Supplementary Online Content

Li C, Ma Y, Yang C, Hua R, Xie W, Zhang L. Association of cystatin C kidney function measures with long-term deficit-accumulation frailty trajectories and physical function decline. JAMA Netw Open. 2022;5(9):e2234208. doi:10.1001/jamanetworkopen.2022.34208

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This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods. Frailty Assessment and Statistical Analysis

1. Frailty assessment
The 29 items used to construct the FI included functional limitations (based on self-reported difficulties in activities of daily living, instrumental activities of daily living, and other activities), self-reported health status and alterations, components of depressive symptoms (based on 8-item version of the Center for Epidemiologic Studies Depression Scale), medical conditions (based on self-reported diagnosis by physicians), and cognitive status (based on a combination of external physician diagnosis and cognition score). These items came from self-reported information by study participants and objective measurements. The functional limitations were derived from the Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs), as well as other self-reported subjective activities limitations. Self-reported health status and alterations were derived using the self-rating of participants’ overall health status. Components of depressive symptoms were extracted from 8-item version of the Center for Epidemiologic Studies Depression Scale, which included 8 questions concerning indicators of participants’ feelings much of the time over the week prior to the interview, with each question consisting of 2 response categories (yes or no). The medical conditions were extracted from self-reported physician diagnosis of relevant diseases, with confirmation procedure applied at each wave. Such procedure was applied to help participants confirm whether they had been diagnosed of the disease at previous wave. The cognitive status was measured based on a combination of self-reported diagnosis and cognition score. We defined dementia cases using either a self-reported physician diagnosis or an alternative approach based on cognition scores. For the HRS, we used a cognition summary score from 0 to 27, with a cutoff point of 6 or less defined as dementia and 7 to 11 defined as cognitive impairment. The cognition summary score comprised the domains of memory and executive function. For the CHARLS, we defined dementia as a coexistence of cognitive and functional impairment. Cognitive impairment was defined as a score that was 1.5 SD below the mean of the population stratified by educational background. Functional impairment was defined as difficulty in performing one or more activities of daily living, including bathing, eating, dressing, getting in/out of bed, and walking across a room. These approaches had been validated.

2. Statistical analysis
Based on the 12-year repeated measurements of FI in the HRS and 7-year data in the CHARLS, we alternatively used the GBTM approach to evaluate long-term frailty trajectories. The GBTM approach assumed that the total population was consisted of several subpopulations with different longitudinal trajectories, and used maximum likelihood estimation to identify participants sharing similar trajectories. The trajectory group of the highest probability was determined for each participant, which was then included in further multivariate analysis. The GBTM approach can fit non-monotonic trajectories and support multiple trajectory shapes including linear, quadratic and cubic. It also allows specification of number of trajectory groups before fitting the model.

After determining that modeling 3 trajectory groups was appropriate for frailty trajectories modeling, we further evaluated different trajectory shapes for each trajectory group by testing the null hypothesis that the shape parameter for the group equals zero. We also used graphics of trajectory group means to help determine which shape best fit each trajectory group. After the procedure, we determined that the best 3-group trajectory model consisted of 3 quadratic trajectories. Then the estimated trajectory groups membership was included as the dependent variable for further multivariate analysis. We analyzed the associations between baseline kidney function metrics and identified frailty trajectories using binary logistic and multinomial logistic regression models, respectively.
### eTable 1. Components of Constructed 29-Item Frailty Index

| Item number | Item definition | Scoring |
|-------------|----------------|---------|
| 1           | Self-reported difficulties in bathing because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 2           | Self-reported difficulties in dressing because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 3           | Self-reported difficulties in getting in/out of bed because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 4           | Self-reported difficulties in walking around the house because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 5           | Self-reported difficulties in eating because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 6           | Self-reported difficulties in finishing daily activities of using the toilet because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 7           | Total number (0-5) of self-reported difficulties in finishing daily activities including bathing, dressing, eating, getting in/out of bed, walking around the house. | Any difficulties=1.00; No difficulties=0.00 |
| 8           | Self-reported difficulties in shopping because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 9           | Self-reported difficulties in preparing hot meal because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 10          | Self-reported difficulties in taking prescribed medications because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 11          | Self-reported difficulties in managing money because of a | Yes=1.00; No=0.00 |

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| Item number | Item definition | Scoring |
|-------------|----------------|---------|
| 12          | Self-reported difficulties in getting up from a chair because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 13          | Self-reported difficulties in climbing several flights of stairs because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 14          | Self-reported difficulties in lifting or carrying weights over 10 pounds because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 15          | Self-reported difficulties in walking one block because of a physical, mental, emotional or memory problem. | Yes=1.00; No=0.00 |
| 16          | Self-reported rating of health status. | Poor=1.00; Fair=0.75; Good=0.50; Very Good=0.25; Excellent=0.00 |
| 17          | Change in self-reported rating of health status. | Worse=1.00; Better/Same=0.00 |
| 18          | Feeling that everything is an effort much of time. | Yes=1.00; No=0.00 |
| 19          | Feeling depressed much of time. | Yes=1.00; No=0.00 |
| 20          | Feeling happy much of time. | No=1.00; Yes=0.00 |
| 21          | Feeling lonely much of time. | Yes=1.00; No=0.00 |
| 22          | Feeling that could not get going much of time. | Yes=1.00; No=0.00 |
| 23          | Self-reported diagnosis of hypertension by physician. | Yes=1.00; No=0.00 |
| 24          | Self-reported diagnosis of stroke by physician. | Yes=1.00; No=0.00 |
| 25          | Self-reported diagnosis of cancer by physician. | Yes=1.00; No=0.00 |
| 26          | Self-reported diagnosis of diabetes by physician. | Yes=1.00; No=0.00 |
| 27          | Self-reported diagnosis of arthritis by physician. | Yes=1.00; No=0.00 |
| 28          | Self-reported diagnosis of chronic lung disease by physician. | Yes=1.00; No=0.00 |
| 29          | Cognitive status, based on combination of self-reported diagnosis, and cognition score. | Dementia=1.00; Cognitive impairment but not demented=0.50; Cognitive healthy=0.00 |
| Item number a | Item definition b | Scoring c |
|---------------|-------------------|-----------|

a An unified 29-item frailty index was utilized across different waves, identical in both the HRS and the CHARLS.
b Item definition was based on self-reported information or objective measurements or both.
c The frailty index was calculated as the sum of scoring divided by the total number of items.
**eTable 2. Descriptive Statistics of Outcome Measurements at Different Waves in the HRS Cohort**

| Waves           | Frailty index | Grip strength (kg) | Gait speed (cm/s) |
|-----------------|---------------|--------------------|-------------------|
|                 | mean (SD)     | median (IQR)       | mean (SD)         | mean (SD)         |
| Wave 8 (year 2006) | 0.11 (0.07)   | 0.11 (0.05-0.16)   | 32.79 (11.03)     | 84.99 (23.87)     |
| Wave 9 (year 2008) | 0.13 (0.10)   | 0.12 (0.07-0.18)   | NA                | NA                |
| Wave 10 (year 2010)  | 0.15 (0.12)   | 0.12 (0.08-0.20)   | 30.78 (10.53)     | 84.21 (23.94)     |
| Wave 11 (year 2012)  | 0.16 (0.13)   | 0.13 (0.08-0.22)   | NA                | NA                |
| Wave 12 (year 2014)  | 0.18 (0.14)   | 0.15 (0.08-0.22)   | 28.94 (10.54)     | 80.70 (23.24)     |
| Wave 13 (year 2016)  | 0.18 (0.14)   | 0.16 (0.09-0.23)   | NA                | NA                |
| Wave 14 (year 2018)  | 0.16 (0.13)   | 0.12 (0.08-0.20)   | 28.56 (12.70)     | 81.00 (23.99)     |

Abbreviations: HRS, Health and Retirement Study; SD, standard deviation; IQR, interquartile range; NA, not applicable.
### eTable 3. Descriptive Statistics of Outcome Measurements at Different Waves in the CHARLS Cohort

| Waves          | Frailty index | Grip strength (kg) | Gait speed (cm/s) |
|----------------|---------------|--------------------|-------------------|
|                | mean (SD)     | median (IQR)       | mean (SD)         | mean (SD)         |
| Wave 1 (year 2011) | 0.10 (0.07) | 0.09 (0.05-0.16) | 32.36 (10.45)    | 64.56 (21.01)    |
| Wave 2 (year 2013)  | 0.15 (0.11) | 0.13 (0.08-0.20) | 31.30 (10.91)    | 69.32 (19.96)    |
| Wave 3 (year 2015)  | 0.17 (0.13) | 0.13 (0.08-0.22) | 29.55 (10.30)    | 78.03 (21.66)    |
| Wave 4 (year 2018)  | 0.18 (0.14) | 0.14 (0.08-0.24) | NA               | NA               |

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; SD, standard deviation; IQR, interquartile range; NA, not applicable.
eTable 4. Comparison of Baseline Characteristics of HRS Participants Included in vs Excluded From Analysis

| Characteristics                      | Excluded (n=9355) | Included (n=9114) | P* |
|--------------------------------------|------------------|------------------|----|
| **Men**                              | 3716 (39.72)     | 3870 (42.46)     | .001 |
| **Age, mean (SD), y**                | 69.74±11.72      | 66.19±10.11      | .001 |
| **Follow-up duration, median (IQR), y** | 8.00 (2.00-12.00) | 12.00 (8.00-12.00) | .001 |
| **White**                            | 7181 (76.76)     | 7755 (85.09)     | .001 |
| **Living alone**                     | 3959 (42.32)     | 2458 (26.97)     | .001 |
| **Education background**             |                  |                  |    |
| Less than high school                | 2784 (29.76)     | 1372 (15.05)     | .001 |
| High school or equivalent            | 3203 (34.24)     | 3316 (36.38)     |    |
| College and above                    | 3368 (36.00)     | 4426 (48.56)     |    |
| **Family annual income thirds**     |                  |                  |    |
| T1                                   | 4076 (43.57)     | 2085 (22.88)     | .001 |
| T2                                   | 2913 (31.14)     | 3238 (35.53)     |    |
| T3                                   | 2366 (25.29)     | 3791 (41.60)     |    |
| **Employment status**                |                  |                  |    |
| Unemployed                           | 1504 (16.08)     | 843 (9.25)       | .001 |
| Employed                             | 7851 (83.92)     | 8271 (90.75)     |    |
| **Medical insurance coverage**       |                  |                  |    |
| Uninsured                            | 530 (5.67)       | 507 (5.56)       | .001 |
| Public insurance                     | 3676 (39.29)     | 2237 (24.54)     |    |
| Private insurance                    | 5149 (55.04)     | 6370 (69.89)     |    |
| **Current smoking**                  | 1390 (14.86)     | 1141 (12.52)     | .001 |
| Alcohol consumption                  | 1226 (13.11)     | 1834 (20.12)     | .001 |
| **Physical activity**                | 5432 (58.07)     | 7487 (82.15)     | .001 |
| **Physical disability**              | 3193 (34.13)     | 193 (2.12)       | .001 |
| **Overweight**                       | 4345 (46.45)     | 6608 (72.50)     | .001 |
| **Frailty index, median (IQR)**      | 0.26 (0.12-0.40) | 0.11 (0.05-0.16) | .001 |
| **Grip strength, mean (SD), kg**     | 28.87±11.02      | 32.79±11.03      | .001 |
| **Gait speed, mean (SD), cm/s**      | 70.56±26.71      | 84.99±23.87      | .001 |
| **Hypertension**                     | 6591 (70.45)     | 5682 (62.34)     | .001 |
| **Diabetes**                         | 2513 (26.86)     | 1470 (16.13)     | .001 |
| **Stroke**                           | 1280 (13.68)     | 344 (3.77)       | .001 |
| **Heart diseases**                   | 2844 (30.40)     | 1572 (17.25)     | .001 |
| **Chronic lung diseases**            | 1213 (12.97)     | 427 (4.69)       | .001 |
| **Cancer**                           | 1535 (16.41)     | 1040 (11.41)     | .001 |

Abbreviations: HRS, Health and Retirement Study; SD, standard deviation; IQR, interquartile range.

*P* value reported for differences between groups using t test, chi-square test, or Wilcoxon rank test.
## eTable 5. Comparison of Baseline Characteristics of CHARLS Participants Included in vs Excluded From Analysis

| Characteristics                              | Excluded n=10873 | Included n=6835 | P a  |
|---------------------------------------------|------------------|-----------------|------|
| Men                                         | 5120 (47.09)     | 3358 (49.13)    | .01  |
| Age, mean (SD), y                           | 58.55±10.41      | 58.41±9.79      | .37  |
| Follow-up duration, median (IQR), y         | 7.00 (4.00-7.00) | 7.00 (7.00-7.00)| .001 |
| Living alone                                | 1501 (13.80)     | 759 (11.10)     | .001 |
| Education background                        |                  |                 |      |
| Less than high school                       | 9525 (87.60)     | 6036 (88.31)    |      |
| High school or equivalent                   | 1117 (10.27)     | 676 (9.89)      | .22  |
| College and above                           | 231 (2.12)       | 123 (1.80)      |      |
| Family annual income thirds                 |                  |                 |      |
| T1                                          | 3722 (34.23)     | 2244 (32.83)    | .15  |
| T2                                          | 3583 (32.95)     | 2288 (33.47)    |      |
| T3                                          | 3568 (32.82)     | 2303 (33.69)    |      |
| Employment status                           |                  |                 |      |
| Unemployed                                  | 603 (5.55)       | 260 (3.80)      | .001 |
| Employed                                    | 10270 (94.45)    | 6575 (96.20)    |      |
| Medical insurance coverage                  |                  |                 |      |
| Uninsured                                   | 1040 (9.56)      | 435 (6.36)      | .001 |
| Public insurance                            | 9581 (88.12)     | 6214 (90.91)    |      |
| Private insurance                           | 252 (2.32)       | 186 (2.72)      |      |
| Current smoking                             | 2817 (25.91)     | 2054 (30.05)    | .001 |
| Alcohol consumption                         | 1298 (11.94)     | 1005 (14.70)    | .001 |
| Physical activity                           | 2488 (22.88)     | 1924 (28.15)    | .001 |
| Physical disability                         | 2386 (21.94)     | 283 (4.14)      | .001 |
| Overweight                                  | 3915 (36.01)     | 2750 (40.23)    | .001 |
| Frailty index, median (IQR)                 | 0.13 (0.06-0.28) | 0.09 (0.05-0.16)| .001 |
| Grip strength, mean (SD), kg                | 30.83±11.06      | 32.36±10.45     | .001 |
| Gait speed, mean (SD), cm/s                 | 59.63±21.79      | 64.56±21.01     | .001 |
| Hypertension                                | 4492 (41.31)     | 2667 (39.02)    | .003 |
| Diabetes                                    | 1461 (13.44)     | 1020 (14.92)    | .006 |
| Stroke                                      | 398 (3.66)       | 88 (1.29)       | .001 |
| Cardiovascular disease                      | 1393 (12.81)     | 737 (10.78)     | .001 |
| Chronic lung disease                        | 1156 (10.63)     | 548 (8.02)      | .001 |
| Cancer                                      | 121 (1.11)       | 46 (0.67)       | .004 |

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; SD, standard deviation; IQR, interquartile range.

a P value reported for differences between groups using t test, chi-square test, or Wilcoxon rank test.
### eTable 6. Association Between Kidney Function Measures and Frailty Trajectories Identified Using the GBTM Approach in 2 Independent Cohorts Based on the Original Unweighted Samples

| Kidney function metrics | HRS (n=9114) | CHARLS (n=6835) |
|-------------------------|--------------|-----------------|
|                         | Accelerated frailty increase | Multinomial logistic regression \(^{a}\) | Accelerated frailty increase | Moderate frailty increase | Accelerated frailty increase | Moderate frailty increase |
|                         | OR (95% CI) | \(P\) | OR (95% CI) | \(P\) | OR (95% CI) | \(P\) |
| **Categories by eGFRCys** |  |  |  |  |  |
| \(\geq 90\) mL/min/1.73m\(^2\) | 1 [Reference] | NA | 1 [Reference] | NA | 1 [Reference] | NA |
| 60-89 mL/min/1.73m\(^2\) | 1.06 (0.85 - 1.32) | .60 | 1.07 (0.85 - 1.37) | .14 | 1.08 (0.94 - 1.24) | .43 |
| \(< 60\) mL/min/1.73m\(^2\) | 1.29 (1.03 - 1.63) | .03 | 1.52 (1.17 - 1.97) | .001 | 1.27 (1.07 - 1.50) | .005 |
| Test for linear trend \(^{c}\) | 1.15 (1.03 - 1.29) | .01 | 1.25 (1.10 - 1.43) | .001 | 1.12 (1.03 - 1.22) | .007 |
| Continuous serum cystatin C, per SD \(^{d}\) | 1.07 (1.01 - 1.14) | .03 | 1.22 (1.12 - 1.33) | .001 | 1.16 (1.08 - 1.25) | .001 |
| Continuous eGFRCys, per SD | 0.89 (0.81 - 0.96) | .005 | 0.81 (0.73 - 0.89) | .001 | 0.88 (0.83 - 0.94) | .001 |
| **Categories by eGFRCys** |  |  |  |  |  |
| \(\geq 90\) mL/min/1.73m\(^2\) | 1 [Reference] | NA | 1 [Reference] | NA | 1 [Reference] | NA |
| 60-89 mL/min/1.73m\(^2\) | 1.03 (0.78 - 1.35) | .83 | 1.06 (0.80 - 1.41) | .16 | 1.08 (0.93 - 1.26) | .58 |
| \(< 60\) mL/min/1.73m\(^2\) | 1.49 (1.07 - 2.07) | .02 | 1.53 (1.08 - 2.17) | .005 | 1.09 (0.88 - 1.36) | .60 |
| Test for linear trend | 1.23 (1.04 - 1.46) | .01 | 1.26 (1.05 - 1.50) | .01 | 1.05 (0.94 - 1.17) | .37 |
| Continuous serum cystatin C, per SD | 1.18 (1.07 - 1.29) | .001 | 1.22 (1.10 - 1.35) | .001 | 1.08 (1.01 - 1.16) | .03 |
| Continuous eGFRCys, per SD | 0.83 (0.73 - 0.94) | .003 | 0.80 (0.70 - 0.91) | .001 | 0.92 (0.85 - 0.99) | .04 |
| Continuous serum creatinine, per SD | 0.91 (0.81 - 1.02) | .12 | 0.92 (0.81 - 1.03) | .16 | 0.99 (0.92 - 1.07) | .85 |
| Continuous eGFRCr, per SD | 1.09 (0.97 - 1.23) | .14 | 1.08 (0.95 - 1.22) | .25 | 0.99 (0.92 - 1.07) | .74 |
| Continuous cystatin C adjusted for creatinine, per SD | 1.33 (1.19 - 1.49) | .001 | 1.40 (1.24 - 1.58) | .001 | 1.12 (1.03 - 1.21) | .008 |
| Continuous eGFRCys adjusted for eGFRCr, per SD | 0.75 (0.66 - 0.87) | .001 | 0.73 (0.63 - 0.84) | .001 | 0.91 (0.83 - 0.99) | .03 |
| eGFRdiff adjusted for eGFRCr, per SD | 0.79 (0.71 - 0.89) | .001 | 0.77 (0.68 - 0.87) | .001 | 0.93 (0.86 - 0.99) | .03 |

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; HRS, Health and Retirement Study; SD, standard deviation; CI, confidence interval; OR, odds ratio; eGFRCys, estimated glomerular filtration rate using serum cystatin C; eGFRCr, estimated glomerular filtration rate using serum creatinine; eGFRdiff, difference between eGFRCys and eGFRCr (calculated as eGFRCys - eGFRCr); NA, not applicable. \(^{a}\) OR was estimated using binary logistic regression models, with the logit link function. Accelerated frailty progression trajectory was the outcome, while the moderate and stable frailty progression trajectories were estimated using multinomial logistic regression models. \(^{c}\) Test for linear trend. \(^{d}\) Continuous variable per SD.

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combined as the reference category for modelling.

OR was estimated using multinomial logistic regression models, with the generalized logit link function. Accelerated frailty progression trajectory and moderate frailty trajectory were outcomes, while the stable frailty progression trajectory was the reference category for modeling. Adjusted covariates included age, sex, ethnicity, living arrangement, education background, family annual income, employment status, medical insurance coverage, current smoking, alcohol consumption, physical activity, overweight status, physical disability, baseline frailty index, hypertension, diabetes, stroke, heart diseases, chronic lung diseases, and cancer.

Performed by treating eGFRCys categories as a numerical variable.

Estimated as the beta coefficient for 1 SD increment in kidney metrics.
### eTable 7. Longitudinal Associations Between Kidney Function Measures and Frailty Trajectories in 2 Independent Cohorts Based on the Original Unweighted Samples

| Kidney function metrics | Rate of change in frailty index (SD/year) | $\beta$ (95% CI) $^a$ | $P$ |
|-------------------------|------------------------------------------|------------------------|-----|
| **HRS (n=9114)**        |                                          |                        |     |
| Categories by eGFRCys   |                                          |                        |     |
| $\geq$ 90 mL/min/1.73m$^2$ | 0 [Reference]                           | NA                     |     |
| 60-89 mL/min/1.73m$^2$  | 0.041 (0.031 to 0.052)                  | .001                   |     |
| $<$ 60 mL/min/1.73m$^2$ | 0.136 (0.124 to 0.148)                  | .001                   |     |
| Test for linear trend $^b$ | 0.066 (0.060 to 0.072)                  | .001                   |     |
| Continuous serum cystatin C, per SD $^c$ | 0.048 (0.043 to 0.053)                  | .001                   |     |
| Continuous eGFRCys, per SD | -0.055 (-0.059 to -0.050)               | .001                   |     |
| **CHARLS (n=6835)**     |                                          |                        |     |
| Categories by eGFRCys   |                                          |                        |     |
| $\geq$ 90 mL/min/1.73m$^2$ | 0 [Reference]                           | NA                     |     |
| 60-89 mL/min/1.73m$^2$  | 0.031 (0.012 to 0.050)                  | .001                   |     |
| $<$ 60 mL/min/1.73m$^2$ | 0.167 (0.142 to 0.193)                  | .001                   |     |
| Test for linear trend $^b$ | 0.074 (0.062 to 0.087)                  | .001                   |     |
| Continuous serum cystatin C, per SD $^c$ | 0.053 (0.044 to 0.062)                  | .001                   |     |
| Continuous eGFRCys, per SD | -0.057 (-0.066 to -0.049)               | .001                   |     |
| Continuous serum creatinine, per SD | 0.004 (-0.005 to 0.013)                | .40                    |     |
| Continuous eGFRCr, per SD | -0.048 (-0.057 to -0.039)             | .001                   |     |
| Continuous cystatin C adjusted for creatinine, per SD | 0.053 (0.044 to 0.062)                  | .001                   |     |
| Continuous eGFRCys adjusted for eGFRCr, per SD | -0.057 (-0.066 to -0.048)             | .001                   |     |
| eGFRCdiff adjusted for eGFRCr, per SD | -0.029 (-0.038 to -0.020)            | .001                   |     |

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; HRS, Health and Retirement Study; SD, standard deviation; CI, confidence interval; eGFRCys, estimated glomerular filtration rate using serum cystatin C; eGFRCr, estimated glomerular filtration rate using serum creatinine; eGFRCdiff, difference between eGFRCys and eGFRCr (calculated as eGFRCys - eGFRCr); NA, not applicable.

$^a$ Beta coefficient was estimated using linear mixed models, positive value represents accelerated frailty. Adjusted covariates included age, sex, ethnicity, living arrangement, education background, family annual income, employment status, medical insurance coverage, current smoking, alcohol consumption, physical activity, overweight status, physical disability, hypertension, diabetes, stroke, heart diseases, chronic lung diseases, and cancer.

eGFRCys: estimated glomerular filtration rate using serum cystatin C; eGFRCr: estimated glomerular filtration rate using serum creatinine; eGFRCdiff: difference between eGFRCys and eGFRCr, calculated as eGFRCys-eGFRCr.

$^b$ Performed by treating eGFRCys categories as a numerical variable.

$^c$ Estimated as the beta coefficient for 1 SD increment in kidney metrics.

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| Kidney function metrics | Rate of change in grip strength (SD/year) | Rate of change in gait speed (SD/year) |
|-------------------------|------------------------------------------|---------------------------------------|
|                         | β (95% CI) a                           | P                                    | β (95% CI) a                           | P                                    |
| **HRS (n=9114)**        |                                          |                                       |                                       |
| ≥ 90 mL/min/1.73m²      | 0 [Reference]                          | NA                                   | 0 [Reference]                          | NA                                   |
| 60-89 mL/min/1.73m²     | -0.007 (-0.011 to -0.002)              | .004                                 | -0.010 (-0.018 to -0.002)             | .02                                  |
| < 60 mL/min/1.73m²      | -0.010 (-0.015 to -0.004)              | .001                                 | -0.020 (-0.030 to -0.011)             | .001                                 |
| Test for linear trend b | -0.005 (-0.008 to -0.002)              | .001                                 | -0.009 (-0.014 to -0.005)             | .001                                 |
| Continuous serum cystatin C, per SD c | -0.005 (-0.008 to -0.003) | .001 | -0.008 (-0.012 to -0.004) | .001 |
| Continuous eGFRCys, per SD | 0.004 (0.002 to 0.006) | .001 | 0.006 (0.003 to 0.010) | .001 |
| **CHARLS (n=6835)**     |                                          |                                       |                                       |
| ≥ 90 mL/min/1.73m²      | 0 [Reference]                          | NA                                   | 0 [Reference]                          | NA                                   |
| 60-89 mL/min/1.73m²     | -0.004 (-0.011)                        | .62                                  | -0.002 (-0.034 to -0.030)             | .91                                  |
| < 60 mL/min/1.73m²      | -0.023 (-0.042 to -0.004)              | .02                                  | -0.048 (-0.083 to -0.014)             | .006                                 |
| Test for linear trend b | -0.010 (-0.019 to -0.001)              | .03                                  | -0.026 (-0.043 to -0.009)             | .003                                 |
| Continuous serum cystatin C, per SD c | -0.008 (-0.015 to -0.002) | .01 | -0.017 (-0.028 to -0.007) | .001 |
| Continuous eGFRCys, per SD | 0.007 (0.001 to 0.014) | .03 | 0.023 (0.010 to 0.035) | .001 |
| Continuous serum creatinine, per SD | -0.001 (-0.008 to -0.005) | .68 | 0.006 (-0.005 to 0.017) | .27 |
| Continuous eGFRCr, per SD | -0.000 (-0.007 to -0.006) | .89 | 0.009 (-0.003 to 0.021) | .15 |
| Continuous cystatin C adjusted for creatinine, per SD | -0.008 (-0.014 to -0.002) | .01 | -0.017 (-0.028 to -0.006) | .002 |
| Continuous eGFRCys adjusted for eGFRCr, per SD | 0.007 (0.001 to 0.013) | .03 | 0.022 (0.010 to 0.034) | .001 |
| eGFRdiff adjusted for eGFRCr, per SD | 0.009 (0.003 to 0.015) | .006 | 0.017 (0.005 to 0.029) | .005 |

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; HRS, Health and Retirement Study; SD, standard deviation; CI, confidence interval; eGFRCys, estimated glomerular filtration rate using serum cystatin C; eGFRCr, estimated glomerular filtration rate using serum creatinine; eGFRdiff, difference between eGFRCys and eGFRCr (calculated as eGFRCys - eGFRCr); NA, not applicable.

a Beta coefficient was estimated using linear mixed models. Adjusted covariates included age, sex, ethnicity, living arrangement, education background, family annual income, employment status, medical insurance coverage, current smoking, alcohol consumption, physical activity, overweight status, physical disability, hypertension, diabetes, stroke, heart diseases, chronic lung diseases, and cancer.

eGFRCys: estimated glomerular filtration rate using serum cystatin C; eGFRCr: estimated glomerular filtration rate using serum creatinine.
filtration rate using serum creatinine; eGFRdiff: difference between eGFRCys and eGFRCr, calculated as eGFRCys-eGFRCr.
b Performed by treating eGFRCys categories as a numerical variable.
c Estimated as the beta coefficient for 1 SD increment in kidney metrics.
eFigure 1. Participant Selection Diagram

HRS
- 6362 Participants excluded due to missing serum cystatin C
- 2819 participants excluded due to developed frailty
- 12107 participants with complete serum cystatin C measurement at wave 8
- 9288 non-frail participants at wave 8
- 9114 participants included in final analysis

CHARLS
- 17708 participants attending wave 1
- 8878 participants with complete serum cystatin C measurement at wave 1
- 7120 non-frail participants at wave 1
- 6835 participants included in final analysis

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eFigure 2. Identified Dynamic Frailty Trajectories in 2 Independent Cohorts Using the GBTM Approach

Panel A: HRS cohort; Panel B: CHARLS cohort.
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