi-state model with three aims: (i) to estimate bidirectional transition intensity ratios; (ii) to evaluate the additive mortality interaction of co-occurring diabetes and frailty; and (iii) to assess robustness through pre-specified sensitivity analyses that separate structural modelling assumptions from secondary robustness checks.

Methods

Study design and population

CHARLS is a nationally representative cohort of community-dwelling adults aged ≥45 years in China, with baseline (2011) and follow-up waves in 2013, 2015, 2018, and 2020 [9]. We included respondents with valid baseline diabetes and frailty data and at least one follow-up observation. The analytic cohort comprised 16,658 participants (Figure 1A).

Diabetes ascertainment

Diabetes was defined as cumulative ever-diagnosed diabetes: self-reported physician diagnosis, current treatment with insulin or oral hypoglycaemic agents, or prior ever-diabetes flag, carried forward. In sensitivity analyses we incorporated HbA1c ≥ 6.5% or fasting glucose ≥ 126 mg/dL (2011/2015) per ADA criteria[10] for undiagnosed diabetes (S6), backfilled diagnosis year from the 2018 question (S7), and restricted diabetes to self-reported cases in 2011–2015 (S5).

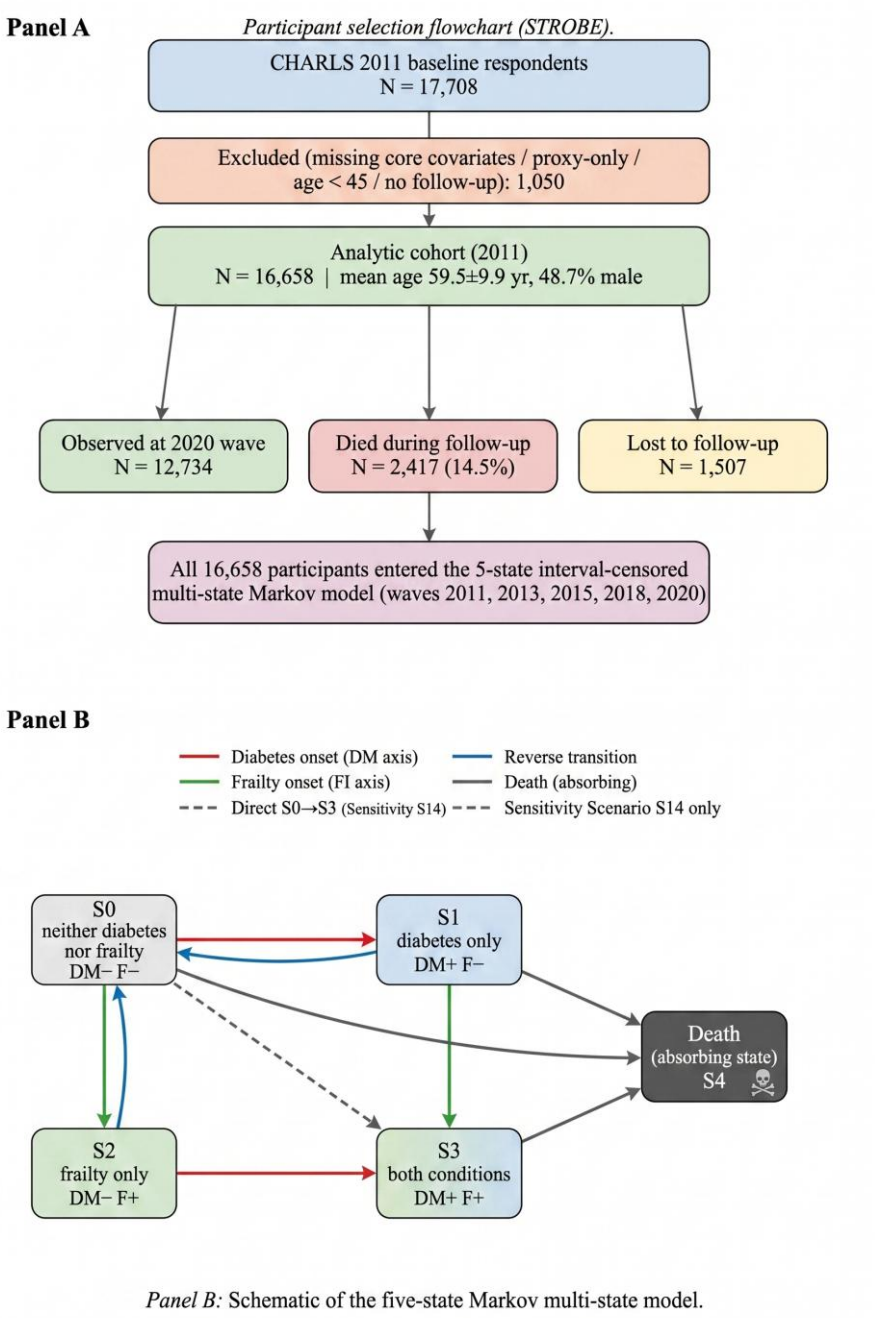
Frailty ascertainment

Frailty was measured with a 30-item Rockwood deficit accumulation frailty index (FI) [11], in contrast to the physical frailty phenotype [12]. The FI comprised 13 chronic conditions (excluding diabetes), 11 ADL and IADL items, self-rated health, pain, sleep, falls, fracture, and multi-site pain. A participant was frail if FI $\geq$ 0.25. We also evaluated FI thresholds of 0.20 and 0.30 (S1) and a 19-item FI without ADL/IADL items (S2).

Multi-state model

We specified a five-state Markov multi-state model (Figure 1B): S0, neither; S1, diabetes only; S2, frailty only; S3, both; S4, death. Allowable transitions followed Figure 1B. When both diabetes and frailty changed between waves, we split the interval at its midpoint and assumed diabetes changed first, consistent with its clinical irreversibility. Death was absorbing. For each allowed transition we discretised the within-wave interval at its midpoint and fitted a transition-specific Cox model via pyMSM (version 0.1.7).[13] We selected the Markov specification as primary because it yielded stable, interpretable transition-intensity ratios across all 50 imputations; the semi-Markov sensitivity (S10), modelling sojourn-time dependence, gave directionally consistent estimates, supporting this choice.

Because diabetes and frailty were already ascertained at baseline, the cohort is a prevalent-case cohort; we modelled transition intensities conditional on the baseline state without left-truncation at onset, so estimates describe associations within the observed population rather than incidence from a disease-free origin. Deaths were identified from respondent or proxy interviews in the CHARLS mortality module and assigned to the interval between the last live wave and the wave at which death was reported. All seven covariates were treated as time-constant baseline characteristics and were not updated across waves.



Panel B: Schematic of the five-state Markov multi-state model.

Figure 1. Study design and five-state multi-state model structure.

Panel A: participant selection flowchart (STROBE). Panel B: schematic of the five-state Markov multi-state model. S0 = neither diabetes nor frailty; S1 = diabetes only; S2 = frailty only; S3 = both conditions; S4 = death (absorbing state). Arrows indicate the ten allowable transitions; the dashed arrow denotes the direct S0→S3 transition permitted only in sensitivity scenario S14.

Covariates and statistical analysis

All transition models adjusted for age, sex, education (four levels), urban residence, BMI, smoking status, and alcohol consumption. We report transition intensity ratios (TIRs) evaluated at t = 5 years: TIR(DM→F) = q(S1→S3) / q(S0→S2); TIR(F→DM) = q(S2→S3) / q(S0→S1). Additive mortality interaction on the rate scale was quantified by the relative excess risk due to interaction, RERI = (h11 − h10 − h01 + h00)/h00, where h00, h10, h01, and h11 are the death transition intensities (per person-year) from S0, S1, S2, and S3; on the absolute intensity scale the additive hazard interaction was AHI = h11 − h10 − h01 + h00 (the numerator of RERI).[8] RERI and AHI were computed within each of the 50 imputations and then pooled with Rubin's rules; because AHI is a linear contrast of the four death intensities, pooling it per imputation is algebraically equivalent to forming it from the pooled intensities, whereas the ratio-form RERI was likewise pooled per imputation (the alternative of computing the ratio from the already-pooled intensities gives a similar, also non-significant, point estimate of -0.21). The full baseline transition-intensity matrix is reported in Supplementary Table S3 [see Additional file 1]. Missing data were multiply imputed (m = 50) using miceforest (version 6.0.5, LightGBM 4.5.0) and pooled with Rubin rules, inflating between-imputation variance by (1 + 1/m) for derived quantities; the imputation model used LightGBM with num_leaves = 8, max_depth = 3, min_data_in_leaf = 100 and two-fold lag/lead mean matching across the five waves, and trace plots indicated convergence by 10 iterations (Supplementary Figure S2).[14, 15, 16] We followed guidance on the potential and pitfalls of multiple imputation in epidemiological research.[16] All analyses were conducted by the authors; no generative artificial intelligence tool was used to generate, analyse or interpret the data.

Sensitivity and robustness analyses

We pre-specified 15 sensitivity analyses addressing FI thresholds (S1), FI composition (S2), baseline exclusions (S3–S4), diabetes ascertainment (S5–S9), semi-Markov duration (S10), complete-case frailty index (S11), chronic disease count (S13), alternative Q-matrix allowing direct S0→S3 transitions (S14), and inverse-probability-of-censoring weights (S15). The frailty index was treated as valid (fi_valid_imp = 1) only at live interviews at which it was assessed and was set to 0 for all death-status records, because the FI is not measured after death (Supplementary Table S6, Panel C). S11

(survivor-only, deaths excluded) therefore repeats the model after excluding every participant who ever lacked a valid FI — which in this cohort is equivalent to excluding all deaths — so S11 is effectively a survivor-only analysis. Death-transition hazards and the mortality interaction are consequently not estimable in S11 and are not reported; S11 thus probes whether the survivor/complete-case restriction biases the FI-defined transition intensities (S0→S2, S0→S1, S1→S3, S2→S3). Full details, full results, and the STROBE checklist are provided in the Supplementary Material.

Results

Baseline characteristics

The analytic cohort included 16,658 participants (mean age 59.5 years, SD 9.9; 48.7% male). At baseline, 5.7% had diabetes, 11.2% were frail, and 1.4% had both conditions (Table 1).

Table 1. Baseline characteristics of the analytic cohort (CHARLS 2011, N = 16,658).

Characteristic	Value
Age, years, mean ± SD	59.5 ± 9.9
Male sex, n (%)	8,112 (48.7%)*
Urban residence, n (%)	3,565 (21.4%)
Body-mass index, kg/m², mean ± SD	22.9 ± 3.6
Current smoker, n (%)	6,697 (40.2%)*
Current drinker, n (%)	5,547 (33.3%)*
Diabetes (cumulative ever-DM), n (%)	950 (5.7%)
Frailty (Rockwood FI ≥ 0.25), n (%)	1,866 (11.2%)
Education	
Primary or less	42.1%
Middle school	22.3%
High school	22.2%
College or above	13.4%

*Note. SD = standard deviation; FI = frailty index; DM = diabetes mellitus. *Percentages and counts are marginal distributions from imputation 0; all analytical estimates were pooled across the 50 imputations with Rubin's rules and differed by <1% across imputations. Education levels are 1 = primary or less, 2 = middle school, 3 = high school, 4 = college or above.*

State distribution over time

The proportion classified as having neither condition declined from 84.5% in 2011 to 70.9% in 2020, while diabetes-only, frailty-only, and both-conditions categories all increased (Figure 2). A total of 2,417 participants (14.5%) died during follow-up.

Figure S1. Distribution of the four live states across five CHARLS waves (2011–2020).

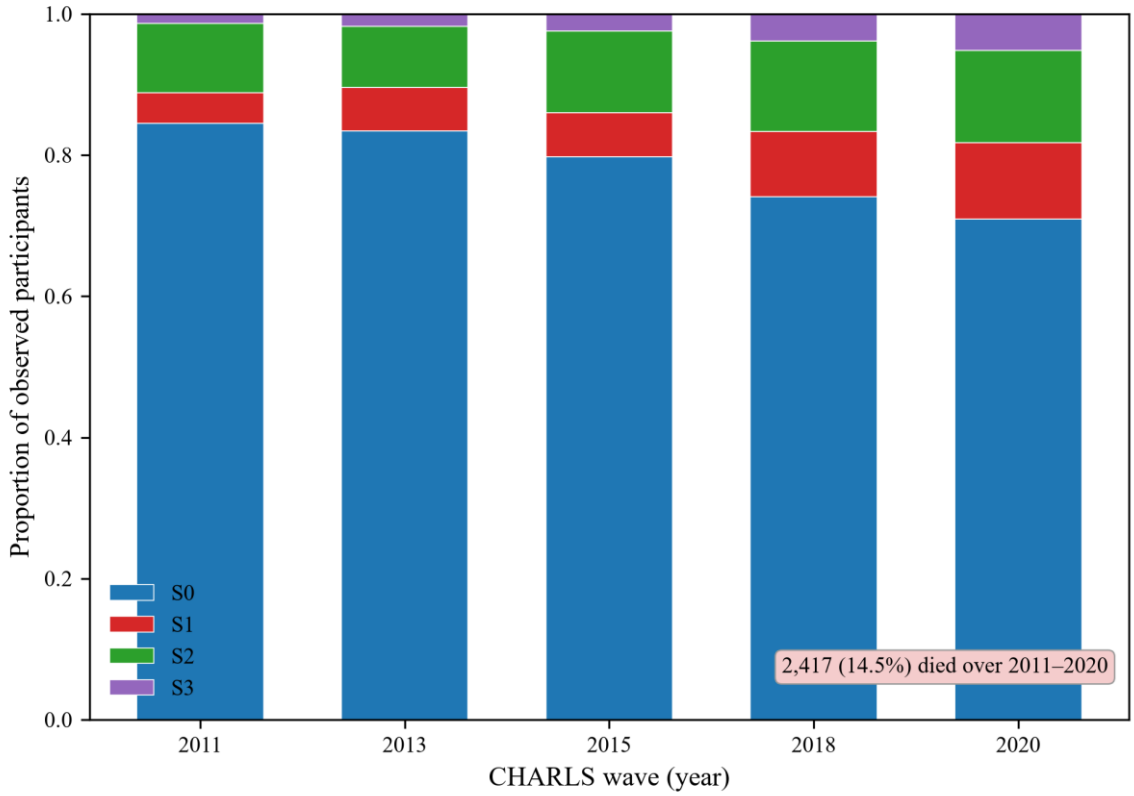


Figure 2. Distribution of the four live states across five waves.

S0 = neither; S1 = diabetes only; S2 = frailty only; S3 = both. States are shown for the five CHARLS waves (2011–2020) conditional on being observed alive at each wave. A total of 2,417 participants (14.5%) died over the follow-up period.

Main model: joint mortality effect and transition intensities

Death intensity differed markedly across states. Frailty alone carried the highest death intensity (h01 ≈ 0.16 per person-year) versus neither condition (h00 ≈ 0.07), whereas the 'both' state was not higher than frailty alone (h11 ≈ 0.09) and diabetes alone added little; there was no clear evidence of additive mortality interaction (RERI = -0.15, 95% CI -1.70 to 1.39; additive hazard interaction AHI = -0.01, 95% CI -0.12 to 0.09 deaths/person-year). Transition intensity ratios were below 1 in both directions: frailty onset among participants with diabetes (evaluated at 5 years) was substantially lower than among those without (TIR DM→F = 0.225, 95% CI 0.176–0.287), and diabetes onset among participants with frailty was also lower (TIR F→DM = 0.649, 95% CI 0.495–0.852). The

complete transition-intensity matrix is in Supplementary Table S3; Figure 3 shows predicted state-occupation probabilities for a representative 60-year-old free of both conditions at baseline. A TIR below 1 indicates a lower intensity in the index state; a RERI below 0 indicates a subadditive joint mortality effect.

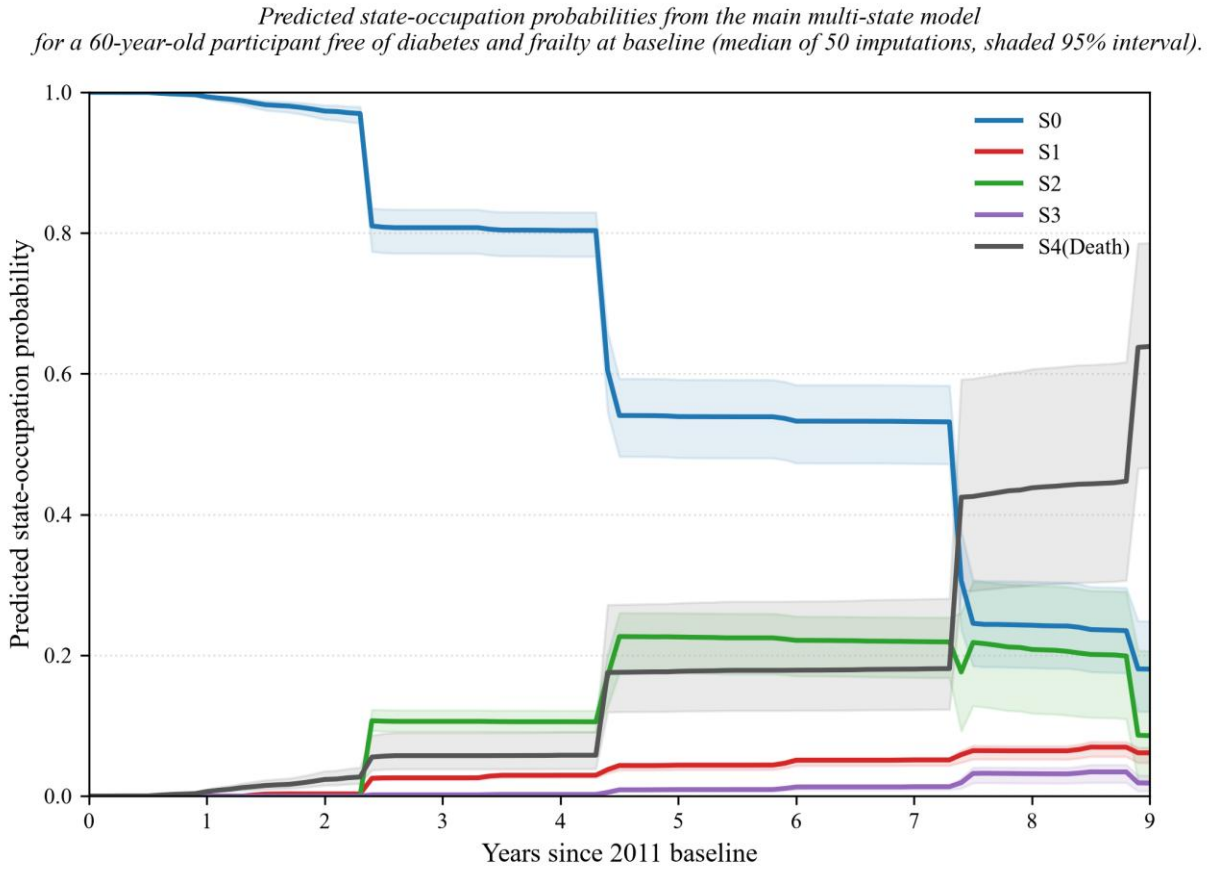


Figure 3. Predicted state-occupation probabilities from the main model.

Predictions are for a 60-year-old participant free of diabetes and frailty at baseline, evaluated with a rural, never-smoker/never-drinker profile and junior-high education (median of 50 imputations; shaded bands show 95% between-imputation intervals). S0 = neither; S1 = diabetes only; S2 = frailty only; S3 = both; S4 = death.

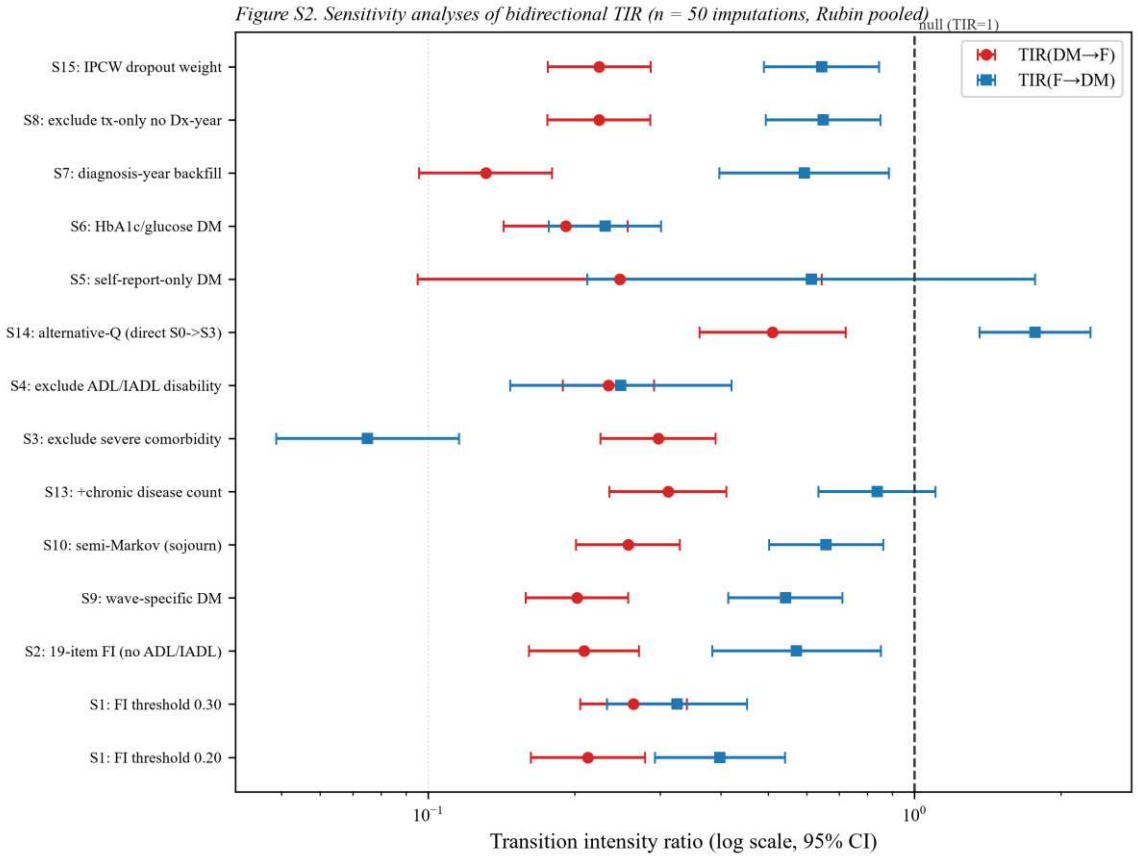


Figure 4. Sensitivity analyses for the two transition intensity ratios.

Forest plot. The 14 plotted points represent 13 estimable sensitivity analyses: S1 is shown at two frailty-index thresholds (0.20 and 0.30), S12 was infeasible, and S11 is omitted because its mortality interaction is not estimable. Red circles: TIR(DM→F); blue squares: TIR(F→DM). Bars show 95% confidence intervals; the vertical dashed line is the null value of 1.0.

Sensitivity analyses

The finding that diabetes is not associated with accelerated frailty onset (TIR DM→F < 1) was robust across all 14 feasible scenarios (point estimates 0.131–0.511; Figure 4, Table S1). The mortality interaction was not robust: the RERI changed sign across structural scenarios, consistent with no clear evidence of additive interaction. TIR F→DM was more sensitive: it fell to 0.233 with biochemical detection (S6), reflecting reclassification of undiagnosed diabetes, and rose to 1.784 under an alternative Q-matrix allowing direct S0→S3 transitions (S14), so the frailty→diabetes

direction was not robust. The IPCW analysis (S15) was essentially identical to the main model. In age-restricted subgroups the mortality pattern was preserved: death intensity was highest with frailty alone in every subgroup, and the additive interaction crossed zero in all of them (Supplementary Table S5). Among the 4,614 participants aged ≥ 65 years at baseline, death intensity with frailty alone was 0.63 per person-year versus 0.21 with neither condition, a ratio of 3.1 compared with 2.2 in the full cohort. The diabetes→frailty ratio, by contrast, became progressively smaller with advancing age — 0.225 in the full cohort, 0.050 (95% CI 0.019–0.082) at age ≥ 60 years and 0.006 (95% CI 0.003–0.009) at age ≥ 65 years — a gradient consistent with intensifying survivor selection rather than with a protective effect of diabetes.

Two further analyses targeted the structural assumptions (Table 2). Restricting the cohort to the 14,061 participants free of both conditions at baseline left the diabetes→frailty ratio unchanged (TIR 0.248, 95% CI 0.191–0.305), whereas the frailty→diabetes ratio fell to 0.099 (95% CI 0.056–0.141), indicating that this direction is shaped by the prevalent-case design. Reversing the assumed order of within-interval changes (frailty first) left both ratios materially unchanged (TIR DM→F 0.285, 95% CI 0.177–0.393; TIR F→DM 0.592, 95% CI 0.438–0.747), so the midpoint-split convention is not driving the estimates; the larger shift under an alternative transition matrix (S14) reflects the added direct S0→S3 pathway. Transitions are observed only at survey waves, so intensities are interpretable only over windows containing a wave (t = 5 and t = 8).

Table 2. Sensitivity of transition intensity ratios and mortality interaction to two structural assumptions

Analysis	Participants	Imputations	TIR diabetes→frailty	TIR frailty→diabetes	RERI (95% CI)
Main model (prevalent cohort)	16,658	50	0.22 (0.18–0.29)	0.65 (0.49–0.85)	−0.15 (−1.70 to 1.39)
Incident cohort (free of both conditions at baseline)	14,061	14	0.25 (0.19–0.31)	0.10 (0.06–0.14)	0.28 (−0.35 to 0.90)
Reversed within-interval order (frailty first)	16,658	12	0.29 (0.18–0.39)	0.59 (0.44–0.75)	−0.01 (−0.13 to 0.10)

Note. Values are point estimates with 95% confidence intervals at t = 5 years and the reference covariate profile. TIR = transition intensity ratio; RERI = relative excess risk due to interaction. Confidence intervals for the two supplementary

analyses were obtained by Rubin's rules over the completed imputations available for that scenario (m = 14 and m = 12 respectively), which is fewer than for the main analysis (m = 50).

Discussion

The dominant finding in this nationally representative cohort concerns mortality, not transitions. Death intensity was more than twice as high in the frailty-only state as in the state with neither condition, diabetes alone added little, and co-occurrence conferred no detectable additive interaction (RERI = -0.15, 95% CI -1.70 to 1.39); the point estimate was negative but the interval was wide and included both subadditive and superadditive effects. Transition intensity ratios were below 1 in both directions, but these estimates proved sensitive to structural assumptions and are most plausibly explained by survivor selection rather than by any protective effect.

The TIR(DM→F) of 0.22 is most plausibly explained by survivor selection: people who have diabetes and survive to the next wave are a relatively healthier subset, so their observed rate of new frailty is lower. Supporting this, backfilling diagnosis year (S7) lowered TIR(DM→F) further and excluding severe baseline comorbidity (S3) raised it. The semi-Markov analysis (S10) raised it to 0.26—still below 1—suggesting some of the pattern reflects state duration. Consistent with increasing selection in older age, the signal strengthened in age-restricted subgroups (TIR(DM→F) 0.05 at ≥60 and 0.01 at ≥65 years), while the RERI became non-significant in those subgroups (Supplementary Table S5).

The F→DM direction was sensitive to diabetes ascertainment: incorporating HbA1c and fasting glucose (S6) lowered TIR(F→DM) to 0.233 because many frail participants with undiagnosed diabetes were reclassified as already diabetic earlier, indicating that the frailty-to-diabetes association under self-report was, if anything, modestly inflated by under-ascertainment among frail participants.

We found no clear evidence that diabetes and frailty act synergistically on mortality: the additive interaction was not statistically significant and its direction was unstable across specifications (RERI = -0.15, 95% CI -1.70 to 1.39). In the intensity matrix (Supplementary Table S3), frailty alone carried by far the highest death intensity ($h01 \approx 0.16$ per person-year) compared with neither condition ($h00 \approx 0.07$), whereas the 'both' state had a lower death intensity ($h11 \approx 0.09$) than frailty alone. We interpret

the negative point estimate cautiously: the S3 (both) state at any wave is a small, survivor-selected subgroup observed alive with both conditions, and the frailty index partially overlaps disability and terminal-decline items, so the apparent 'protection' of adding diabetes to frailty is most plausibly an artefact of selection and deficit-index circularity rather than a true biological effect. The clinically salient signal is therefore the dominant mortality burden of frailty itself.

Strengths include five waves spanning nearly a decade, a large representative sample, explicit modelling of bidirectional transitions and competing mortality, 50 MICE imputations, and 15 sensitivity analyses. We also corrected a common pitfall in CHARLS 2018: the incremental diabetes diagnosis-year question can misclassify long-standing cases as newly incident unless the diagnosis year is backfilled. Limitations include reliance on self-report and proxy interviews for most diabetes and frailty items, biochemical confirmation only in 2011 and 2015, the Markov assumption, and limited generalisability to younger adults or institutionalised populations. Because diabetes and frailty were already present at baseline, the cohort is a prevalent-case cohort and estimates describe associations conditional on the baseline state rather than incidence from a disease-free origin. The TIRs are relative intensities at a fixed covariate profile and should not be interpreted as causal effects without stronger assumptions. All covariates were measured at baseline and held constant; because body mass index, smoking and alcohol use can change materially over nine years, residual and time-varying confounding cannot be excluded.

Implications for public health practice and research. Two aspects of these findings are actionable at the population level. First, risk stratification in middle-aged and older adults should not be organised around glycaemic status alone: in this cohort the diabetes-only state carried a death intensity close to that of the state with neither condition, whereas frailty alone more than doubled it, so a diabetes-centred register would direct attention away from most of the excess mortality risk. Second, frailty can be operationalised as a deficit-accumulation index from items that population surveys and routine primary-care assessments already collect, so adding it to periodic health assessment for older adults is feasible at low marginal cost rather than requiring new measurement infrastructure. For research, our results argue against using transitions between diagnosed diabetes

and frailty as an intervention target or surrogate endpoint: the corresponding intensity ratios moved substantially with ascertainment and design assumptions, whereas the ordering of death intensities across states was stable in every scenario we examined. Evaluations of integrated chronic disease management in ageing populations should therefore be designed around mortality and functional outcomes rather than around transitions in comorbidity status.

Conclusions

Frailty carries the dominant mortality burden in this cohort, diabetes adds little beyond it, and their co-occurrence shows no clear evidence of additive mortality interaction. Transition intensity ratios between diabetes and frailty were below 1 in both directions, but they were sensitive to structural assumptions and most plausibly reflect survivor selection, so they should not be interpreted as evidence that neither condition accelerates the other. Prevention strategies should prioritise early frailty detection and shared risk-factor reduction.

List of abbreviations

ADL: activities of daily living

AHI: additive hazard interaction

BMI: body-mass index

CHARLS: China Health and Retirement Longitudinal Study

CI: confidence interval

DM: diabetes mellitus

FI: frailty index

HbA1c: glycated haemoglobin

IADL: instrumental activities of daily living

IPCW: inverse probability of censoring weighting

MICE: multiple imputation by chained equations

RERI: relative excess risk due to interaction

SD: standard deviation

STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

TIR: transition intensity ratio

S0–S4: states of the multi-state model (S0, neither diabetes nor frailty; S1, diabetes only; S2, frailty only; S3, both conditions; S4, death)

Declarations

Ethics approval and consent to participate. CHARLS was approved by the Biomedical Ethics Review Committee of Peking University (approval number IRB00001052-11015); all participants provided informed consent. This secondary analysis used de-identified public-use data.

Clinical trial number: not applicable.

Consent for publication. Not applicable.

Availability of data and materials. The datasets analysed during the current study are available in the CHARLS repository, https://charls.pku.edu.cn/. Analysis code and sensitivity outputs are available from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests.

Funding. The authors declare that no external funding or financial support was received for this research; this work was self-funded by the authors without grant support.

Authors' contributions. TC conceived the study, designed the multi-state modelling strategy, curated the CHARLS data, performed the statistical analyses including multiple imputation and all sensitivity scenarios, prepared the figures, and drafted the manuscript. AX contributed clinical and geriatric interpretation of the findings, critically revised the manuscript for important intellectual

content, and contributed to the discussion of clinical implications. Both authors reviewed and approved the final manuscript. TC is the guarantor and takes responsibility for the integrity of the work as a whole.

Acknowledgements. The authors thank the CHARLS research team and all study participants. This analysis uses CHARLS public-use data.

Reporting guidelines. This study was reported in accordance with the STROBE statement.[17] [see Additional file 1]

Declaration of generative AI and AI-assisted technologies in the writing process. During the preparation of this work the authors used WorkBuddy (an AI-assisted writing assistant developed by Tencent, China) for language editing, for reorganising and condensing text drafted by the authors, and for preparing the cover letter and the point-by-point response to reviewers. The tool was not used to generate or analyse data, to produce any scientific content, interpretation or conclusion, or to create figures; all analyses were performed by the authors using the software described in the Methods section. The authors reviewed and edited all AI-assisted output and take full responsibility for the content of the published article.

Additional files

File name: Additional file 1

File format: .docx (Microsoft Word).

Title of data: Supplementary material — Transitions between diabetes and frailty and their joint association with mortality in older Chinese adults.

Description of data: Supplementary Methods describing the pre-specified sensitivity analysis scenarios; Figure S2, convergence diagnostics for the multiple imputation algorithm; Tables S1–S6 (baseline characteristics by baseline state, covariate hazard ratios across the ten transitions, full results of the sensitivity analyses, age-subgroup analyses, and multiple imputation diagnostics); and the completed STROBE checklist.

References

1. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.

2. O'Caoimh R, Sezgin D, O'Donovan MR, et al. Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies. Age Ageing. 2021;50(1):96-104.

3. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-762.

4. Sinclair AJ, Abdelhafiz AH, Rodríguez-Mañas L. Frailty and sarcopenia — newly emerging and long standing complications of diabetes in older people. Diabetes Res Clin Pract. 2017;130:111-117.

5. Vermeiren S, Vella-Azzopardi R, Beckwée D, et al. Frailty and the prediction of negative health outcomes: a meta-analysis. J Am Med Dir Assoc. 2016;17(12):1163.e1-1163.e17.

6. Jackson CH. Multi-state models for panel data: the msm package for R. J Stat Softw. 2011;38(8):1-29.

7. Putter H, Fiocco M, Geskus RB. Tutorial in biostatistics: competing risks and multi-state models. Stat Med. 2007;26(11):2389-2430.

8. VanderWeele TJ. On the distinction between interaction and effect modification. Curr Epidemiol Rep. 2014;1(1):51-57.

9. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). Int J Epidemiol. 2014;43(1):61-68.

10. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S20-S42.

11. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine. Age Ageing. 2007;36(6):614-616.

12. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-M156.

13. Perelshtein S, Holtzman E, Ben Arie A, et al. PyMSM: Python package for multi-state survival analysis. J Mach Learn Res. 2023;24(289):1-8.

14. Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons; 1987.

15. Wilson S. miceforest: multiple imputation with LightGBM in Python (version 6.0.5). 2023. Available at: https://github.com/AnotherSamWilson/miceforest. Accessed 11 Sept 2026.

16. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009;338:b2393.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335(7624):806-808.

Supplementary Files

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

- Additionalfile1.docx