

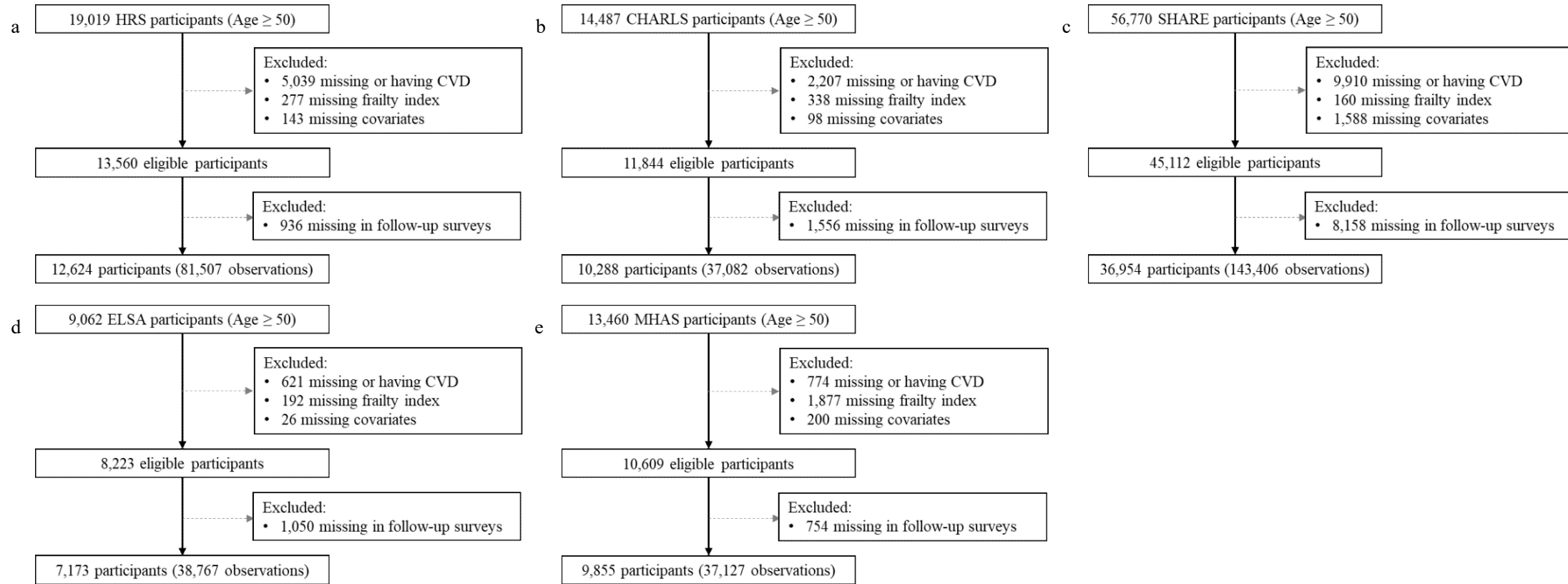
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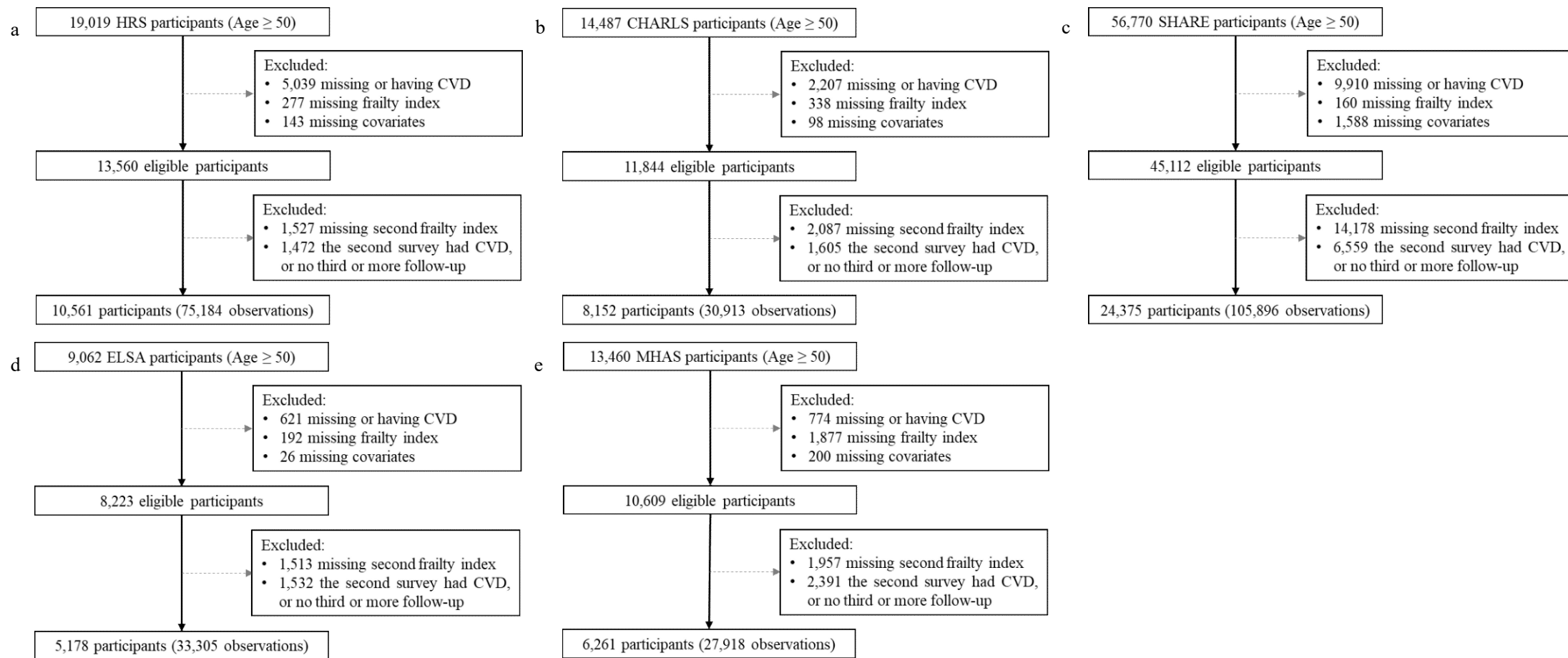
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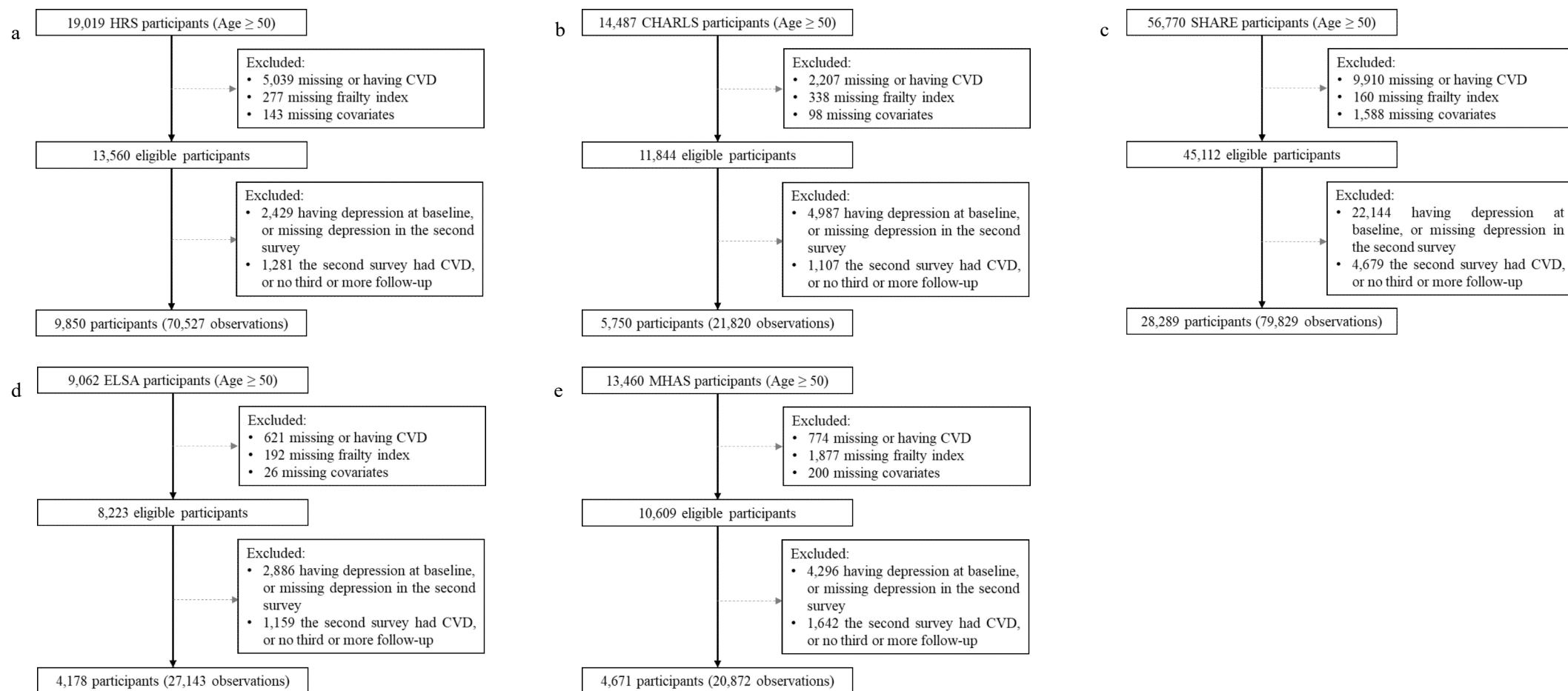
Supplementary Figure 1. The flowcharts of baseline frailty status analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



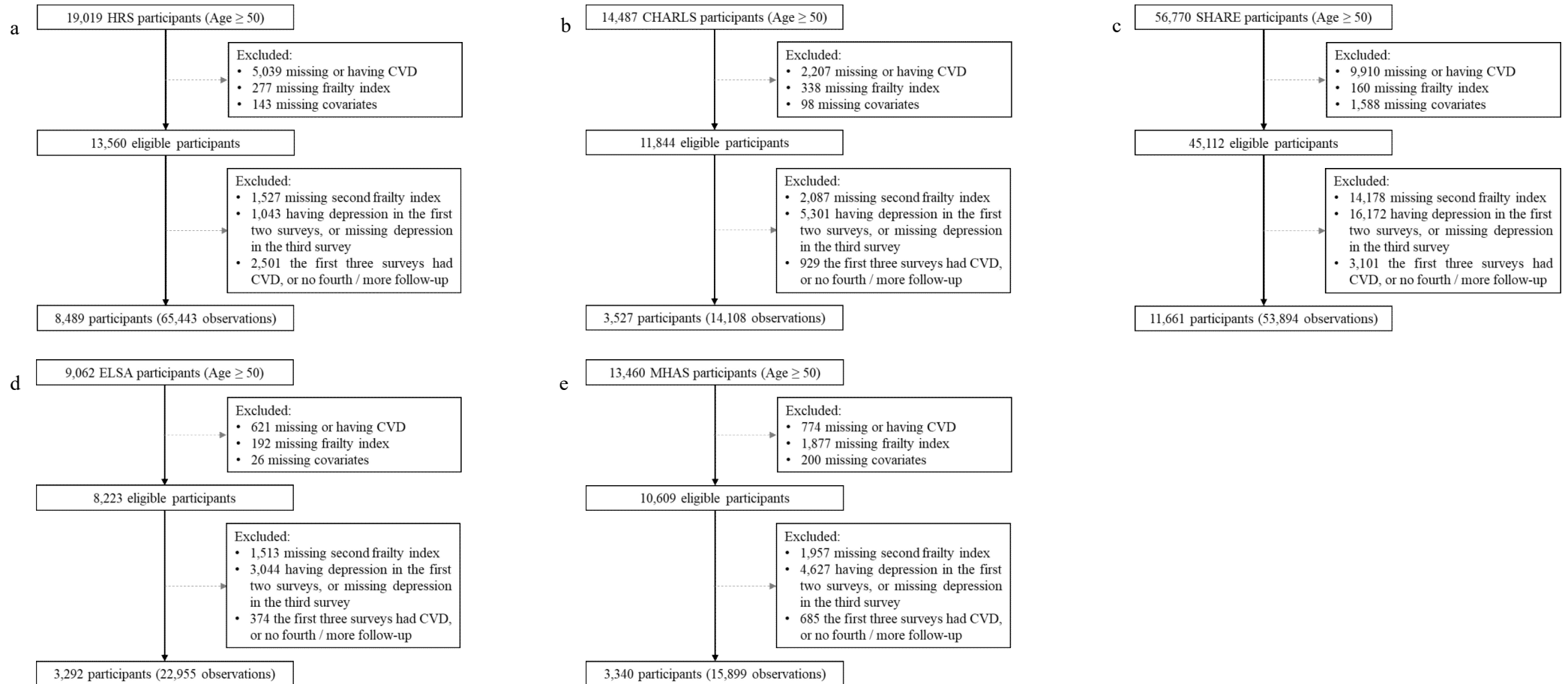
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(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



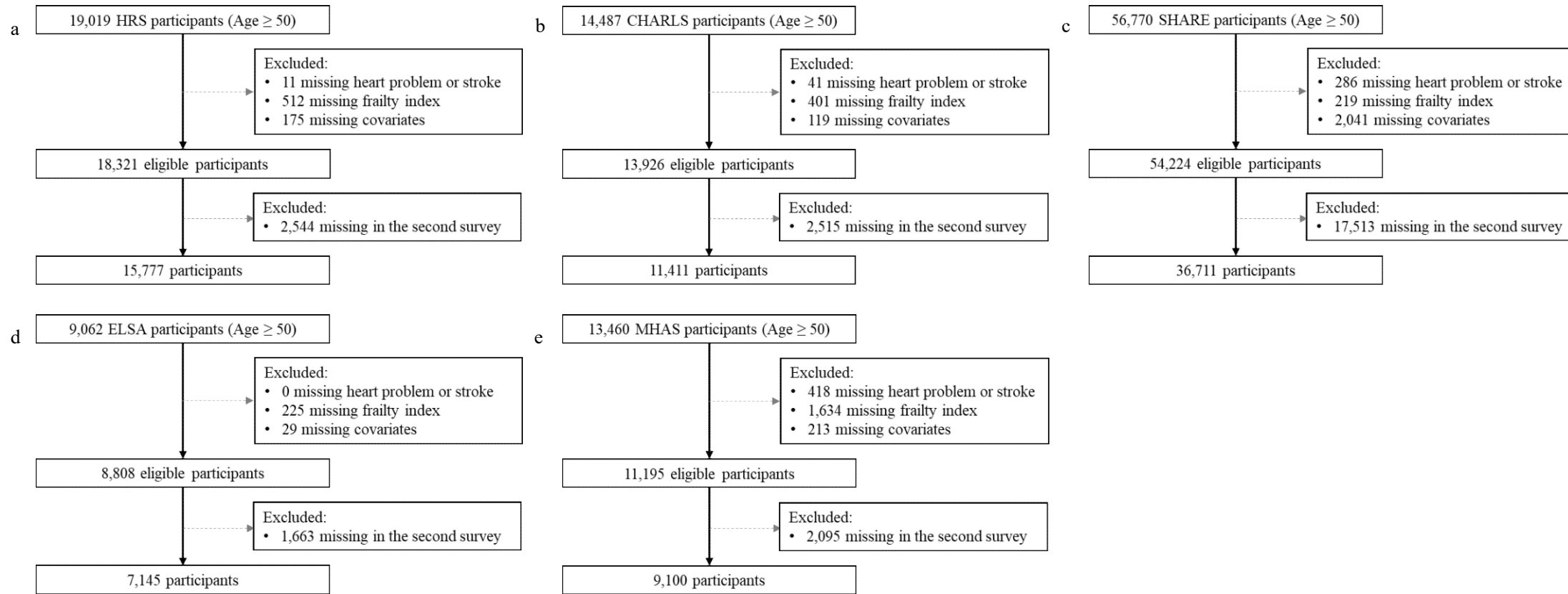
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(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



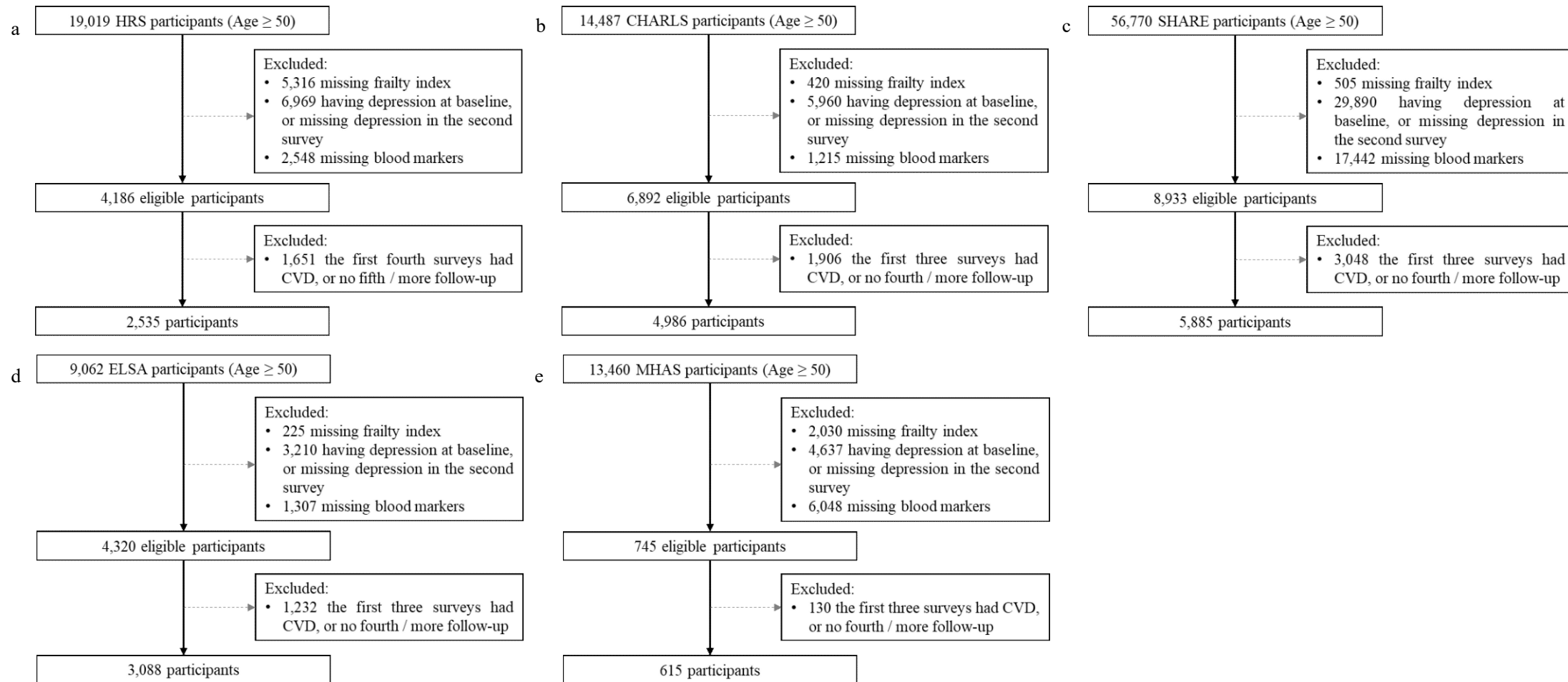
Supplementary Figure 4. The flowcharts of mediating role of depression in changes in frailty status analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



Supplementary Figure 5. The flowcharts of cross-lagged panel network analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.

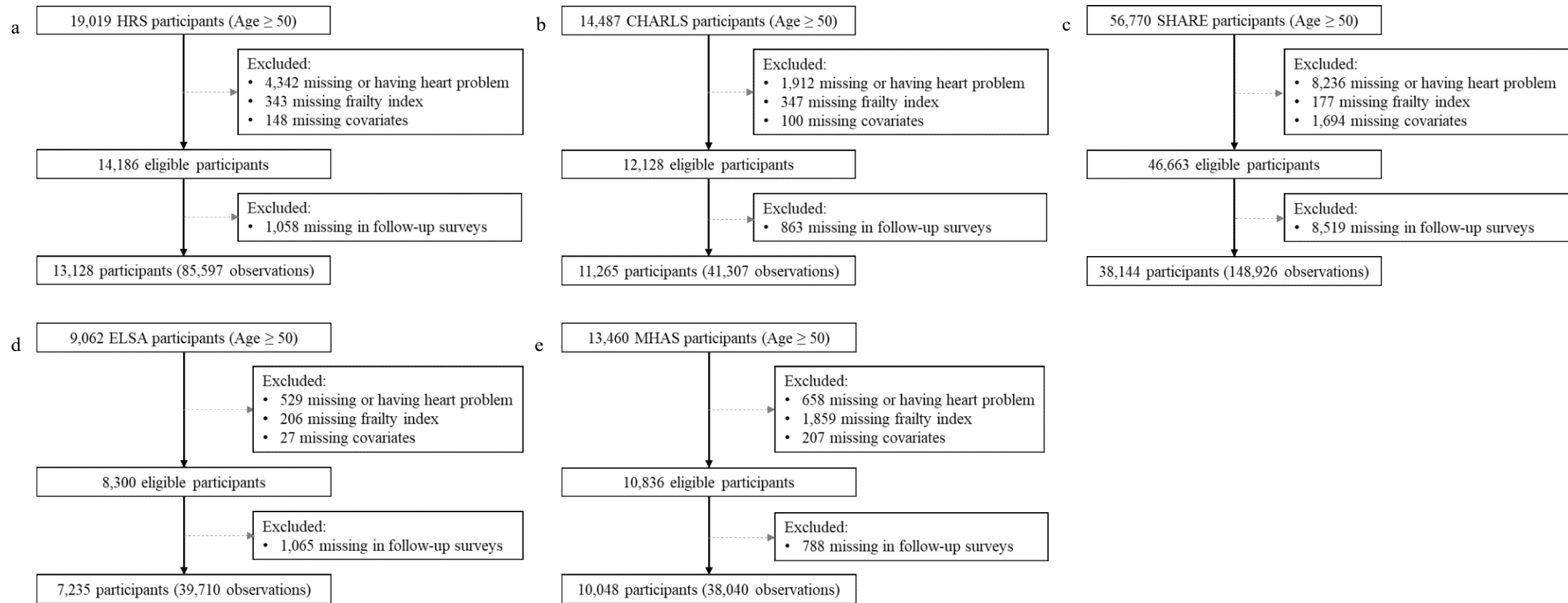


Supplementary Figure 6. The flowcharts of blood markers correlation analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in

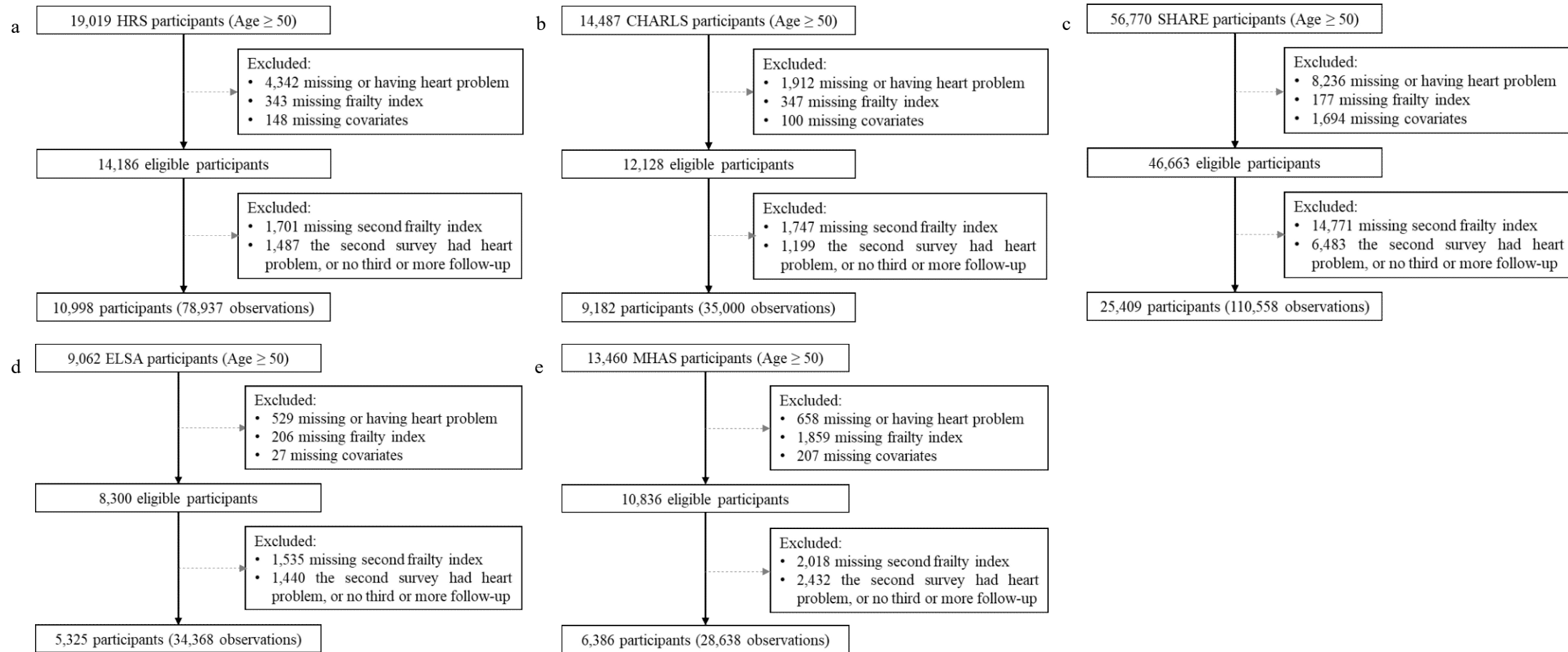
Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.

In the analysis, HRS used frailty status in 2000, depressive symptoms in 2002, blood markers in 2006, and incident CVD in 2008, 2010, 2012, 2014, 2016, and 2018; CHARLS used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2018; SHARE used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2017 and 2019; ELSA used frailty status in 2004, depressive symptoms in 2006, blood markers in 2008, and incident CVD in 2010, 2012, 2014, 2016, and 2018; MHAS used frailty status in 2001, depressive symptoms in 2003, blood markers in 2012, and incident CVD in 2015 and 2018.



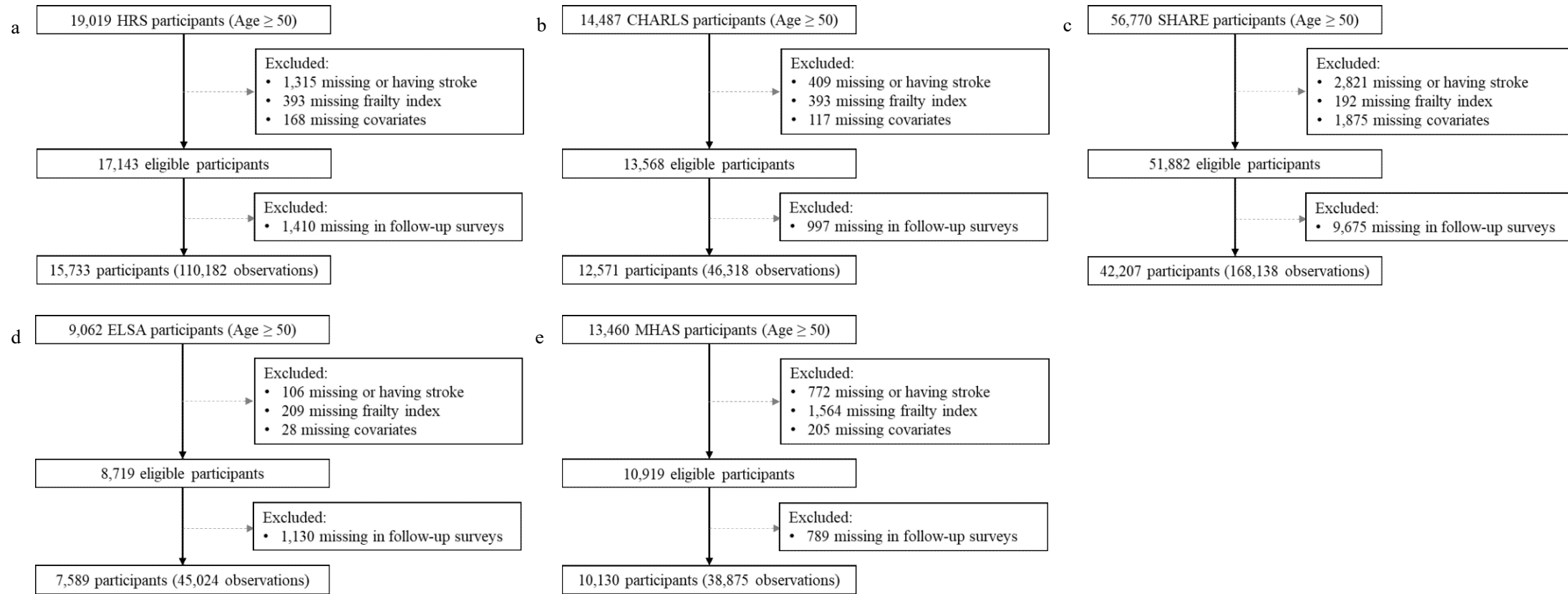
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(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



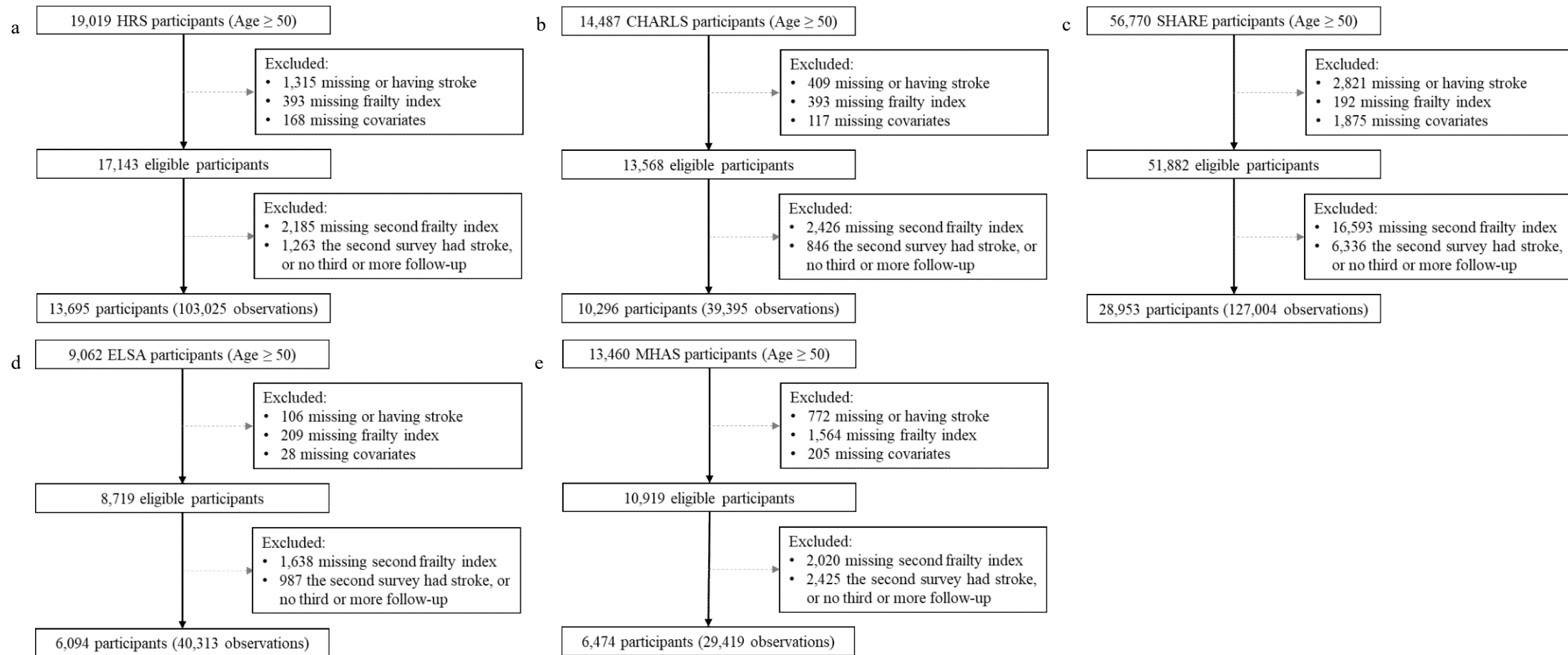
Supplementary Figure 8. The flowcharts of changes in frailty status on heart problem analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



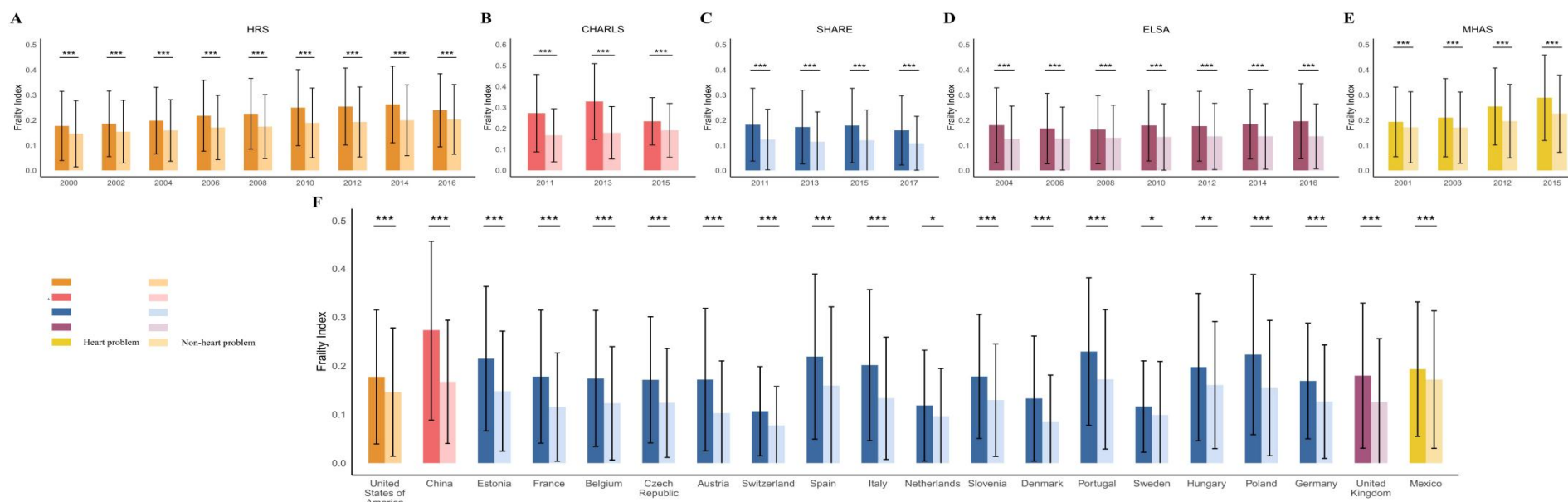
Supplementary Figure 9. The flowcharts of baseline frailty status on stroke analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



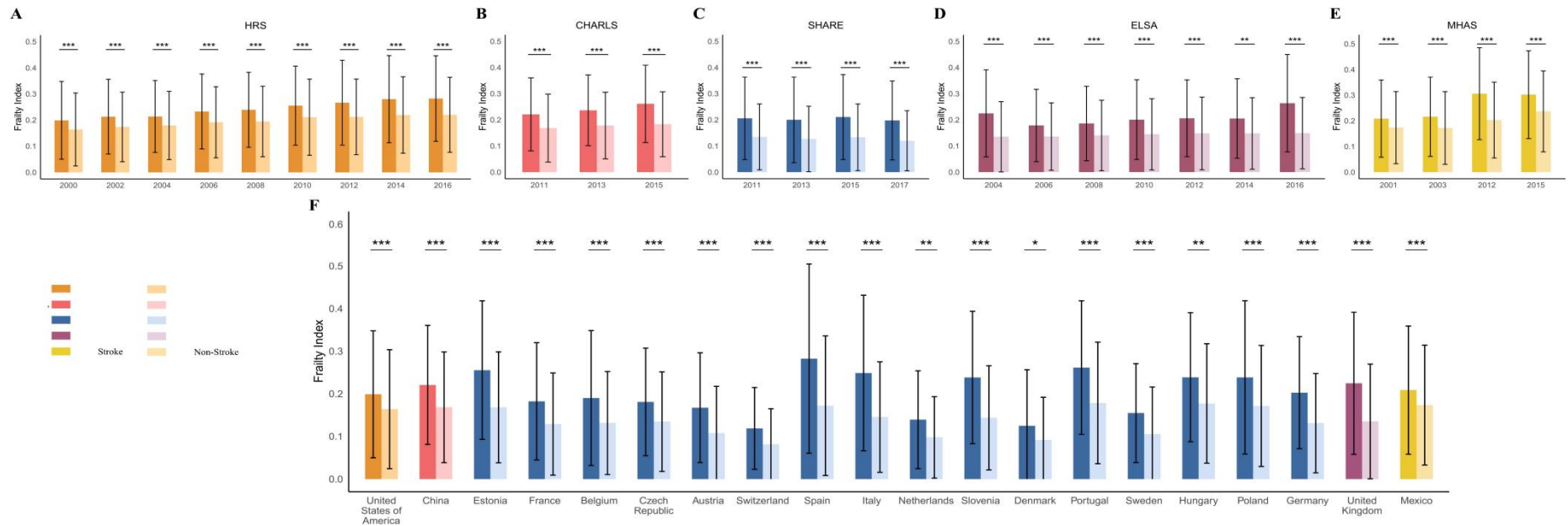
Supplementary Figure 10. The flowcharts of changes in frailty status on stroke analysis participants selection in HRS, CHARLS, SHARE, ELSA, and MHAS.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study.



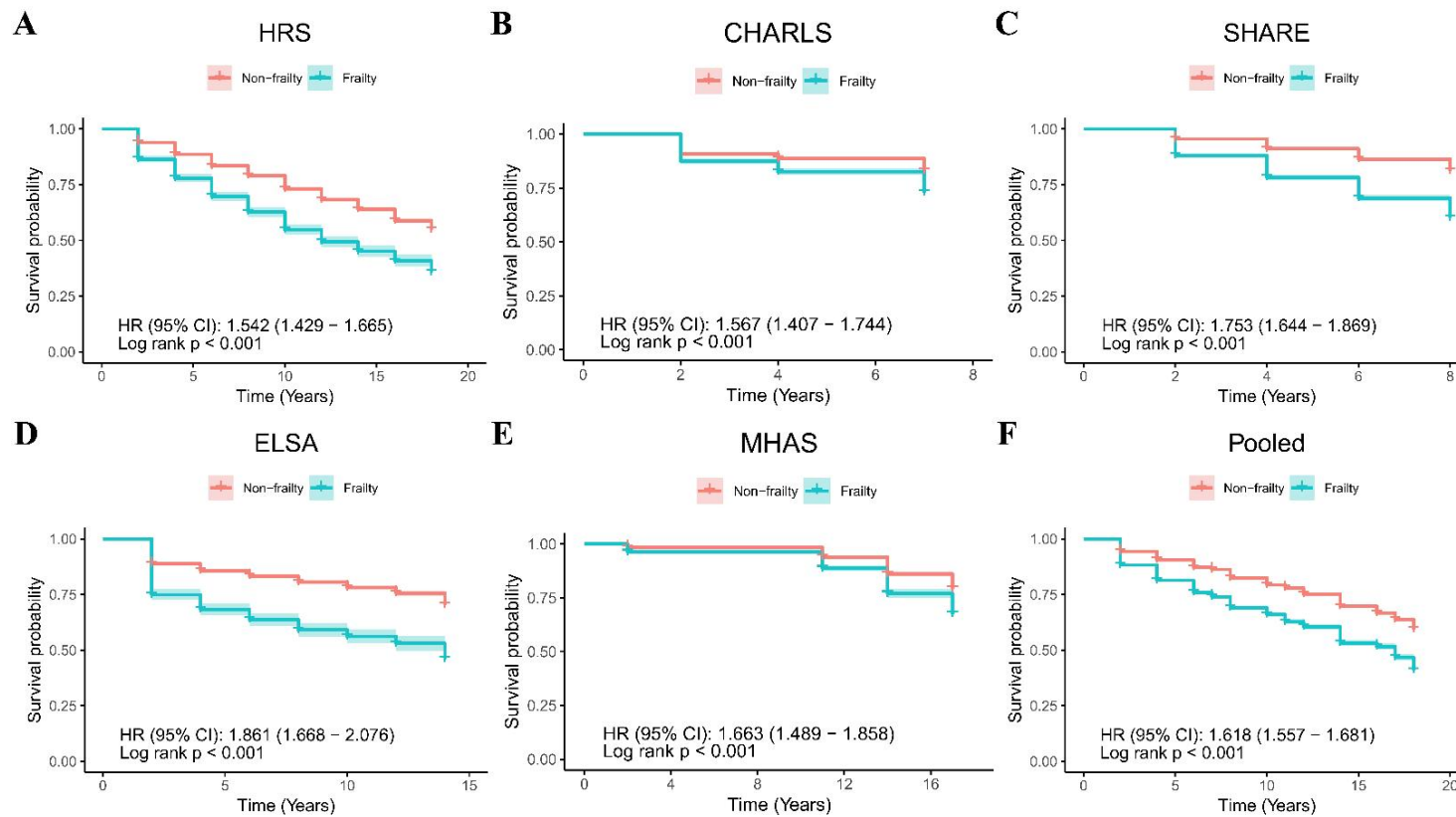
Supplementary Figure 11. Differences in frailty index across heart disease.

Note: The images A, B, C, D and E illustrated the differences in frailty index across heart disease by survey year in the following studies: HRS (Health and Retirement Study), MHAS (Mexican Health and Ageing Study), CHARLS (China Health and Retirement Longitudinal Study), ELSA (English Longitudinal Study of Ageing), and SHARE (Survey of Health, Ageing and Retirement in Europe), respectively. Additionally, image F presented the differences in frailty index across heart disease categorized by country. For all countries, the sample size of the heart disease group is smaller than the non-heart disease group; detailed sample sizes are provided in Supplementary Table 50. T test (two-tailed independent t-test) was used to compare the trends in frailty index and heart disease across different survey waves. The years corresponding to the horizontal coordinates in images A, B, C, D, and E represented the FI using this survey period and the incident heart disease at follow-up (e.g., The 2000 results in HRS corresponded to the use of FI for 2000 and the prevalence for 2002-2018, and so on). In image F, baseline FI and incident heart disease at follow-up were used. Frailty index are presented as mean values, with error bars representing $\pm SD$. The p value indicates the difference in frailty index between heart disease and Non-heart disease groups. * $p < 0.1$, ** $p < 0.01$, *** $p < 0.001$.



Supplementary Figure 12. Differences in frailty index across stroke.

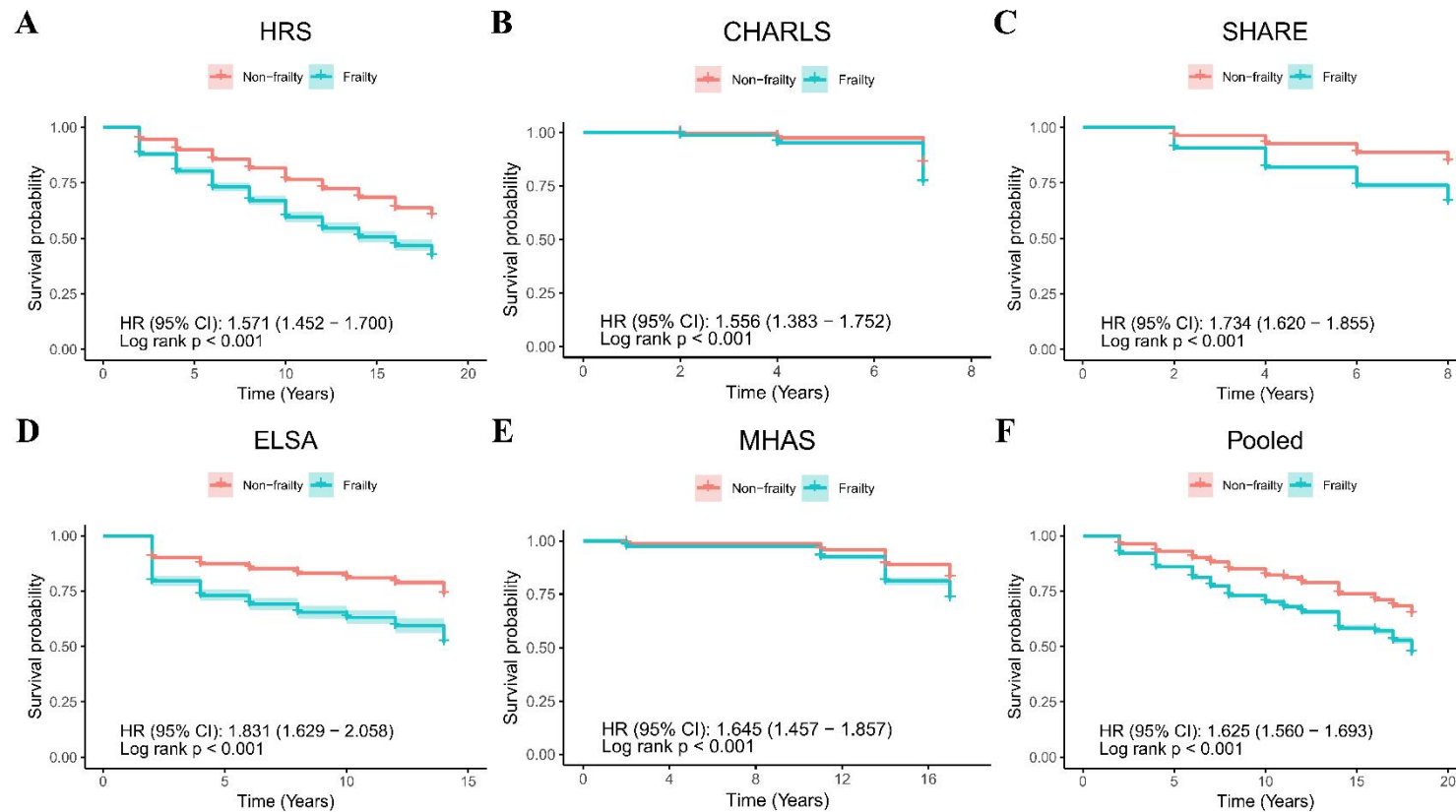
Note: The images A, B, C, D and E illustrated the differences in frailty index across stroke by survey year in the following studies: HRS (Health and Retirement Study), MHAS (Mexican Health and Ageing Study), CHARLS (China Health and Retirement Longitudinal Study), ELSA (English Longitudinal Study of Ageing), and SHARE (Survey of Health, Ageing and Retirement in Europe), respectively. Additionally, image F presented the differences in frailty index across stroke categorized by country. For all countries, the sample size of the stroke group is smaller than the non-stroke group; detailed sample sizes are provided in Supplementary Table 51. T test (two-tailed independent t-test) was used to compare the trends in frailty index and stroke across different survey waves. The years corresponding to the horizontal coordinates in images A, B, C, D, and E represented the FI using this survey period and the incident stroke at follow-up (e.g., The 2000 results in HRS corresponded to the use of FI for 2000 and the prevalence for 2002-2018, and so on). In image F, baseline FI and incident stroke at follow-up were used. Frailty index are presented as mean values, with error bars representing $\pm SD$. The p value indicates the difference in frailty index between stroke and Non-stroke groups. * $p < 0.1$, ** $p < 0.01$, *** $p < 0.001$.



Supplementary Figure 13. Kaplan-Meier survival curve of CVD based on baseline frailty status subgroup in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

(A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled.

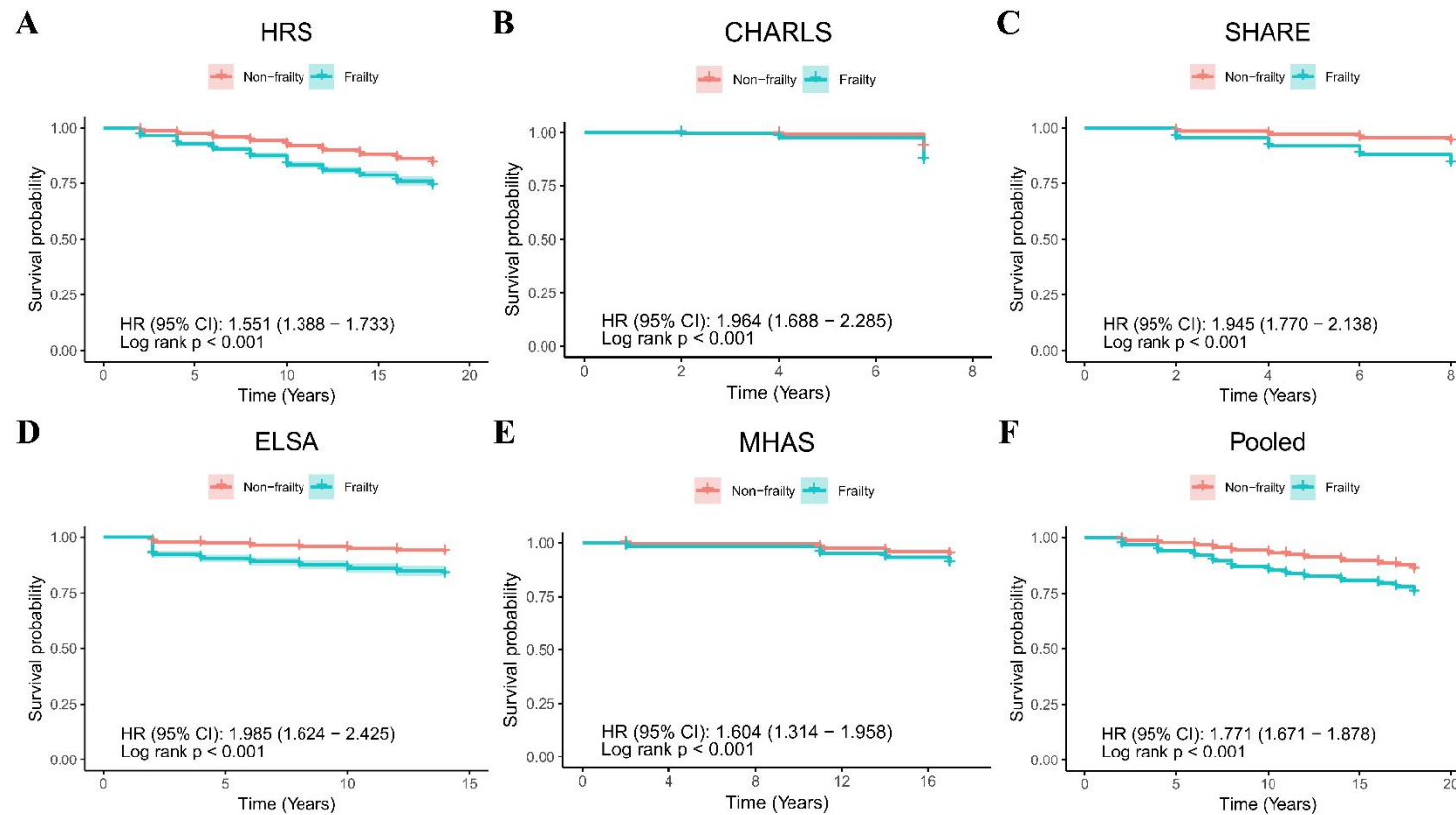
All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country.



Supplementary Figure 14. Kaplan-Meier survival curve of heart disease based on baseline frailty status subgroup in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

(A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled.

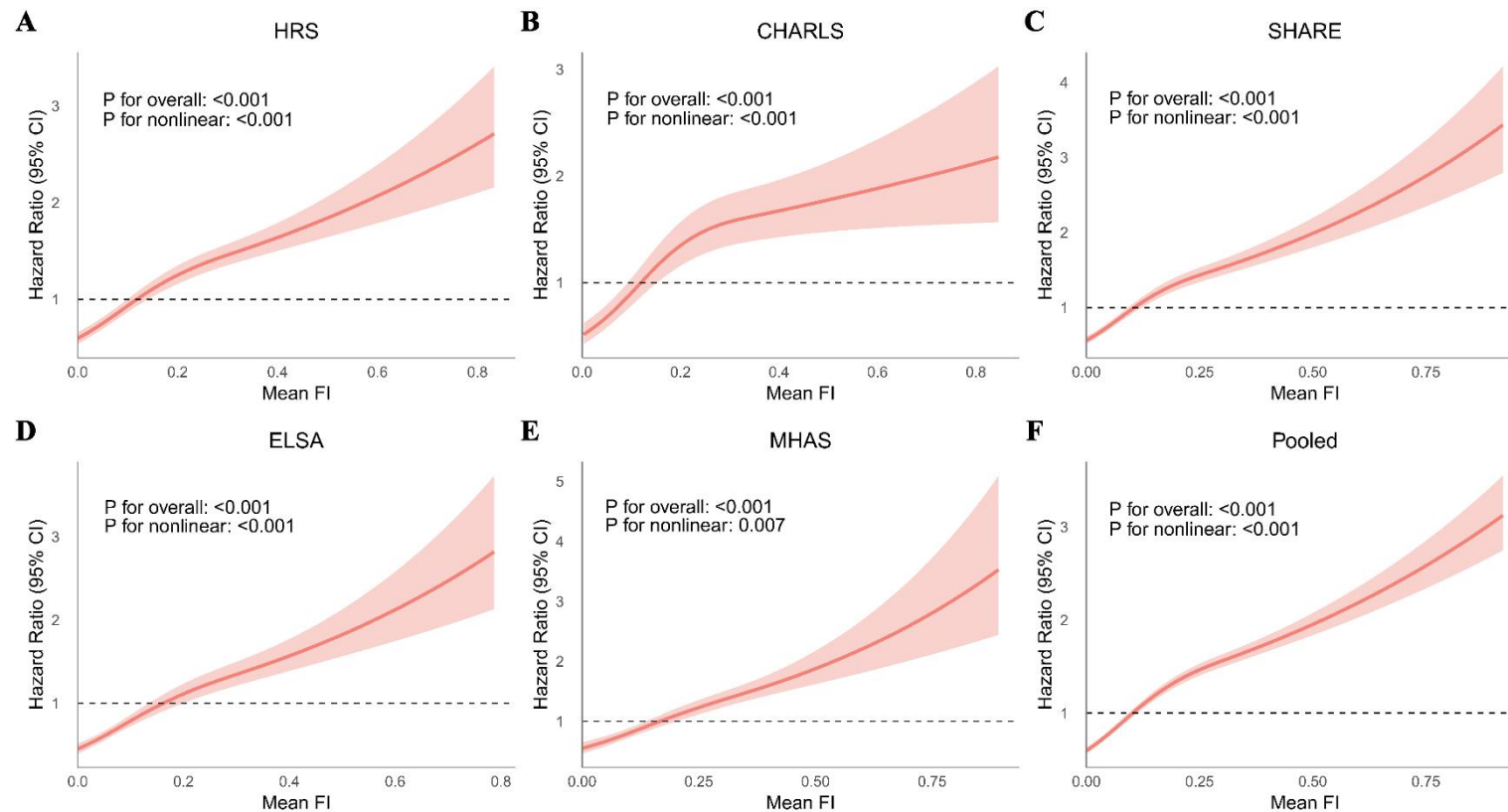
All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country.



Supplementary Figure 15. Kaplan-Meier survival curve of stroke based on baseline frailty status subgroup in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

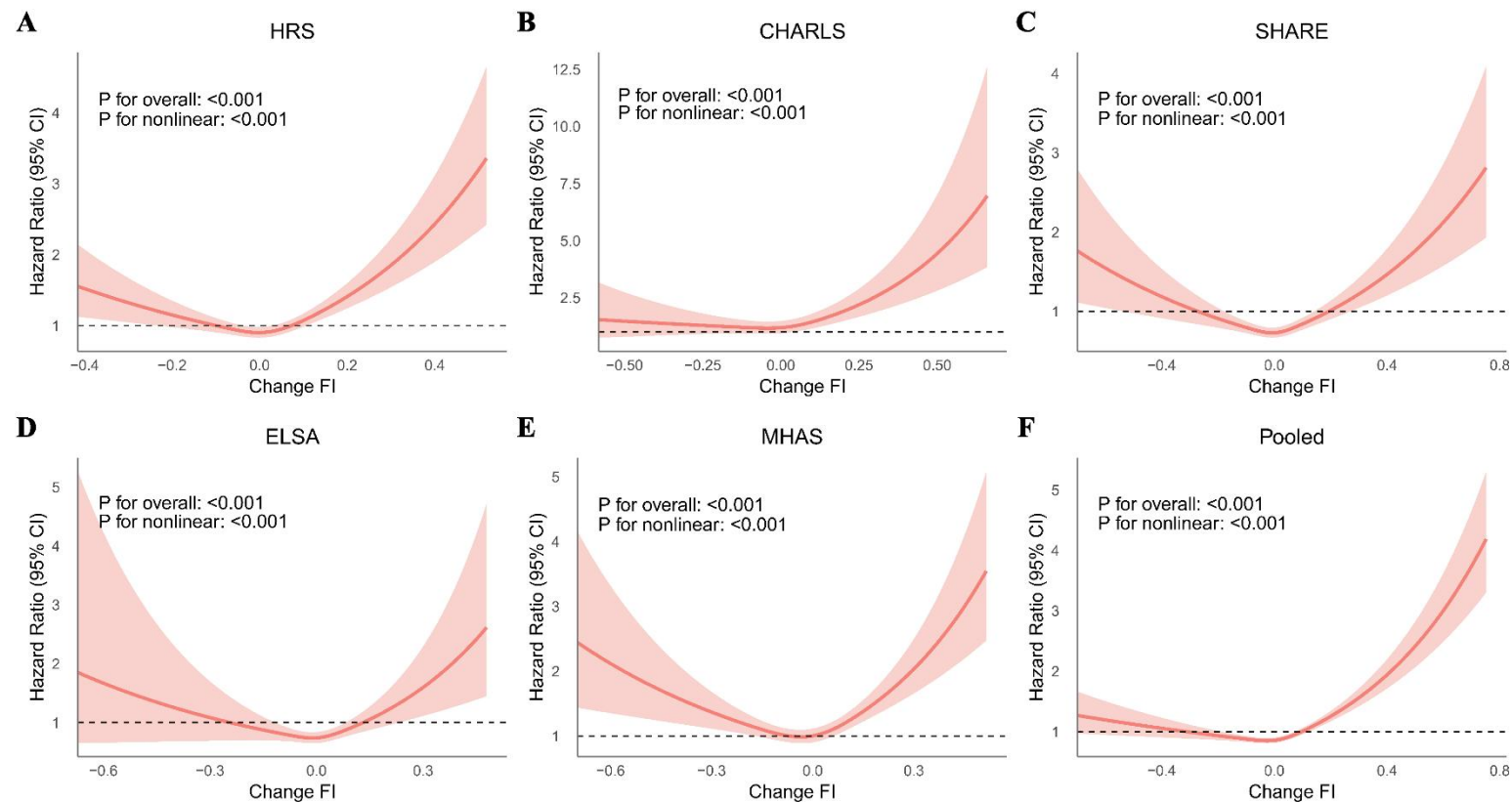
(A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled.

All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country.



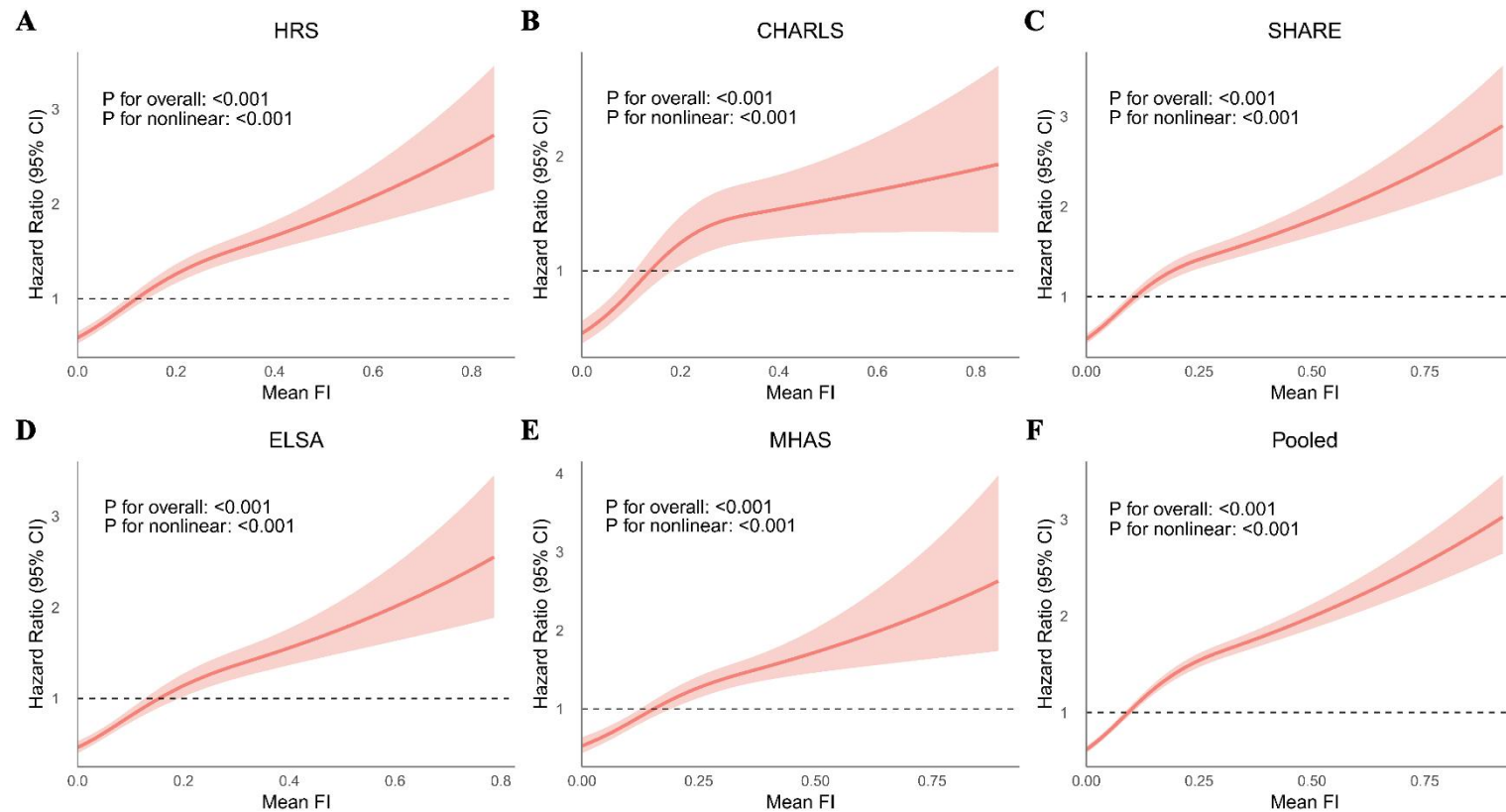
Supplementary Figure 16. RCS curve of the relationship between mean FI and incident CVD in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since mean FI was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).



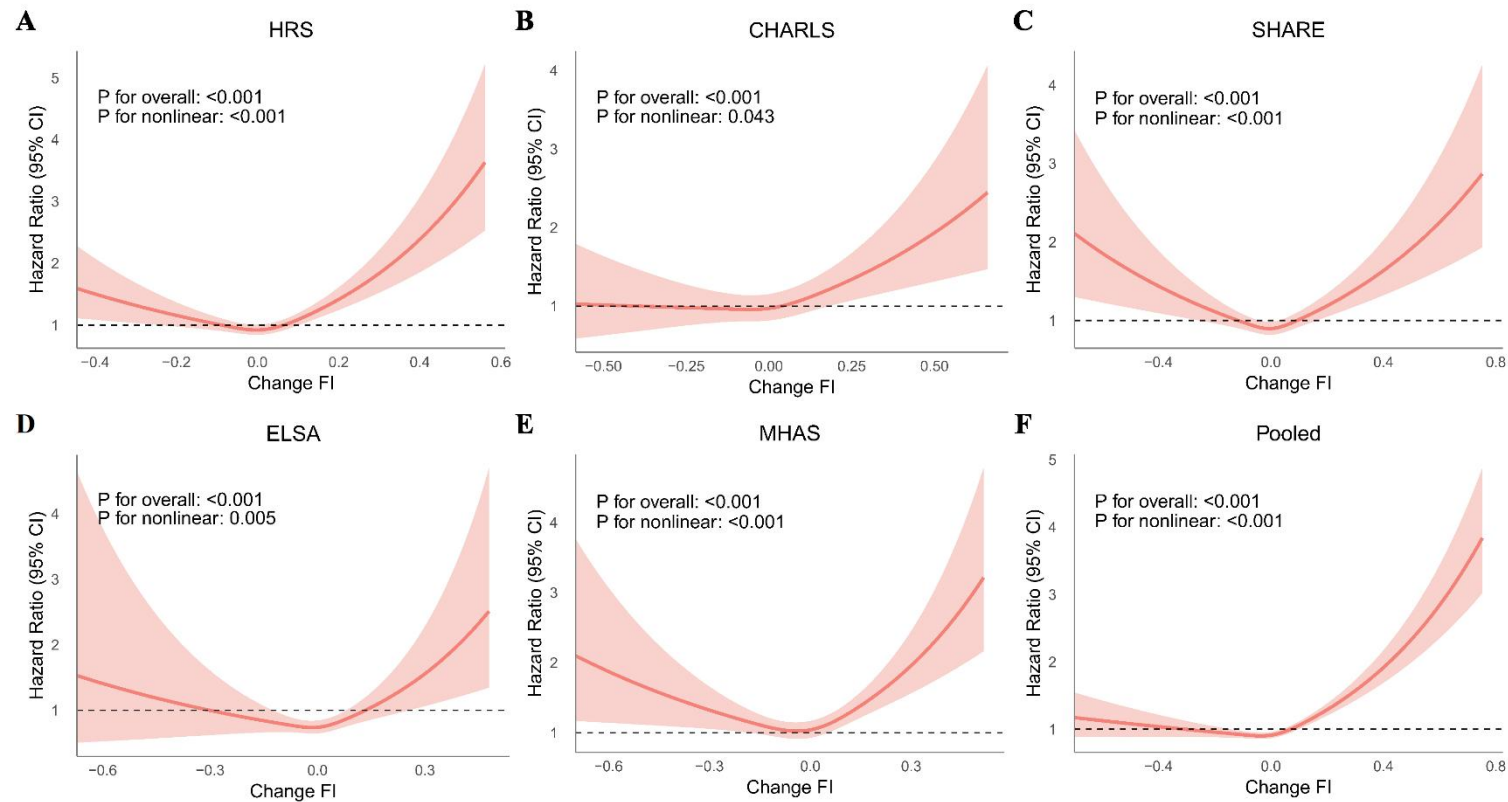
Supplementary Figure 17. RCS curve of the relationship between FI change and incident CVD in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since FI change was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).



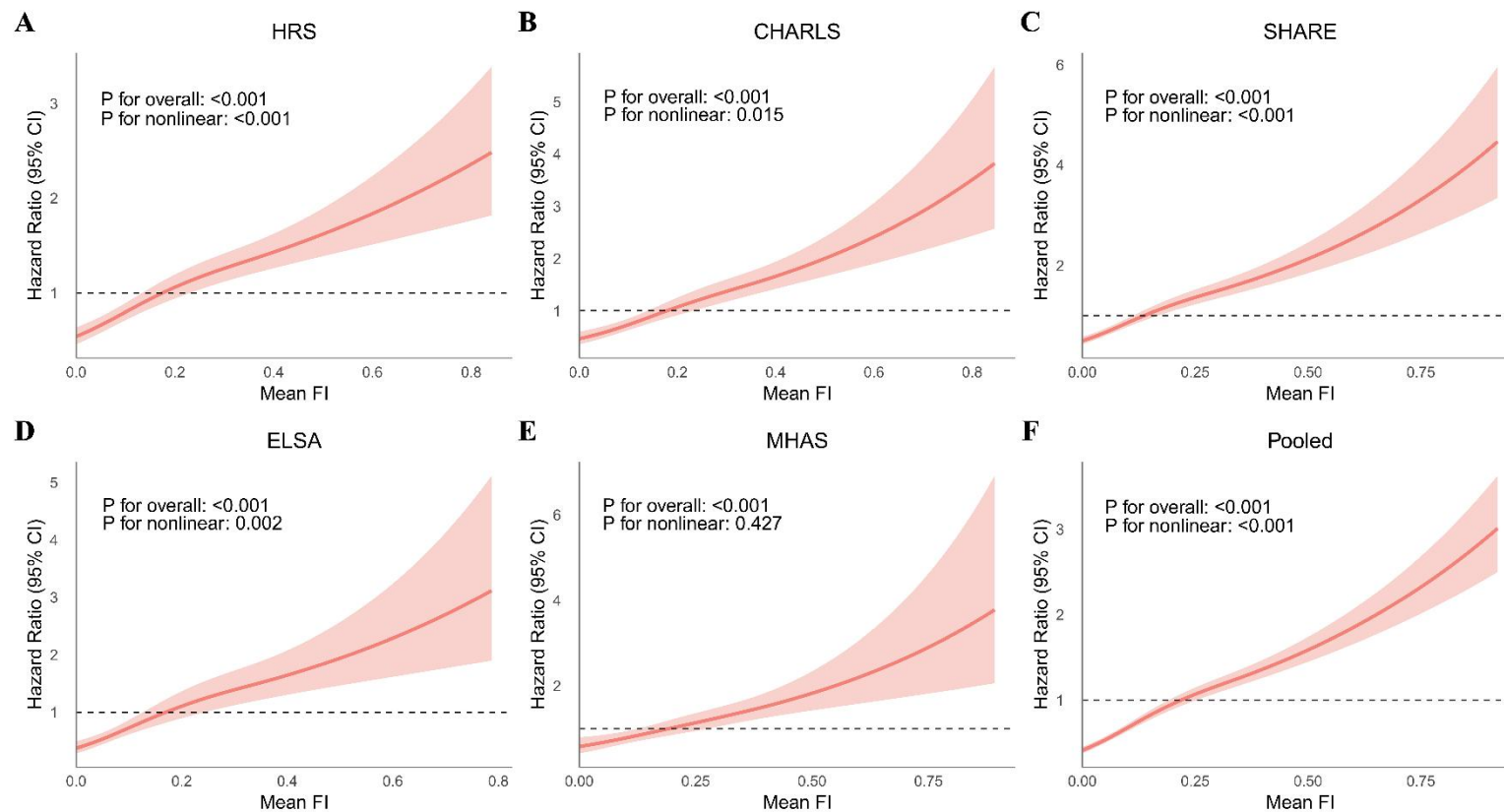
Supplementary Figure 18. RCS curve of the relationship between mean FI and incident heart disease in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since mean FI was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).



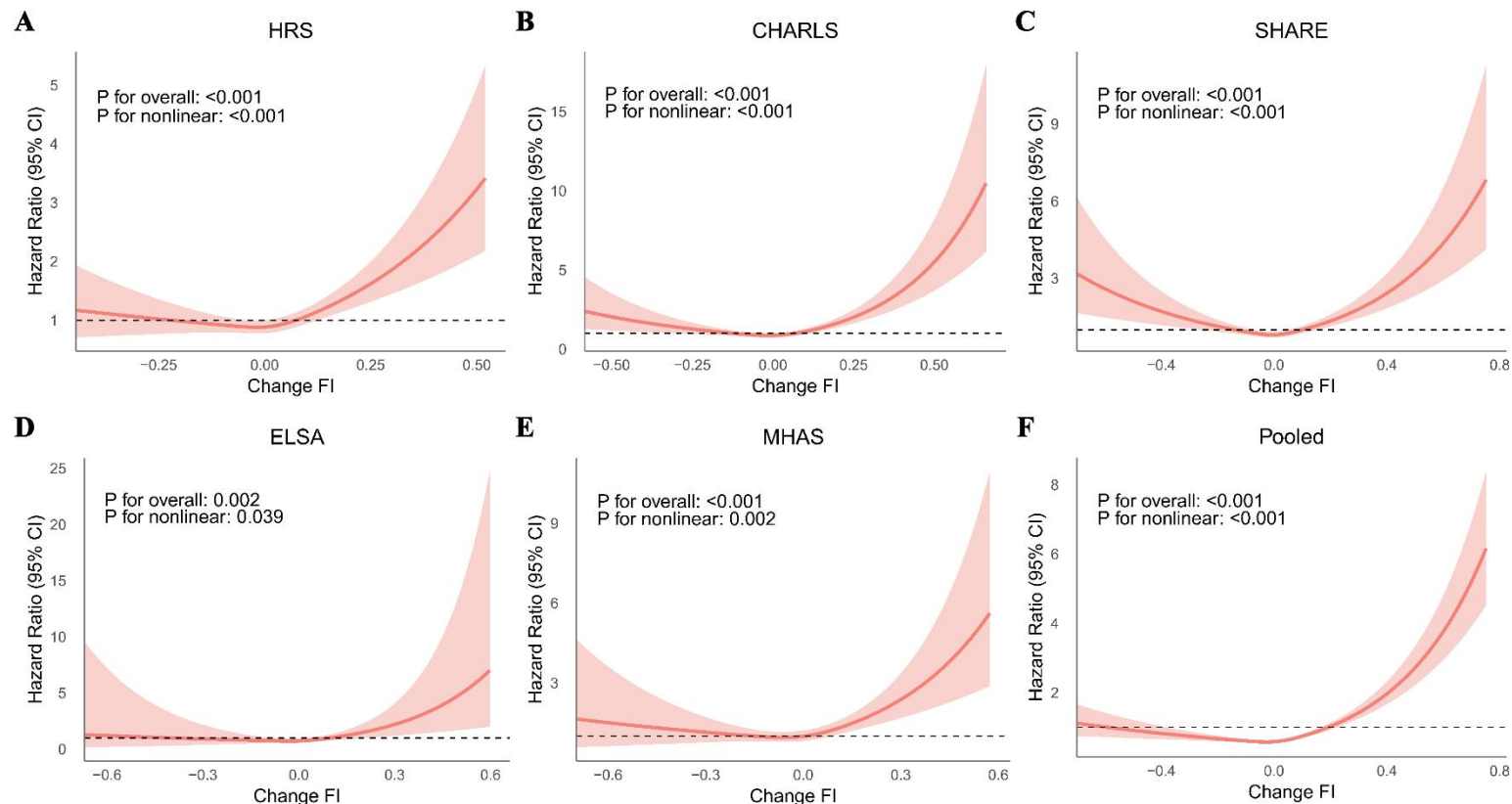
Supplementary Figure 19. RCS curve of the relationship between FI change and incident heart disease in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since FI change was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).



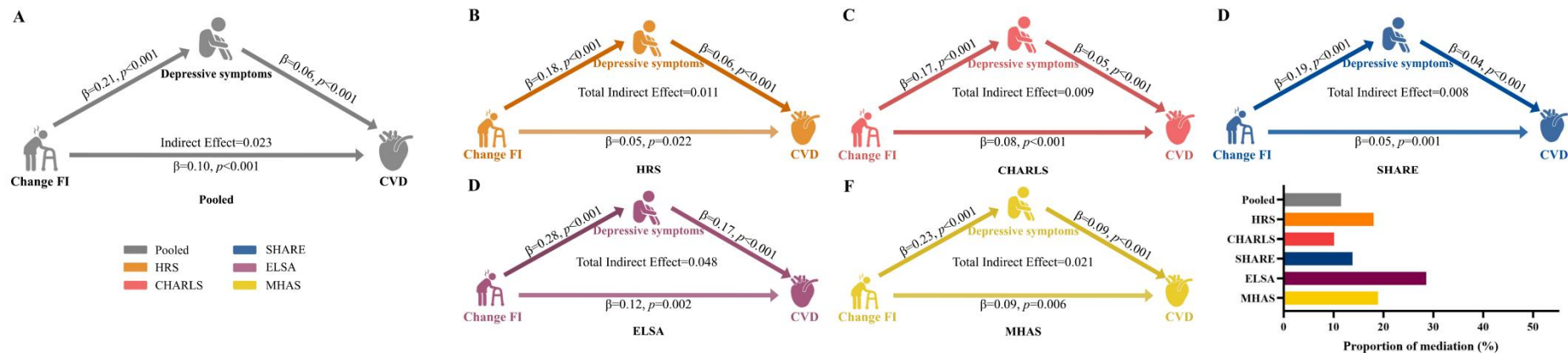
Supplementary Figure 20. RCS curve of the relationship between mean FI and incident stroke in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since mean FI was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).



Supplementary Figure 21. RCS curve of the relationship between FI change and incident stroke in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

FI: frailty index; CVD: cardiovascular disease; (A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study; (F) Pooled. All analyses were adjusted age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we further controlled the different country. Since FI change was calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity. The dashed horizontal line at $y = 1$ denotes the baseline hazard ratio ($HR = 1$).

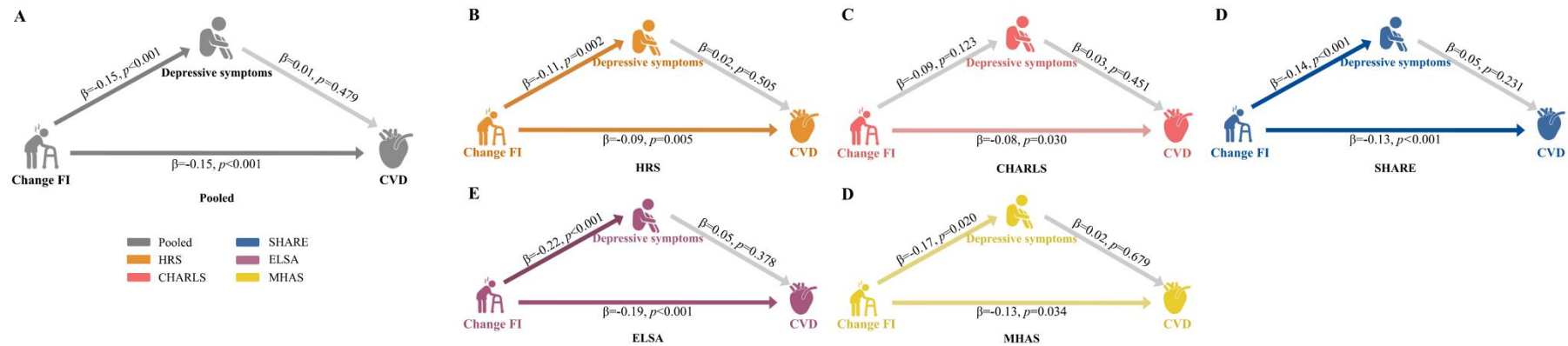


Supplementary Figure 22. Association between non-frailty to frailty, depressive symptoms and CVD.

CVD: cardiovascular disease; (A) Pooled; (B) HRS, Health and Retirement Study; (C) CHARLS, China Health and Retirement Longitudinal Study; (D) SHARE, Survey of Health, Ageing and Retirement in Europe; (E) ELSA, English Longitudinal Study of Ageing; (F) MHAS, Mexican Health and Aging Study.

All analyses have been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

In the analyses, HRS used changes in frailty status in 2000-2002, depressive symptoms in 2004, and incident CVD in 2006-2018; CHARLS used changes in frailty status in 2011-2013, depressive symptoms in 2015, and incident CVD in 2018; SHARE used changes in frailty status in 2011-2013, depressive symptoms in 2015, and incident CVD in 2017-2019; ELSA used changes in frailty status in 2004-2006, depressive symptoms in 2008, and incident CVD in 2010-2018; MHAS used changes in frailty status in 2001-2003, depressive symptoms in 2012, and incident CVD in 2015-2018.

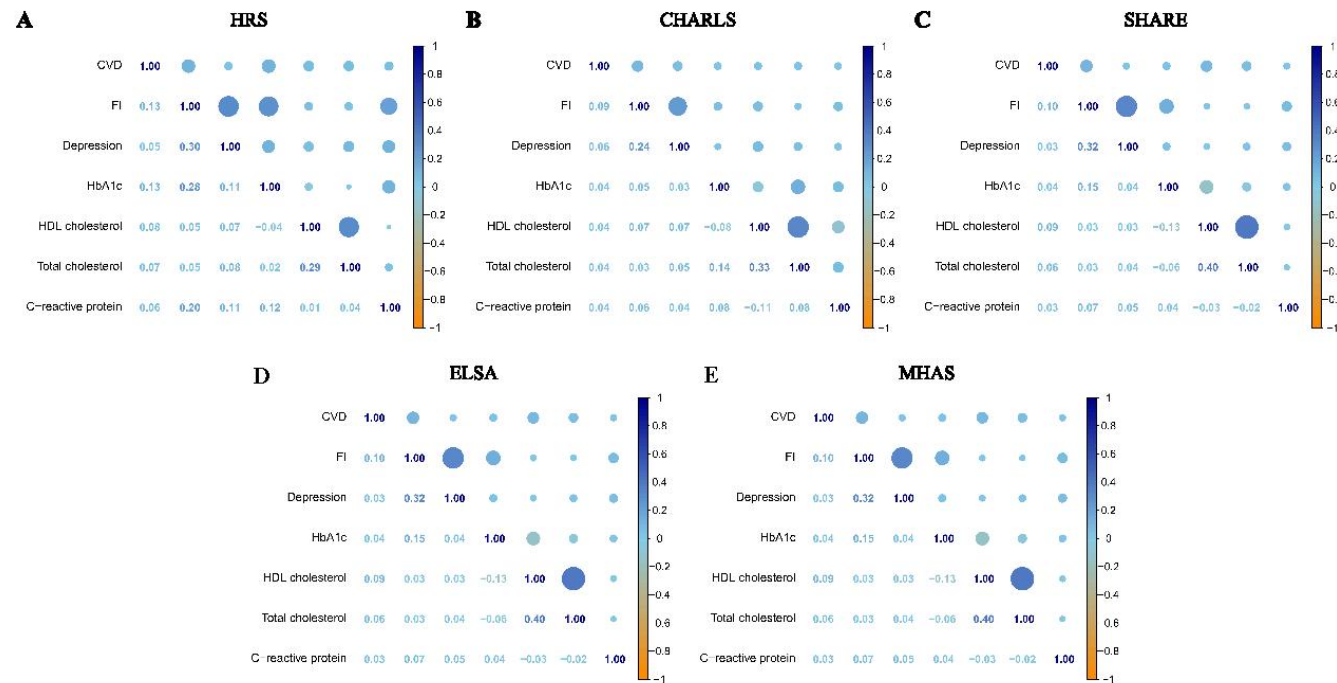


Supplementary Figure 23. Association between frailty to non-frailty, depressive symptoms and CVD.

CVD: cardiovascular disease; (A) Pooled; (B) HRS, Health and Retirement Study; (C) CHARLS, China Health and Retirement Longitudinal Study; (D) SHARE, Survey of Health, Ageing and Retirement in Europe; (E) ELSA, English Longitudinal Study of Ageing; (F) MHAS, Mexican Health and Aging Study.

All analyses have been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

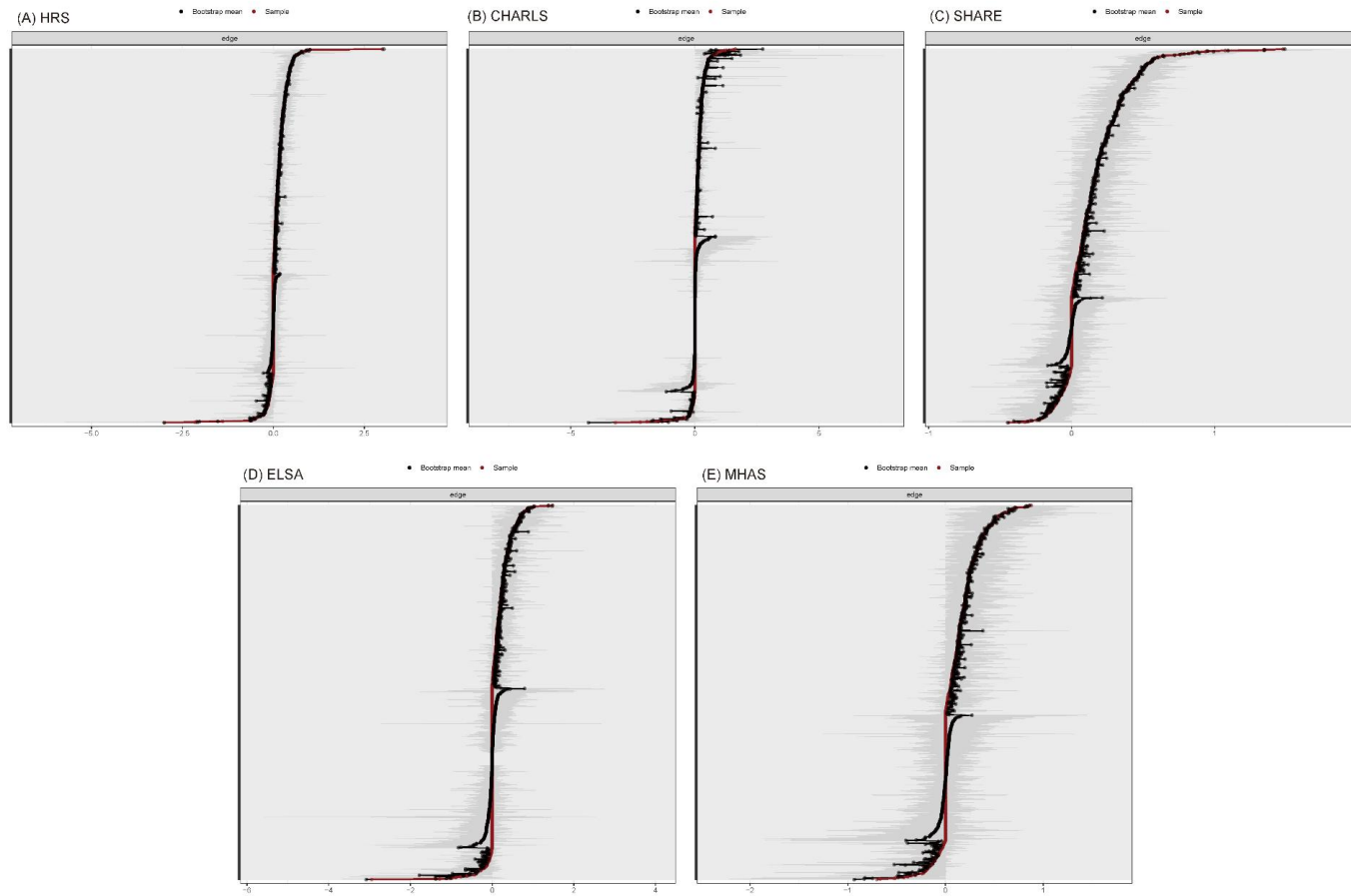
In the analyses, HRS used changes in frailty status in 2000-2002, depressive symptoms in 2004, and incident CVD in 2006-2018; CHARLS used changes in frailty status in 2011-2013, depressive symptoms in 2015, and incident CVD in 2018; SHARE used changes in frailty status in 2011-2013, depressive symptoms in 2015, and incident CVD in 2017-2019; ELSA used changes in frailty status in 2004-2006, depressive symptoms in 2008, and incident CVD in 2010-2018; MHAS used changes in frailty status in 2001-2003, depressive symptoms in 2012, and incident CVD in 2015-2018.



Supplementary Figure 24. Correlation analyses between baseline FI, depressive symptoms, blood markers, and incident CVD in HRS, CHARLS, SHARE, ELSA, and MHAS.

FI: frailty index; CVD: cardiovascular disease; (A) HRS, Health and Retirement Study; (B) CHARLS, China Health and Retirement Longitudinal Study; (C) SHARE, Survey of Health, Ageing and Retirement in Europe; (D) ELSA, English Longitudinal Study of Ageing; (E) MHAS, Mexican Health and Aging Study.

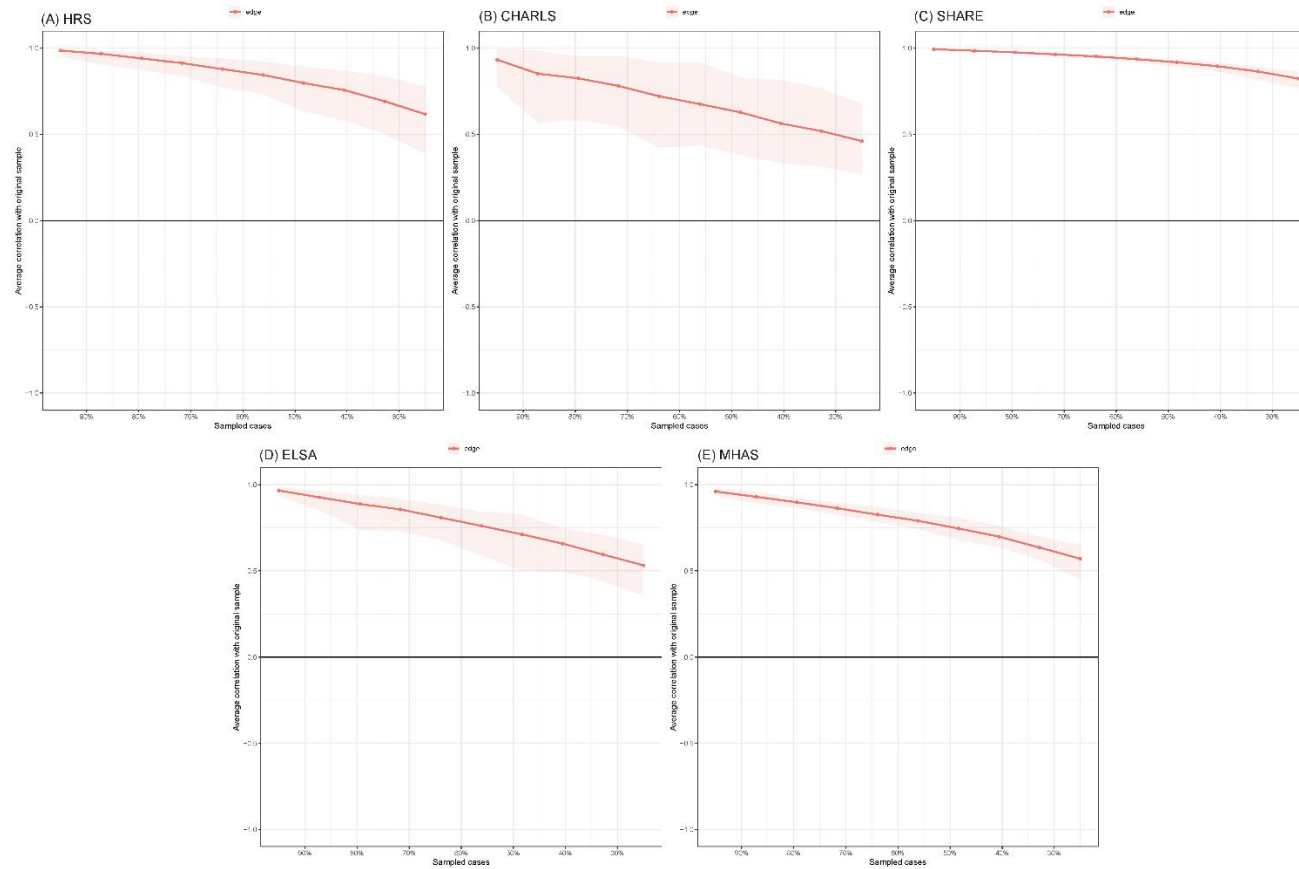
In the analyses, HRS used frailty status in 2000, depressive symptoms in 2002, blood markers in 2006, and incident CVD in 2008, 2010, 2012, 2014, 2016, and 2018; CHARLS used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2018; SHARE used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2017 and 2019; ELSA used frailty status in 2004, depressive symptoms in 2006, blood markers in 2008, and incident CVD in 2010, 2012, 2014, 2016, and 2018; MHAS used frailty status in 2001, depressive symptoms in 2003, blood markers in 2012, and incident CVD in 2015 and 2018. Blue indicates positive correlations, and orange indicates negative correlations.



Supplementary Figure 25. Bootstrapped confidence intervals of estimated edges across HRS, CHARLS, SHARE, ELSA, and MHAS.

(A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study.

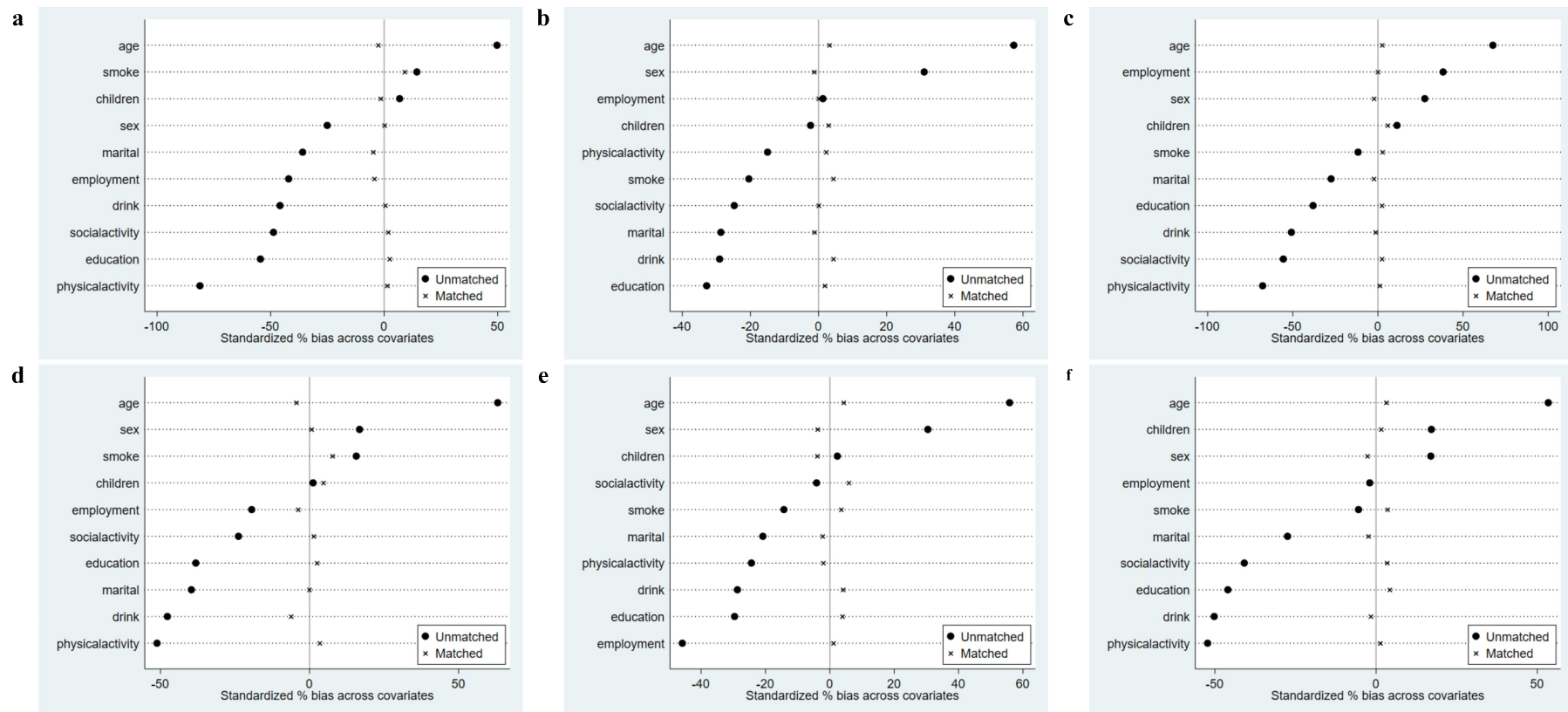
The red line depicted the sample edge weights and the gray bar depicted the bootstrapped confidence interval.



Supplementary Figure 26. Case-dropping analysis across HRS, CHARLS, SHARE, ELSA, and MHAS.

(A) HRS: Health and Retirement Study; (B) CHARLS: China Health and Retirement Longitudinal Study; (C) SHARE: Survey of Health, Ageing and Retirement in Europe; (D) ELSA: English Longitudinal Study of Ageing; (E) MHAS: Mexican Health and Aging Study.

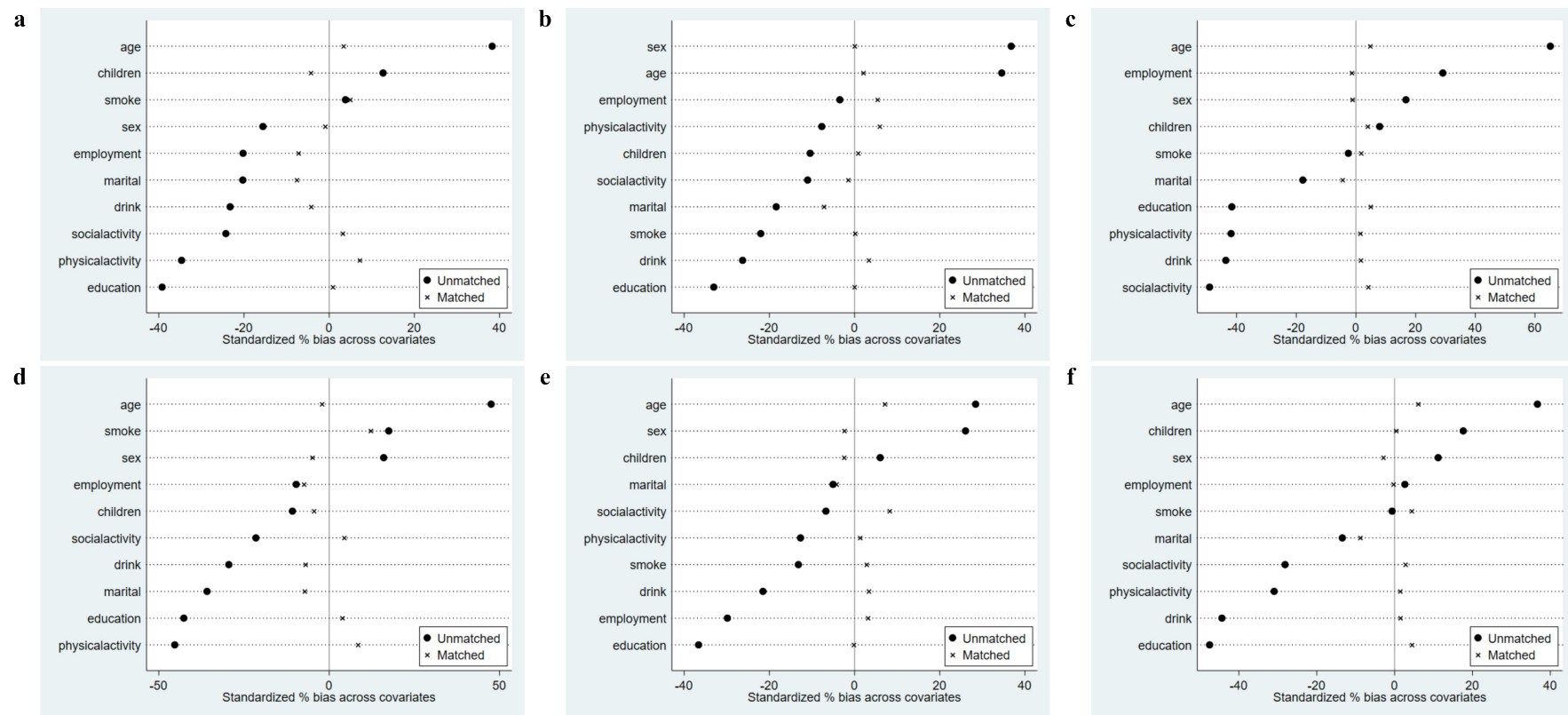
The x-axis represented the proportion of cases included, while the y-axis showed the correlation between the original centrality indices and the estimated centrality after excluding a portion of the cases.



Supplementary Figure 27. Comparison of covariates standardization deviation before and after PSM treatment based on baseline frailty status in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study; (f) Pooled.

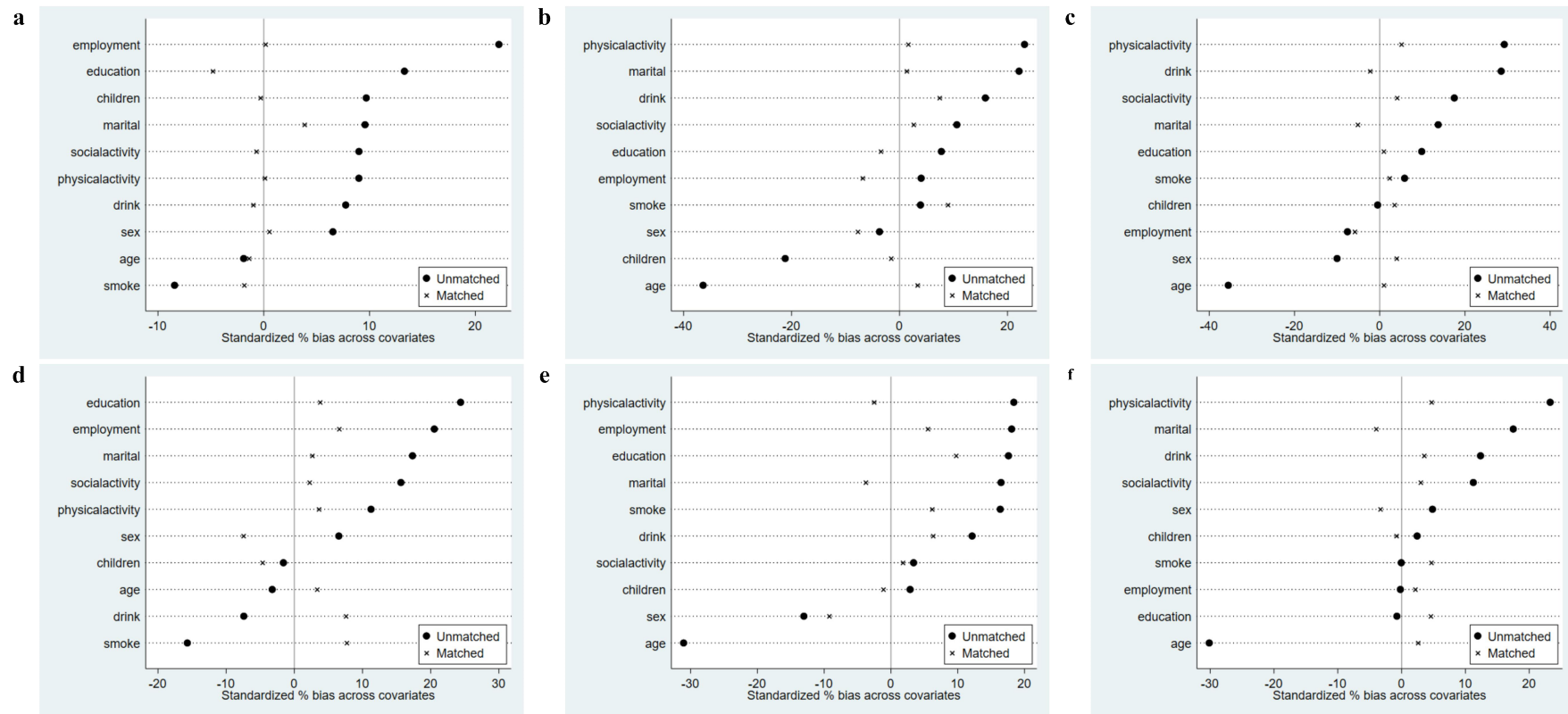
(b) The results showed that after the 1-to-3 PSM matching processing, there were no longer significant differences in covariates between baseline frail and non-frail samples in each cohort. The vertical line at $x = 0$ represents the reference line indicating no standardized deviation.



Supplementary Figure 28. Comparison of covariates standardization deviation before and after PSM treatment based on non-frail to frail in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study; (f) Pooled.

The results showed that after the 1-to-3 PSM matching processing, there were no longer significant differences in covariates between stable non-frail and non-frail to frail samples in each cohort. The vertical line at $x = 0$ represents the reference line indicating no standardized deviation.



Supplementary Figure 29. Comparison of covariates standardization deviation before and after PSM treatment based on frail to non-frail in HRS, CHARLS, SHARE, ELSA, MHAS and Pooled.

(a) HRS: Health and Retirement Study; (b) CHARLS: China Health and Retirement Longitudinal Study; (c) SHARE: Survey of Health, Ageing and Retirement in Europe; (d) ELSA: English Longitudinal Study of Ageing; (e) MHAS: Mexican Health and Aging Study; (f) Pooled.

The results showed that after the 1-to-3 PSM matching processing, there were no longer significant differences in covariates between stable frail and frail to non-frail samples in each cohort. The vertical line at $x = 0$ represents the reference line indicating no standardized deviation.

Supplementary Table 1. The items used to construct the frailty index in HRS, CHARLS, SHARE, ELSA, and MHAS.

No	Description of the items					Cut-off value
	HRS (2000-2018)	CHARLS (2011-2018)	SHARE (2011-2019)	ELSA (2004-2018)	MHAS (2001-2018)	
1	Self-reported diagnosed hypertension by doctors					Yes=1, No=0
2	Self-reported diagnosed diabetes by doctors					Yes=1, No=0
3	Self-reported diagnosed cancer by doctors					Yes=1, No=0
4	Self-reported diagnosed arthritis by doctors					Yes=1, No=0
5	Self-reported diagnosed chronic lung disease by doctors				Self-reported diagnosed respiratory disease by doctors	Yes=1, No=0
6	Self-reported diagnosed any emotional, nervous, or psychiatric problems by doctors	Unavailable	Diagnosed psychiatric problems by doctors	Unavailable	Yes=1, No=0	
7	Self-reported diagnosed memory-related disease, including Alzheimer’s disease or dementia, organic brain senility, or other serious memory impairment			Unavailable	Yes=1, No=0	
8	Self-reported general eyesight	Self-reported eyesight for seeing thing up close		Self-reported general eyesight		Blind, poor or fair=1, Good, very good or excellent=0
9	Self-reported hearing while wearing hearing aid or as usual					Deaf, poor or fair=1, Good, very good or excellent=0
10	Self-reported healthy status					Poor or fair=1, Good, very good or excellent=0
11	BADL: Any difficulty in dressing					Yes=1, No=0
12	BADL: Any difficulty in bathing or showering					Yes=1, No=0
13	BADL: Any difficulty in eating					Yes=1, No=0
14	BADL: Any difficulty in getting in/out bed					Yes=1, No=0
15	BADL: Any difficulty in using the toilet					Yes=1, No=0
16	IADL: Any difficulty in preparing meals					Yes=1, No=0

17	IADL: Any difficulty in shopping	Yes=1, No=0
18	IADL: Any difficulty in managing money	Yes=1, No=0
19	IADL: Any difficulty in taking medications	Yes=1, No=0
20	Mobility: Any difficulty in walking 1 block	Yes=1, No=0
21	Mobility: Any difficulty in getting up from a chair after sitting for long periods	Yes=1, No=0
22	Mobility: Any difficulty in climbing several flights of stairs without resting	Yes=1, No=0
23	Mobility: Any difficulty in stooping, kneeling or crouching	Yes=1, No=0
24	Mobility: Any difficulty in reaching arms above shoulder level	Yes=1, No=0
25	Mobility: Any difficulty in lifting or carrying weights over 10 pounds	Yes=1, No=0
26	Mobility: Any difficulty in picking up a coin from table	Yes=1, No=0
27	Cognition: (total score - (immediate and delayed word recall + date naming)) / total score	Continuous, from 0 to 1

HRS, Health and Retirement Study; CHARLS, China Health and Retirement Longitudinal Study; SHARE, Survey of Health, Ageing and Retirement in Europe; ELSA, English Longitudinal Study of Ageing; MHAS, Mexican Health and Aging Study.

Cognition test consists of three components, including immediate, delayed word recall, and date naming. For word recall, participants are required to recite 10 words in HRS, CHARLS, SHARE, and ELSA; and 8 words in MHAS. For date naming, participants are asked whether they could remember the date of that day (day of week, day of month, month, and year in HRS, CHARLS, SHARE, and ELSA; and day of month, month, and year in MHAS). 1 is given for each right answer, and the cognition score is calculated by the formula: (total score-(immediate and delayed word recall + date naming))/total score. Total score refers to the theoretical maximum score of all tests. Hence, a higher cognition score indicated lower cognition function.

It should be noted that since 2011 was the baseline for the analysis of the SHARE cohort, there was no diagnosis data of emotional, nervous or psychiatric problems in this survey, and this item was not included in the follow-up to maintain the statistical consistency. As a result, the total number of items for calculating the frailty index of SHARE has changed from 27 to 26.

Supplementary Table 2. The items used to diagnose depressive symptoms in HRS, CHARLS, SHARE, ELSA, and MHAS.

Category	CESD-8	CESD-9	CSED-10	EUROD-12
Items	Please tell me if each of the following was true for you much of the time during the past week. Q1: I felt depressed. Q2: I felt that everything I did was an effort. Q3: My sleep was restless. Q4: I was happy. Q5: I felt lonely. Q6: I enjoyed life. Q7: I felt sad. Q8: I could not get “going”.	Please tell me if each of the following was true for you majority of the time during the past week. Q1: I felt depressed. Q2: I felt that everything I did was an effort. Q3: My sleep was restless. Q4: I was happy. Q5: I felt lonely. Q6: I enjoyed life. Q7: I felt sad. Q8: I felt tired. Q9: I felt very energetic.	Please tell me how you have felt and behaved during the past week. Q1: I was bothered by things that don't usually bother me. Q2: I had trouble keeping my mind on what I was doing. Q3: I felt depressed. Q4: I felt everything I did was an effort. Q5: I felt hopeful about the future. Q6: I felt fearful. Q7: My sleep was restless. Q8: I was happy. Q9: I felt lonely. Q10: I could not get “going”.	Please tell me if each of the following was true for you much of the time in the last month. Q1: Have you been sad or depressed? Q2: Have you hoped for the future? Q3: Have you felt that you would rather be dead? Q4: Do you tend to blame yourself or feel guilty about anything? Q5: Have you had trouble sleeping recently? Q6: Do you have any interest in things? Q7: Have you been irritable recently? Q8: Have you been eating more or less than usual? Q9: Have you had too little energy to do the things you wanted to do? Q10: Can you concentrate on a television programme, film or radio programme? Q11: Have you enjoyed doing any activity recently? Q12: Have you cried at all?

Response	Yes=1, No=0	Yes=1, No=0	Rarely or none of the time (<1 day)=0, Some or a little of the time (1-2 days)=1, Occasionally or a moderate amount of the time (3-4 days)=2, Most or all of the time (5-7 days)=3.	Yes=1, No=0
Scores	Range from 0 to 8	Range from 0 to 9	Range from 0 to 30	Range from 0 to 12
Cutoff	A score of 3 or higher	A score of 5 or higher	A score of 10 or higher	A score of 4 or higher
Surveys	HRS, ELSA	MHAS	CHARLS	SHARE

HRS, Health and Retirement Study; CHARLS, China Health and Retirement Longitudinal Study; SHARE, Survey of Health, Ageing and Retirement in Europe; ELSA, English Longitudinal Study of Ageing; MHAS, Mexican Health and Aging Study.

Items Q4 and Q6 in the CESD-8 scale, Q4, Q6 and Q9 in the CESD-9 scale, Q5, Q8 in the CESD-10 scale, and Q2, Q6, Q10 and Q11 in the EURO-D-12 scale are positive. In this paper, these items are assigned in reverse, and then added with other items to calculate the final total score.

Supplementary Table 3. Definitions of covariates.

Variables	HRS	CHARLS	SHARE	ELSA	MHAS
sex	1 = Male, 2 = Female				
Age	Continuous variable in the model analysis. Categorical variable as a subgroup analysis: 0 = 50~64, 1 = 65years and above				
Education	0 = Below high school, 1 = High school, 2 = Above high school				
Employment	<i>Are you working now, temporarily laid off, unemployed and looking for work, disabled and unable to work, retired, or what?</i> 0 = Unemployed, 1 = Currently working or retired	<i>What sort of work do you do?</i> 0 = Unemployed, 1 = Currently working or retired	<i>In general, which of the following best describes your current employment situation?</i> 0 = Unemployed, 1 = Currently working or retired	<i>Which one of these, would you say best describes your current situation?</i> 0 = Unemployed, 1 = Currently working or retired	<i>Last week did you work, look for work, retired, or what?</i> 0 = Unemployed, 1 = Currently working or retired
Marital status	0 = Others (separated, divorced, widowed, or never married), 1 = Married (first married, remarried, or civil partner)				
Co-residence with children	<i>Do any of your children live with you?</i> 0 = No, 1 = Yes	<i>Does your children normally live with you?</i> 0 = No, 1 = Yes	<i>Where does your children live?</i> 0 = No, 1 = Yes (live together)	<i>On average, how often do you do each of the following with any of your children?</i> 0 = No, 1 = Yes (three or more times a week)	<i>Do you live with any of your children?</i> 0 = No, 1 = Yes

Smoking	0 = No (never smoked, or ever smoked but stopped at present), 1 = Yes (smoke at present)				
Drinking	0 = No (never drink), 1 = Yes (drink any cups of wine)				
Social activity	<i>Have you participated in the following activities last month (Do volunteer work; Do charity work; Go to a sport, social, or other club; Attend non-religious organizations)?</i> 0 = No, 1 = Yes (at least one social activity)	<i>Have you done any of these activities in the last month (Interacted with friends; Played Ma-jong, played chess, played cards, or went to community club; Went to a sport, social, or other kind of club; Took part in a community-related organization; Done voluntary or charity work)?</i> 0 = No, 1 = Yes (at least one social activity)	<i>Have you done any of these activities in the past twelve months (Done voluntary or charity work; Gone to a sport, social or other kind of club; Taken part in activities of a religious organization; Taken part in a political or community-related organization)?</i> 0 = No, 1 = Yes (at least one social activity)	<i>Are you a member of any of these organisations, clubs or societies (Political party; Church or other religious groups; Charitable associations; Social clubs; Sports clubs, gyms, exercise classes; Any other organisations, clubs or societies)?</i> 0 = No, 1 = Yes (at least one social activity)	<i>If you did some of these activities during the past year (Work as a volunteer or help a non-profit organization without pay or compensation; Attend a sporting or social club)?</i> 0 = No, 1 = Yes (at least one social activity)
Physical activity	<i>On average over the last 12 months, have you participated in vigorous physical activity or exercise three times a week or more?</i> 0 = No, 1 = Yes	<i>Are you do vigorous physical activities for 10+ minutes at least 1 day a week?</i> 0 = No, 1 = Yes	<i>How often do you take part in vigorous sports or activities?</i> 0 = No (less than once a week), 1 = Yes (at least once a week)	<i>During the last two years, have you exercised or done hard physical work three or more times a week?</i> 0 = No, 1 = Yes	

HRS, Health and Retirement Study; CHARLS, China Health and Retirement Longitudinal Study; SHARE, Survey of Health, Ageing and Retirement in Europe; ELSA, English Longitudinal Study of Ageing; MHAS, Mexican Health and Aging Study.

Supplementary Table 4. The proportion of frailty status and CVD across countries.

		Frailty status	CVD
HRS	United States	2,217 (17.56%)	4,763 (37.73%)
CHARLS	China	2,177 (21.16%)	1,826 (17.75%)
SHARE	Austria	328 (9.62%)	576 (16.90%)
	Belgium	425 (12.15%)	499 (14.26%)
	Czech Republic	444 (12.91%)	630 (18.32%)
	Denmark	125 (7.20%)	274 (15.78%)
	Estonia	782 (18.57%)	909 (21.59%)
	France	459 (12.91%)	545 (15.33%)
	Germany	119 (12.91%)	181 (19.63%)
	Hungary	219 (18.75%)	159 (13.61%)
	Italy	423 (17.46%)	423 (17.46%)
	Netherlands	126 (6.53%)	177 (9.18%)
	Poland	207 (21.54%)	253 (26.33%)
	Portugal	309 (24.22%)	179 (14.03%)
	Slovenia	271 (14.74%)	353 (19.20%)
	Spain	584 (22.57%)	431 (16.66%)
	Sweden	87 (6.69%)	185 (14.23%)
	Switzerland	116 (4.29%)	313 (11.58%)
ELSA	England	1,204 (16.79%)	1,962 (27.35%)
MHAS	Mexico	2,778 (28.19%)	1,550 (15.73%)

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Supplementary Table 5. The association of baseline frailty status with risks of incident CVD across countries.

		HR (95%CI)	<i>P</i>
HRS	United States	1.51 (1.40, 1.63)	<0.001
CHARLS	China	1.54 (1.38, 1.71)	<0.001
SHARE	Austria	1.70 (1.36, 2.13)	<0.001
	Belgium	1.79 (1.42, 2.25)	<0.001
	Czech Republic	1.50 (1.22, 1.85)	<0.001
	Denmark	2.04 (1.41, 2.93)	<0.001
	Estonia	1.68 (1.44, 1.96)	<0.001
	France	1.53 (1.22, 1.91)	<0.001
	Germany	1.79 (1.21, 2.63)	0.003
	Hungary	1.55 (1.07, 2.25)	0.021
	Italy	1.49 (1.17, 1.90)	0.001
	Netherlands	1.99 (1.24, 3.19)	0.004
	Poland	1.58 (1.19, 2.09)	0.002
	Portugal	1.79 (1.30, 2.46)	<0.001
	Slovenia	1.60 (1.23, 2.08)	<0.001
	Spain	1.64 (1.31, 2.06)	<0.001
	Sweden	1.85 (1.18, 2.91)	0.007
	Switzerland	1.95 (1.27, 2.99)	0.002
ELSA	England	1.77 (1.59, 1.98)	<0.001
MHAS	Mexico	1.63 (1.46, 1.82)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 6. The association of baseline frailty status with risks of incident heart disease.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.62 (1.51, 1.75)	<0.001	1.50 (1.33, 1.68)	<0.001	1.79 (1.68, 1.92)	<0.001	1.78 (1.59, 1.99)	<0.001	1.64 (1.45, 1.84)	<0.001	1.66 (1.60, 1.73)	<0.001
Model 2	1.68 (1.56, 1.81)	<0.001	1.52 (1.35, 1.71)	<0.001	1.76 (1.65, 1.88)	<0.001	1.78 (1.59, 2.00)	<0.001	1.63 (1.44, 1.84)	<0.001	1.68 (1.61, 1.75)	<0.001
Model 3	1.68 (1.56, 1.81)	<0.001	1.53 (1.36, 1.72)	<0.001	1.75 (1.64, 1.87)	<0.001	1.78 (1.58, 1.99)	<0.001	1.63 (1.44, 1.83)	<0.001	1.68 (1.62, 1.75)	<0.001
Model 4	1.55 (1.43, 1.68)	<0.001	1.51 (1.34, 1.70)	<0.001	1.64 (1.53, 1.76)	<0.001	1.76 (1.57, 1.98)	<0.001	1.62 (1.43, 1.82)	<0.001	1.61 (1.54, 1.68)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 7. The association of baseline frailty status with risks of incident heart disease across countries.

		HR (95%CI)	<i>P</i>
HRS	United States	1.55 (1.43, 1.68)	<0.001
CHARLS	China	1.51 (1.34, 1.70)	<0.001
SHARE	Austria	1.85 (1.46, 2.35)	<0.001
	Belgium	1.74 (1.36, 2.22)	<0.001
	Czech Republic	1.43 (1.14, 1.78)	0.002
	Denmark	1.98 (1.35, 2.90)	<0.001
	Estonia	1.53 (1.31, 1.79)	<0.001
	France	1.83 (1.45, 2.30)	<0.001
	Germany	1.74 (1.13, 2.66)	0.011
	Hungary	1.51 (1.01, 2.26)	0.045
	Italy	1.44 (1.11, 1.86)	0.006
	Netherlands	1.92 (1.15, 3.23)	0.013
	Poland	1.58 (1.18, 2.12)	0.002
	Portugal	1.59 (1.12, 2.25)	0.009
	Slovenia	1.64 (1.23, 2.18)	0.001
	Spain	1.62 (1.27, 2.05)	<0.001
	Sweden	2.05 (1.26, 3.33)	0.004
	Switzerland	1.88 (1.19, 2.97)	0.007
ELSA	England	1.76 (1.57, 1.98)	<0.001
MHAS	Mexico	1.62 (1.43, 1.82)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 8. The association of baseline frailty status with risks of incident stroke.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.71 (1.54, 1.90)	<0.001	1.89 (1.63, 2.20)	<0.001	2.16 (1.97, 2.37)	<0.001	2.22 (1.82, 2.69)	<0.001	1.66 (1.36, 2.02)	<0.001	1.89 (1.78, 2.00)	<0.001
Model 2	1.65 (1.48, 1.83)	<0.001	1.92 (1.65, 2.23)	<0.001	2.11 (1.93, 2.32)	<0.001	2.13 (1.75, 2.60)	<0.001	1.62 (1.33, 1.97)	<0.001	1.86 (1.76, 1.97)	<0.001
Model 3	1.63 (1.47, 1.82)	<0.001	1.93 (1.66, 2.24)	<0.001	2.10 (1.91, 2.30)	<0.001	2.14 (1.75, 2.60)	<0.001	1.62 (1.33, 1.97)	<0.001	1.86 (1.75, 1.97)	<0.001
Model 4	1.54 (1.38, 1.72)	<0.001	1.92 (1.65, 2.23)	<0.001	1.94 (1.77, 2.14)	<0.001	1.95 (1.60, 2.39)	<0.001	1.59 (1.31, 1.95)	<0.001	1.76 (1.66, 1.86)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 9. The association of baseline frailty status with risks of incident stroke across countries.

		HR (95%CI)	<i>P</i>
HRS	United States	1.54 (1.38, 1.72)	<0.001
CHARLS	China	1.92 (1.65, 2.23)	<0.001
SHARE	Austria	1.88 (1.42, 2.49)	<0.001
	Belgium	2.12 (1.51, 2.97)	<0.001
	Czech Republic	1.64 (1.23, 2.20)	0.001
	Denmark	2.62 (1.47, 4.68)	0.001
	Estonia	1.78 (1.42, 2.24)	<0.001
	France	1.55 (1.10, 2.18)	0.013
	Germany	2.29 (1.28, 4.10)	0.005
	Hungary	2.04 (1.15, 3.63)	0.015
	Italy	1.55 (1.03, 2.31)	0.034
	Netherlands	2.62 (1.34, 5.13)	0.005
	Poland	1.68 (1.03, 2.72)	0.036
	Portugal	2.54 (1.56, 4.14)	<0.001
	Slovenia	2.16 (1.50, 3.11)	<0.001
	Spain	1.69 (1.17, 2.47)	0.006
	Sweden	2.76 (1.57, 4.82)	<0.001
	Switzerland	2.51 (1.29, 4.85)	0.006
ELSA	England	1.95 (1.60, 2.39)	<0.001
MHAS	Mexico	1.59 (1.31, 1.95)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 10. The association of changes in frailty status with risks of incident CVD in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.16 (1.02, 1.31)	0.022	1.87 (1.50, 2.34)	<0.001	1.32 (1.15, 1.52)	<0.001	1.59 (1.20, 2.10)	0.001	1.47 (1.22, 1.77)	<0.001	1.34 (1.24, 1.44)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.73 (0.61, 0.88)	0.001	0.54 (0.40, 0.74)	<0.001	0.74 (0.61, 0.88)	0.001	0.51 (0.34, 0.76)	0.001	0.74 (0.60, 0.92)	0.006	0.70 (0.63, 0.77)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 11. The association of mean FI, FI change with risks of incident CVD in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.38 (1.24, 1.53)	<0.001	2.16 (1.64, 2.85)	<0.001	1.28 (1.13, 1.45)	<0.001	1.47 (1.18, 1.83)	0.001	1.28 (1.06, 1.55)	0.010	1.39 (1.30, 1.49)	<0.001
T3	1.73 (1.56, 1.91)	<0.001	2.95 (2.25, 3.86)	<0.001	1.55 (1.38, 1.76)	<0.001	1.85 (1.49, 2.29)	<0.001	1.76 (1.47, 2.11)	<0.001	1.74 (1.63, 1.86)	<0.001
T4	2.15 (1.94, 2.39)	<0.001	4.42 (3.39, 5.77)	<0.001	2.22 (1.97, 2.51)	<0.001	2.53 (2.03, 3.15)	<0.001	2.34 (1.95, 2.81)	<0.001	2.35 (2.20, 2.51)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.89 (0.81, 0.98)	0.020	1.05 (0.85, 1.30)	0.650	0.88 (0.80, 0.98)	0.023	0.95 (0.79, 1.16)	0.621	0.82 (0.69, 0.98)	0.027	0.89 (0.84, 0.95)	<0.001
T3	0.93 (0.85, 1.02)	0.123	0.90 (0.72, 1.12)	0.335	0.90 (0.81, 1.00)	0.060	0.95 (0.78, 1.15)	0.586	0.96 (0.81, 1.13)	0.622	0.92 (0.87, 0.97)	0.004
T4	1.16 (1.06, 1.26)	0.001	1.46 (1.20, 1.78)	<0.001	1.15 (1.04, 1.26)	0.005	1.28 (1.07, 1.53)	0.006	1.32 (1.13, 1.54)	<0.001	1.20 (1.14, 1.27)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 12. The association of changes in frailty status with risks of incident heart disease in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.16 (1.02, 1.33)	0.022	1.46 (1.23, 1.73)	<0.001	1.23 (1.06, 1.43)	0.008	1.56 (1.16, 2.10)	0.003	1.93 (1.59, 2.34)	<0.001	1.36 (1.26, 1.46)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.71 (0.59, 0.87)	0.001	0.68 (0.54, 0.86)	0.002	0.70 (0.58, 0.84)	<0.001	0.44 (0.28, 0.68)	<0.001	0.52 (0.41, 0.66)	<0.001	0.65 (0.58, 0.72)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 13. The association of mean FI, FI change with risks of incident heart disease in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.33 (1.20, 1.49)	<0.001	1.68 (1.38, 2.03)	<0.001	1.31 (1.15, 1.50)	<0.001	1.34 (1.07, 1.67)	0.012	1.30 (1.06, 1.60)	0.012	1.37 (1.27, 1.46)	<0.001
T3	1.78 (1.60, 1.98)	<0.001	2.33 (1.94, 2.81)	<0.001	1.60 (1.40, 1.83)	<0.001	1.60 (1.28, 2.01)	<0.001	1.75 (1.43, 2.13)	<0.001	1.76 (1.65, 1.89)	<0.001
T4	2.21 (1.98, 2.47)	<0.001	2.89 (2.39, 3.49)	<0.001	2.38 (2.08, 2.71)	<0.001	2.51 (2.00, 3.15)	<0.001	2.37 (1.94, 2.88)	<0.001	2.39 (2.23, 2.55)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.89 (0.81, 0.99)	0.028	0.94 (0.80, 1.10)	0.441	0.91 (0.81, 1.01)	0.086	0.94 (0.77, 1.15)	0.531	0.85 (0.71, 1.03)	0.102	0.90 (0.84, 0.95)	0.001
T3	0.97 (0.88, 1.07)	0.501	0.92 (0.78, 1.08)	0.318	0.94 (0.84, 1.04)	0.233	0.95 (0.78, 1.16)	0.597	1.01 (0.84, 1.21)	0.954	0.95 (0.90, 1.01)	0.100
T4	1.18 (1.08, 1.30)	<0.001	1.24 (1.06, 1.44)	0.006	1.14 (1.03, 1.26)	0.013	1.22 (1.01, 1.47)	0.038	1.35 (1.14, 1.60)	<0.001	1.21 (1.14, 1.28)	<0.001

FI: frailty index; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 14. The association of changes in frailty status with risks of incident stroke in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.33 (1.11, 1.58)	0.001	1.83 (1.44, 2.31)	<0.001	1.81 (1.49, 2.20)	<0.001	2.01 (1.27, 3.19)	0.003	2.96 (2.20, 3.99)	<0.001	1.68 (1.52, 1.87)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.67 (0.51, 0.87)	0.003	0.53 (0.39, 0.72)	<0.001	0.76 (0.59, 0.98)	0.033	0.26 (0.10, 0.67)	0.005	0.62 (0.42, 0.92)	0.018	0.63 (0.55, 0.73)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 15. The association of mean FI, FI change with risks of incident stroke in HRS, CHARLS, SHARE, ELSA, MHAS, and Pooled.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.40 (1.19, 1.64)	<0.001	2.03 (1.55, 2.66)	<0.001	1.48 (1.20, 1.84)	<0.001	1.70 (1.07, 2.69)	0.025	1.71 (1.17, 2.50)	0.006	1.55 (1.39, 1.72)	<0.001
T3	1.75 (1.49, 2.05)	<0.001	2.45 (1.87, 3.20)	<0.001	2.04 (1.66, 2.50)	<0.001	2.22 (1.41, 3.49)	0.001	2.15 (1.48, 3.12)	<0.001	1.97 (1.77, 2.19)	<0.001
T4	2.26 (1.91, 2.66)	<0.001	4.50 (3.47, 5.84)	<0.001	3.03 (2.46, 3.73)	<0.001	2.81 (1.77, 4.45)	<0.001	2.96 (2.05, 4.26)	<0.001	2.82 (2.54, 3.13)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.92 (0.80, 1.07)	0.268	0.86 (0.69, 1.08)	0.195	0.79 (0.67, 0.94)	0.008	1.04 (0.71, 1.53)	0.824	1.20 (0.85, 1.69)	0.307	0.89 (0.81, 0.98)	0.016
T3	0.94 (0.82, 1.08)	0.396	0.95 (0.76, 1.18)	0.631	0.85 (0.72, 1.00)	0.050	0.99 (0.68, 1.46)	0.978	1.36 (0.97, 1.90)	0.076	0.94 (0.86, 1.03)	0.185
T4	1.19 (1.04, 1.36)	0.011	1.44 (1.18, 1.76)	<0.001	1.17 (1.02, 1.35)	0.030	1.66 (1.19, 2.33)	0.003	2.08 (1.53, 2.83)	<0.001	1.30 (1.20, 1.41)	<0.001

FI: frailty index; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 16. Correlation results between baseline FI, depressive symptoms, blood markers, and incident CVD in HRS.

Variables	CVD	FI	Depression	HbA1c	HDL cholesterol	Total cholesterol	C-reactive protein
CVD	1.000						
FI	0.127 (<i>P</i> < 0.001)	1.000					
Depression	0.046 (<i>P</i> = 0.020)	0.303 (<i>P</i> < 0.001)	1.000				
HbA1c	0.129 (<i>P</i> < 0.001)	0.278 (<i>P</i> < 0.001)	0.113 (<i>P</i> < 0.001)	1.000			
HDL cholesterol	0.077 (<i>P</i> < 0.001)	0.050 (<i>P</i> = 0.011)	0.070 (<i>P</i> < 0.001)	-0.043 (<i>P</i> = 0.032)	1.000		
Total cholesterol	0.072 (<i>P</i> < 0.001)	0.048 (<i>P</i> = 0.015)	0.082 (<i>P</i> < 0.001)	0.016 (<i>P</i> = 0.421)	0.294 (<i>P</i> < 0.001)	1.000	
C-reactive protein	0.056 (<i>P</i> = 0.005)	0.204 (<i>P</i> < 0.001)	0.113 (<i>P</i> < 0.001)	0.122 (<i>P</i> < 0.001)	0.011 (<i>P</i> = 0.569)	0.040 (<i>P</i> = 0.043)	1.000

FI: frailty index; CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

In the analyses, HRS used frailty status in 2000, depressive symptoms in 2002, blood markers in 2006, and incident CVD in 2008, 2010, 2012, 2014, 2016, and 2018.

Supplementary Table 17. Correlation results between baseline FI, depressive symptoms, blood markers, and incident CVD in CHARLS.

Variables	CVD	FI	Depression	HbA1c	HDL cholesterol	Total cholesterol	C-reactive protein
CVD	1.000						
FI	0.090 (<i>P</i> < 0.001)	1.000					
Depression	0.064 (<i>P</i> < 0.001)	0.243 (<i>P</i> < 0.001)	1.000				
HbA1c	0.040 (<i>P</i> = 0.005)	0.050 (<i>P</i> < 0.001)	0.031 (<i>P</i> = 0.029)	1.000			
HDL cholesterol	0.041 (<i>P</i> = 0.004)	0.065 (<i>P</i> < 0.001)	0.074 (<i>P</i> < 0.001)	-0.079 (<i>P</i> < 0.001)	1.000		
Total cholesterol	0.044 (<i>P</i> = 0.002)	0.033 (<i>P</i> = 0.020)	0.051 (<i>P</i> < 0.001)	0.143 (<i>P</i> < 0.001)	0.327 (<i>P</i> < 0.001)	1.000	
C-reactive protein	0.037 (<i>P</i> = 0.009)	0.060 (<i>P</i> < 0.001)	0.038 (<i>P</i> = 0.007)	0.079 (<i>P</i> < 0.001)	-0.109 (<i>P</i> < 0.001)	0.080 (<i>P</i> < 0.001)	1.000

FI: frailty index; CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

In the analyses, CHARLS used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2018.

Supplementary Table 18. Correlation results between baseline FI, depressive symptoms, blood markers, and incident CVD in SHARE.

Variables	CVD	FI	Depression	HbA1c	HDL cholesterol	Total cholesterol	C-reactive protein
CVD	1.000						
FI	0.104 (<i>P</i> < 0.001)	1.000					
Depression	0.034 (<i>P</i> = 0.010)	0.324 (<i>P</i> < 0.001)	1.000				
HbA1c	0.042 (<i>P</i> = 0.001)	0.146 (<i>P</i> < 0.001)	0.042 (<i>P</i> = 0.001)	1.000			
HDL cholesterol	0.092 (<i>P</i> < 0.001)	0.029 (<i>P</i> = 0.029)	0.029 (<i>P</i> = 0.024)	-0.131 (<i>P</i> < 0.001)	1.000		
Total cholesterol	0.063 (<i>P</i> < 0.001)	0.027 (<i>P</i> = 0.037)	0.039 (<i>P</i> = 0.003)	-0.056 (<i>P</i> < 0.001)	0.397 (<i>P</i> < 0.001)	1.000	
C-reactive protein	0.032 (<i>P</i> = 0.014)	0.071 (<i>P</i> < 0.001)	0.055 (<i>P</i> < 0.001)	0.039 (<i>P</i> = 0.003)	-0.028 (<i>P</i> = 0.029)	-0.024 (<i>P</i> = 0.064)	1.000

FI: frailty index; CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

In the analyses, SHARE used frailty status in 2011, depressive symptoms in 2013, blood markers in 2015, and incident CVD in 2017, and 2019.

Supplementary Table 19. Correlation results between baseline FI, depressive symptoms, blood markers, and incident CVD in ELSA.

Variables	CVD	FI	Depression	HbA1c	HDL cholesterol	Total cholesterol	C-reactive protein
CVD	1.000						
FI	0.059 (<i>P</i> = 0.001)	1.000					
Depression	0.050 (<i>P</i> = 0.005)	0.293 (<i>P</i> < 0.001)	1.000				
HbA1c	0.086 (<i>P</i> < 0.001)	0.177 (<i>P</i> < 0.001)	0.043 (<i>P</i> = 0.018)	1.000			
HDL cholesterol	0.088 (<i>P</i> < 0.001)	0.042 (<i>P</i> = 0.019)	0.043 (<i>P</i> = 0.016)	-0.104 (<i>P</i> < 0.001)	1.000		
Total cholesterol	0.038 (<i>P</i> = 0.037)	0.046 (<i>P</i> = 0.010)	0.047 (<i>P</i> = 0.009)	-0.118 (<i>P</i> < 0.001)	0.393 (<i>P</i> < 0.001)	1.000	
C-reactive protein	0.069 (<i>P</i> < 0.001)	0.157 (<i>P</i> < 0.001)	0.050 (<i>P</i> = 0.006)	0.120 (<i>P</i> < 0.001)	-0.100 (<i>P</i> < 0.001)	-0.015 (<i>P</i> = 0.419)	1.000

FI: frailty index; CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

In the analyses, ELSA used frailty status in 2004, depressive symptoms in 2006, blood markers in 2008, and incident CVD in 2010-2018.

Supplementary Table 20. Correlation results between baseline FI, depressive symptoms, blood markers, and incident CVD in MHAS.

Variables	CVD	FI	Depression	HbA1c	HDL cholesterol	Total cholesterol	C-reactive protein
CVD	1.000						
FI	0.127 (<i>P</i> < 0.001)	1.000					
Depression	0.092 (<i>P</i> = 0.022)	0.309 (<i>P</i> < 0.001)	1.000				
HbA1c	0.180 (<i>P</i> < 0.001)	0.110 (<i>P</i> = 0.007)	0.104 (<i>P</i> = 0.010)	1.000			
HDL cholesterol	0.109 (<i>P</i> = 0.007)	0.222 (<i>P</i> < 0.001)	0.116 (<i>P</i> = 0.004)	0.133 (<i>P</i> < 0.001)	1.000		
Total cholesterol	0.130 (<i>P</i> = 0.001)	0.139 (<i>P</i> < 0.001)	0.084 (<i>P</i> = 0.037)	0.146 (<i>P</i> < 0.001)	0.377 (<i>P</i> < 0.001)	1.000	
C-reactive protein	0.242 (<i>P</i> < 0.001)	0.281 (<i>P</i> < 0.001)	0.097 (<i>P</i> = 0.016)	0.115 (<i>P</i> = 0.005)	0.247 (<i>P</i> < 0.001)	0.114 (<i>P</i> = 0.005)	1.000

FI: frailty index; CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

In the analyses, MHAS used frailty status in 2001, depressive symptoms in 2003, blood markers in 2012, and incident CVD in 2015 and 2018.

Supplementary Table 21. The edge weights matrices of the HRS network.

	CVD1	CVD2	FI1	FI2	FI3	FI4	FI5	FI6	FI7	FI8	FI9	FI10	FI11	FI12	FI13	FI14	FI15	FI16	FI17	FI18	FI19	FI20	FI21	FI22	FI23	FI24	FI25	FI26	FI27
CVD1	5.42	0.01	0.00	0.08	0.04	0.04	0.20	0.08	0.02	0.07	0.08	0.42	0.13	0.00	0.00	0.14	0.00	0.02	0.03	0.01	0.12	0.21	0.02	0.17	0.00	0.05	0.05	0.09	-0.07
CVD2	0.06	6.23	0.16	-0.03	0.00	-0.02	-0.09	0.00	0.45	0.00	-0.13	0.02	0.13	0.27	0.59	0.08	0.00	0.18	0.00	0.43	0.23	0.08	0.02	0.00	-0.09	0.10	0.00	0.00	0.24
FI1	0.18	0.41	5.11	0.68	0.00	0.22	-0.19	0.03	-0.10	0.11	0.00	0.14	0.00	-0.10	-0.22	0.00	0.00	0.00	0.04	0.00	0.00	0.20	0.11	0.18	0.15	0.05	0.06	0.00	0.09
FI2	0.26	0.08	0.23	6.29	0.00	0.00	-0.11	0.00	-0.18	0.22	0.00	0.51	0.21	0.24	0.10	0.12	0.00	0.05	0.11	0.29	0.18	0.28	0.12	0.20	0.09	0.26	0.07	0.04	0.08
FI3	0.14	0.00	0.00	0.00	6.55	0.13	0.36	0.00	-0.05	-0.09	-0.08	0.17	0.05	0.10	0.10	0.00	0.00	0.00	-0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	-0.02
FI4	0.23	0.00	0.08	0.00	0.00	4.72	0.27	0.02	-0.21	0.09	0.12	0.20	0.28	0.00	0.00	0.12	0.32	0.00	0.02	-0.03	0.00	0.35	0.55	0.28	0.43	0.40	0.23	0.50	-0.04
FI5	0.21	0.00	-0.09	-0.12	0.38	0.01	6.09	0.24	0.14	0.05	0.08	0.40	0.05	0.17	0.08	-0.10	0.00	0.00	0.11	-0.36	0.00	0.25	-0.05	0.18	0.04	0.12	0.14	0.12	-0.20
FI6	0.00	0.00	0.00	0.00	0.00	0.19	0.53	5.35	0.41	0.12	0.04	0.32	0.01	0.19	0.17	0.13	0.21	0.35	0.28	0.55	0.45	0.20	0.17	0.15	0.17	0.09	0.14	0.22	0.05
FI7	0.00	-3.00	-1.25	0.00	0.00	-2.05	-1.97	0.00	3.57	-0.13	-0.20	0.00	0.09	0.00	0.76	0.34	0.00	0.09	0.00	0.35	0.90	0.00	-0.01	0.00	-0.08	0.00	-0.11	0.00	3.30
FI8	0.03	0.00	-0.07	0.00	0.00	0.09	-0.18	0.00	0.21	1.76	0.26	0.41	0.03	0.00	0.25	0.08	0.13	0.28	0.16	0.34	0.17	0.01	0.07	0.00	0.00	0.06	0.00	0.18	0.00
FI9	0.10	-0.01	0.00	-0.10	0.00	0.14	0.00	0.00	0.01	0.33	2.36	0.15	0.06	0.00	0.00	0.22	0.00	0.06	0.00	0.00	0.20	0.00	0.05	0.04	0.04	0.16	0.12	0.29	0.22
FI10	0.18	0.38	0.00	0.19	0.00	-0.02	0.22	0.20	0.07	0.44	0.23	1.71	0.17	0.30	0.36	0.39	0.05	0.27	0.31	0.00	0.00	0.35	0.11	0.12	0.18	0.23	0.34	0.11	0.18
FI11	0.00	0.00	0.19	0.05	0.00	0.02	0.02	0.00	0.00	0.14	0.08	0.10	1.43	0.46	0.48	0.37	0.41	0.29	0.44	0.07	0.33	0.15	0.30	0.00	0.07	0.28	0.16	0.32	0.01
FI12	0.00	0.21	0.00	0.00	0.00	-0.20	-0.09	0.00	0.00	-0.12	0.00	0.00	0.38	1.34	0.27	0.18	0.47	0.49	0.02	0.12	0.24	-0.34	0.00	-0.36	-0.29	-0.01	-0.25	0.00	0.17
FI13	0.00	0.58	0.00	-0.21	-0.48	-0.10	0.09	0.19	0.00	0.33	0.00	0.22	0.56	0.45	2.15	0.54	0.35	0.23	0.24	0.16	0.61	-0.60	-0.56	-0.49	-0.52	0.08	-0.14	0.51	0.50
FI14	0.00	0.14	0.12	-0.05	-0.15	-0.14	0.00	0.00	0.11	0.00	0.01	0.00	0.00	-0.22	0.04	0.84	0.06	0.00	0.05	-0.29	0.00	-0.23	0.00	-0.20	-0.16	0.00	-0.04	0.05	0.06
FI15	0.00	0.00	0.00	0.00	0.00	0.00	-0.13	0.18	0.12	-0.11	0.00	0.04	0.00	0.32	0.03	0.16	1.10	0.00	-0.01	0.00	0.00	0.00	0.04	-0.05	0.00	0.00	-0.07	0.06	-0.19
FI16	0.00	0.00	0.00	0.00	0.00	-0.01	-0.55	0.00	0.08	0.14	0.00	0.12	0.28	0.35	0.35	0.11	0.17	1.05	0.19	0.32	0.20	0.00	0.00	-0.11	-0.03	-0.09	0.00	0.11	-0.04
FI17	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	-0.08	0.18	0.09	0.08	0.00	0.15	0.13	0.09	-0.02	0.42	1.12	0.34	0.26	0.17	0.03	0.00	0.00	0.18	0.21	0.00	0.02
FI18	0.00	0.10	0.00	0.00	-0.10	0.00	-0.42	0.26	0.93	0.07	0.08	-0.03	0.00	0.27	0.52	0.25	0.31	0.20	0.23	1.70	0.63	-0.13	0.00	0.02	-0.09	-0.03	0.00	0.00	0.53
FI19	-0.48	0.00	0.00	0.00	0.00	0.00	0.00	0.41	0.77	0.35	0.27	0.00	0.20	0.46	0.00	0.31	0.00	0.00	-0.41	0.00	1.20	-0.23	-0.11	-0.11	0.00	0.01	-0.24	0.00	0.36
FI20	0.17	0.01	0.03	0.25	0.00	0.05	0.41	0.00	0.00	0.11	0.00	0.45	0.51	0.90	0.66	0.55	0.70	0.42	0.79	0.00	0.22	1.62	0.40	0.57	0.21	0.16	0.48	0.15	0.04
FI21	0.00	0.33	0.01	0.03	0.00	0.41	0.00	0.25	-0.15	0.00	0.04	0.08	0.31	0.18	0.00	0.48	0.38	0.05	0.24	0.06	0.00	0.35	1.38	0.41	0.53	0.07	0.36	0.32	0.05
FI22	0.02	0.00	0.00	0.00	0.00	-0.07	0.41	0.00	0.00	0.05	0.03	0.18	0.31	0.26	0.00	0.19	0.32	0.53	0.02	0.05	0.11	0.13	0.04	0.00	0.00	0.00	0.05	0.01	0.18

FI23	0.05	0.00	0.04	0.12	0.00	0.31	0.00	0.04	0.00	0.00	0.07	0.08	0.43	0.21	0.19	0.55	0.45	0.00	0.07	0.09	0.10	0.32	0.56	0.45	1.38	0.37	0.19	0.15	-0.08
FI24	0.00	0.00	0.00	0.00	0.00	0.28	0.25	0.00	0.00	0.11	0.03	0.23	0.17	0.07	0.11	0.14	0.10	0.00	0.00	0.00	0.00	0.01	0.15	-0.02	0.06	1.57	0.30	0.11	0.02
FI25	0.08	0.00	0.00	0.06	0.00	0.04	0.00	0.05	0.30	0.06	0.08	0.32	0.26	0.43	0.09	0.49	0.23	0.39	0.46	0.33	0.26	0.22	0.09	0.12	0.06	0.31	1.10	0.08	0.11
FI26	0.00	-0.13	0.00	0.00	0.00	0.27	0.00	0.21	0.06	0.05	-0.08	0.16	0.16	0.02	0.58	-0.08	0.00	0.02	0.23	0.17	0.00	0.13	0.23	0.12	0.10	0.20	0.04	2.09	-0.11
FI27	0.00	0.00	0.00	0.00	0.00	-0.10	0.00	0.00	1.03	0.11	0.17	0.15	0.07	0.24	0.21	0.26	0.01	0.28	0.05	0.79	0.72	0.14	0.01	0.01	0.00	0.12	0.03	0.00	1.51

HRS: Health and Retirement Study; CVD1: Heart problem; CVD2: Stroke; FI1: Hypertension; FI2: Diabetes; FI3: Cancer; FI4: Arthritis; FI5: Chronic lung; FI6: Psychiatric; FI7: Memory; FI8: Eyesight; FI9: Hearing; FI10: Health; FI11: Dressing; FI12: Bathing; FI13: Eating; FI14: Getting in/out bed; FI15: Using toilet; FI16: Preparing meals; FI17: Shopping; FI18: Managing money; FI19: Taking medications; FI20: Walking; FI21: Getting up from chair; FI22: Climbing; FI23: Stooping; FI24: Reaching arms; FI25: Lifting; FI26: Picking up coin; FI27: Cognition. In the analysis, cognition was binary, assigning a value of 1 to those above the median and 0 to others. That was, all indicators were binary variables.

All analyses were adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 22. The edge weights matrices of the CHARLS network.

	CVD1	CVD2	FI1	FI2	FI3	FI4	FI5	FI6	FI7	FI8	FI9	FI10	FI11	FI12	FI13	FI14	FI15	FI16	FI17	FI18	FI19	FI20	FI21	FI22	FI23	FI24	FI25	FI26	FI27
CVD1	16.06	0.00	0.43	0.00	0.00	0.25	0.51	0.00	0.00	0.11	0.12	0.27	0.00	0.07	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.22	0.10	0.23	0.06	0.10	0.20	0.20	-0.29
CVD2	0.00	15.82	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.12	-0.09	0.55	0.68	0.66	0.61	0.10	0.13	0.75	0.63	0.49	0.07	0.24	0.31	0.09	0.35	0.09	0.19	0.52	0.16
FI1	0.00	0.00	17.15	0.00	0.00	1.28	0.00	0.00	0.00	0.03	0.00	0.22	0.00	0.13	0.07	0.04	0.22	0.05	0.03	0.02	0.04	0.03	0.11	0.16	0.16	0.09	0.00	0.00	-0.12
FI2	0.00	0.00	0.09	15.02	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.27	0.00	0.24	0.00	0.04	0.16	0.00	0.00	0.00	0.00	0.00	0.20	0.24	0.23	0.03	0.18	0.31	0.00
FI3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.16	-0.05	0.02	-0.01	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.44	-0.12	-0.46	0.00	0.00
FI4	0.16	0.00	1.17	0.00	0.00	22.04	0.26	0.00	0.00	0.20	0.19	0.24	0.19	0.06	0.00	0.39	0.45	0.00	0.01	0.00	0.00	0.10	0.40	0.16	0.42	0.24	0.23	0.23	-0.08
FI5	0.00	0.00	-0.50	0.00	0.00	0.00	15.43	0.00	0.00	0.14	0.18	0.34	0.09	0.16	0.00	0.00	0.06	0.08	0.03	0.00	0.00	0.28	0.09	0.40	0.10	0.05	0.20	0.00	0.00
FI6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.27	-0.21	0.25	0.00	0.00	0.06	0.00	-0.13	0.22	0.16	0.18	0.39	0.00	-0.06	0.12	0.00	0.00	0.00	0.10	0.19
FI7	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	16.10	-0.29	-0.21	0.00	0.00	0.22	0.15	0.00	-0.13	0.21	0.00	0.12	0.50	-0.03	0.00	0.00	-0.08	0.00	0.00	-0.14	0.00
FI8	0.00	0.00	0.60	0.00	0.00	0.00	0.00	0.00	0.00	0.66	0.10	0.08	0.00	-0.04	0.00	0.00	-0.02	0.00	0.01	0.00	0.00	0.00	0.03	0.12	0.12	0.01	-0.02	-0.13	0.00
FI9	0.00	0.00	0.00	0.00	0.00	-0.71	0.13	0.00	0.00	0.11	1.05	0.19	0.10	0.07	0.00	0.06	0.08	0.01	0.17	0.24	0.29	0.00	0.01	0.13	0.00	0.10	0.00	0.19	0.13
FI10	0.00	0.00	-0.04	0.00	0.00	1.56	0.00	0.00	0.00	0.06	0.02	0.28	0.17	0.17	0.00	0.00	0.00	0.18	0.00	0.15	0.05	0.08	0.05	0.12	0.12	0.07	0.06	0.06	0.00
FI11	0.00	0.00	0.00	0.00	0.00	0.38	0.00	0.00	0.00	-0.04	0.00	0.00	0.41	-0.14	0.00	0.08	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	-0.08	-0.16	0.00
FI12	0.00	0.00	0.00	0.00	0.00	0.24	0.23	0.00	0.00	0.00	0.00	0.38	0.45	0.80	0.30	0.56	0.25	0.46	0.41	0.16	0.30	0.15	0.21	0.17	0.21	0.51	0.24	0.51	0.11
FI13	0.00	0.00	-1.60	0.00	0.00	0.00	-0.41	0.00	0.00	0.10	0.00	0.00	0.26	0.19	1.01	0.28	0.20	0.03	0.01	0.12	0.06	0.00	0.00	0.00	0.00	0.17	0.15	0.55	-0.15
FI14	0.00	0.00	1.26	0.00	0.00	0.83	0.00	0.00	0.00	-0.06	-0.19	0.04	0.05	-0.05	0.00	0.33	0.16	-0.05	0.01	-0.18	0.00	0.20	0.15	0.20	0.09	0.00	0.09	-0.21	0.00
FI15	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00	0.14	-0.02	0.01	0.14	0.14	0.00	0.20	0.61	0.00	0.00	0.00	0.00	0.13	0.11	0.23	0.39	0.00	0.07	0.06	0.10
FI16	0.00	0.00	0.00	0.00	0.00	0.26	0.17	0.00	0.00	-0.15	-0.05	0.24	0.40	0.50	0.90	0.22	0.16	1.00	0.47	0.45	0.29	0.21	0.04	0.17	0.13	0.19	0.35	0.29	0.10
FI17	0.00	0.00	-0.40	0.00	0.00	0.07	0.23	0.00	0.00	-0.23	-0.07	0.00	0.01	0.17	0.00	0.03	0.11	0.38	0.73	0.31	0.10	0.12	0.00	0.00	0.07	0.12	0.11	0.03	0.14
FI18	0.00	0.00	0.00	0.00	0.00	0.86	0.27	0.00	0.00	0.00	0.00	0.11	0.01	0.03	0.19	0.10	0.00	0.17	0.40	0.77	0.50	0.11	0.00	0.00	0.00	0.17	0.00	0.19	0.35
FI19	0.00	0.00	1.11	0.00	0.00	0.14	0.00	0.00	0.00	-0.07	-0.07	0.07	0.11	0.13	0.00	0.11	0.00	0.00	0.26	0.21	0.75	-0.01	0.03	0.00	0.00	0.00	0.13	0.26	0.20
FI20	0.00	0.00	-0.80	0.00	0.00	1.20	0.69	0.00	0.00	0.00	0.00	0.24	0.31	0.50	0.26	0.41	0.36	0.51	0.54	0.25	0.27	1.34	0.25	0.64	0.37	0.29	0.48	0.31	0.08
FI21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.01	0.02	0.05	0.20	0.06	0.35	0.36	0.07	0.00	0.00	0.02	0.18	0.56	0.21	0.31	0.03	0.07	0.22	0.00
FI22	0.76	0.00	1.86	0.00	0.00	0.00	0.00	0.00	0.00	0.16	0.18	0.19	0.36	0.31	0.02	0.31	0.28	0.41	0.25	0.23	0.21	0.55	0.30	0.73	0.24	0.31	0.32	0.22	0.16

FI23	0.00	0.00	0.00	0.00	0.00	-2.20	0.00	0.00	0.00	0.11	0.08	0.20	0.00	0.05	0.00	0.29	0.34	0.00	0.00	0.00	0.00	0.07	0.41	0.19	0.64	0.08	0.17	0.00	0.03
FI24	0.00	0.00	-0.81	0.00	0.00	0.00	-0.10	0.00	0.00	0.00	-0.03	0.00	0.53	0.33	0.31	0.10	0.00	0.03	0.00	0.07	0.04	0.00	0.00	0.00	0.00	0.83	0.15	0.27	0.09
FI25	0.00	0.00	0.70	0.00	0.00	1.01	0.66	0.00	0.00	-0.05	-0.03	0.23	0.26	0.35	0.05	0.01	0.18	0.25	0.12	0.00	0.00	0.07	0.09	0.15	0.16	0.21	0.85	0.11	0.09
FI26	0.00	0.00	-1.34	0.00	0.00	-1.94	-3.12	0.00	0.00	-0.17	-0.20	0.05	0.32	0.27	0.31	0.06	0.07	0.27	0.35	0.26	0.13	0.25	0.16	0.09	0.05	0.36	0.16	0.85	0.00
FI27	0.00	0.00	0.00	0.00	0.00	-1.28	0.00	0.00	0.00	-0.03	0.00	0.13	0.23	0.16	0.25	0.13	0.05	0.17	0.32	0.38	0.41	0.16	0.15	0.11	0.04	0.22	0.26	0.31	1.06

CHARLS: China Health and Retirement Longitudinal Study; CVD1: Heart problem; CVD2: Stroke; FI1: Hypertension; FI2: Diabetes; FI3: Cancer; FI4: Arthritis; FI5: Chronic lung; FI6: Psychiatric; FI7: Memory; FI8: Eyesight; FI9: Hearing; FI10: Health; FI11: Dressing; FI12: Bathing; FI13: Eating; FI14: Getting in/out bed; FI15: Using toilet; FI16: Preparing meals; FI17: Shopping; FI18: Managing money; FI19: Taking medications; FI20: Walking; FI21: Getting up from chair; FI22: Climbing; FI23: Stooping; FI24: Reaching arms; FI25: Lifting; FI26: Picking up coin; FI27: Cognition. In the analysis, cognition was binary, assigning a value of 1 to those above the median and 0 to others. That was, all indicators were binary variables.

All analyses were adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 23. The edge weights matrices of the SHARE network.

	CVD1	CVD2	FI1	FI2	FI3	FI4	FI5	FI6	FI7	FI8	FI9	FI10	FI11	FI12	FI13	FI14	FI15	FI16	FI17	FI18	FI19	FI20	FI21	FI22	FI23	FI24	FI25	FI26
CVD1	2.66	0.25	0.02	0.03	0.00	-0.11	0.09	0.00	0.00	0.04	0.40	0.03	0.06	0.00	0.00	0.00	-0.05	0.00	0.00	-0.13	0.22	0.06	0.27	0.03	0.05	0.20	-0.03	-0.02
CVD2	0.18	3.17	0.13	0.15	0.00	0.00	0.00	0.22	0.01	0.09	0.33	0.22	0.47	0.33	0.15	0.20	0.48	0.32	0.39	0.40	0.44	0.14	0.22	0.18	0.25	0.36	0.47	0.02
FI1	0.17	0.04	2.98	0.28	0.00	0.09	-0.05	-0.15	0.00	0.00	0.19	0.01	-0.07	-0.23	-0.09	-0.09	-0.18	-0.08	-0.20	-0.22	0.01	0.07	0.14	0.16	0.01	0.00	0.00	0.02
FI2	0.17	0.28	0.24	4.50	0.00	0.11	0.00	0.02	0.06	0.04	0.30	0.14	0.25	0.00	0.13	0.04	0.16	0.20	0.13	0.31	0.19	0.06	0.29	0.24	0.01	0.07	0.11	0.08
FI3	-0.02	0.00	-0.04	-0.14	3.21	-0.09	0.00	0.00	0.00	-0.03	0.19	0.00	-0.05	0.00	0.00	0.00	0.00	0.00	-0.07	-0.11	-0.08	-0.04	-0.10	-0.04	0.00	0.04	0.05	-0.20
FI4	0.08	-0.13	0.00	-0.02	0.00	1.34	0.00	0.00	0.02	0.12	0.31	0.32	0.15	-0.08	0.15	0.00	-0.07	0.02	-0.20	-0.15	0.18	0.30	0.18	0.36	0.21	0.26	0.29	0.00
FI5	0.12	0.02	0.00	0.00	0.09	0.07	3.23	0.00	0.00	0.14	0.40	0.03	0.14	0.06	-0.15	0.05	0.08	0.08	0.12	0.14	0.29	0.00	0.49	0.05	0.08	0.22	0.00	0.00
FI6	0.17	0.00	-0.43	-0.01	0.00	0.00	0.00	2.67	0.22	0.17	0.03	0.85	0.72	0.94	0.50	0.88	1.34	1.07	1.34	1.48	0.03	0.36	0.35	0.09	0.13	0.20	0.33	0.76
FI7	-0.02	0.00	0.00	-0.06	-0.09	0.08	-0.04	0.00	1.01	0.00	0.18	0.00	0.00	0.13	0.13	0.00	0.14	0.09	0.28	0.13	0.06	0.07	0.02	0.03	0.04	0.01	0.10	0.08
FI8	0.00	0.00	-0.03	-0.08	-0.01	0.00	0.00	0.00	0.14	2.03	0.10	-0.04	-0.05	-0.01	0.09	0.02	-0.10	-0.01	0.10	0.08	-0.06	0.04	0.00	-0.02	0.14	0.00	0.11	0.10
FI9	0.40	0.40	0.15	0.20	0.47	0.42	0.44	0.35	0.21	0.35	1.77	0.50	0.54	0.46	0.58	0.45	0.47	0.56	0.47	0.22	0.64	0.53	0.53	0.48	0.57	0.64	0.52	0.18
FI10	0.00	0.08	0.00	0.00	0.06	-0.09	0.05	0.09	0.02	0.00	0.15	1.46	0.35	0.24	0.53	0.47	0.18	0.17	0.00	0.24	0.26	0.26	0.24	0.43	0.26	0.15	0.15	-0.02
FI11	-0.17	0.00	0.00	0.00	0.00	-0.01	0.00	0.07	0.14	0.08	0.14	0.35	1.35	0.42	0.26	0.60	0.51	0.56	0.36	0.30	0.30	0.17	0.20	0.27	0.04	0.24	0.05	0.25
FI12	-0.14	0.39	-0.01	-0.29	0.08	0.07	0.00	-0.36	0.00	-0.17	-0.13	0.06	-0.13	1.62	0.10	0.02	0.29	0.01	0.24	0.21	-0.16	-0.04	-0.12	-0.09	0.35	0.11	0.51	-0.12
FI13	0.05	0.00	0.03	0.00	0.00	0.10	0.00	-0.04	0.06	0.07	0.13	0.24	0.10	0.10	1.00	0.50	0.17	0.08	0.10	0.19	0.00	0.33	0.07	0.01	0.08	0.00	0.21	-0.06
FI14	0.05	0.00	0.09	0.00	0.00	0.18	-0.02	0.00	0.00	0.00	0.00	-0.09	0.00	-0.13	0.00	0.69	0.06	-0.09	-0.03	-0.18	0.16	0.09	0.02	0.00	-0.12	0.11	-0.31	-0.14
FI15	-0.17	0.22	0.00	-0.10	0.00	-0.01	-0.06	0.29	0.00	0.00	-0.19	0.26	0.44	0.51	0.35	0.35	1.32	0.31	0.40	0.49	0.09	0.00	0.00	-0.01	0.02	0.00	0.04	0.13
FI16	0.00	0.00	-0.23	0.00	-0.01	-0.25	-0.01	-0.06	0.07	0.00	0.25	0.24	0.55	0.36	0.18	0.30	0.57	1.42	0.48	0.37	0.55	0.14	0.18	0.15	0.26	0.45	0.07	0.05
FI17	-0.09	0.14	-0.05	0.00	0.00	-0.15	-0.04	0.63	0.33	0.16	0.08	0.15	0.30	0.24	0.20	0.35	0.32	0.60	1.50	0.58	0.00	0.00	0.01	0.00	-0.02	0.04	0.18	0.48
FI18	0.00	0.00	-0.28	0.03	0.00	-0.01	0.03	0.96	0.17	0.00	-0.03	0.14	0.15	-0.11	0.09	0.00	0.11	-0.09	0.15	1.09	-0.05	0.00	0.00	-0.09	-0.07	0.00	0.29	0.45
FI19	0.11	0.20	-0.01	0.00	0.05	0.02	0.19	0.00	0.05	0.00	0.24	0.12	0.40	0.26	0.24	0.25	0.15	0.49	0.02	0.13	1.47	0.24	0.52	0.37	0.06	0.33	0.04	0.14
FI20	-0.07	0.00	0.06	0.00	0.00	0.20	0.00	0.07	0.07	0.11	0.15	0.33	0.18	0.00	0.39	0.33	0.08	0.09	0.13	0.07	0.09	0.99	0.21	0.33	0.16	0.14	0.11	0.00
FI21	0.19	0.31	0.16	0.20	0.06	0.12	0.51	0.04	0.13	0.00	0.32	0.29	0.42	0.22	0.30	0.20	0.35	0.44	0.22	0.31	0.50	0.34	1.27	0.34	0.20	0.26	0.13	0.10
FI22	0.02	0.00	0.08	0.13	0.09	0.05	0.00	0.00	0.02	0.00	0.18	0.43	0.25	0.09	0.33	0.28	0.10	0.14	0.09	0.00	0.32	0.56	0.31	1.25	0.25	0.21	0.19	-0.05

FI23	0.01	0.00	0.00	0.06	0.00	0.10	0.00	0.00	0.00	0.01	0.16	0.12	0.03	0.03	0.06	-0.14	-0.07	0.03	-0.03	-0.19	0.01	0.10	0.00	0.13	1.29	0.26	0.17	0.08
FI24	0.17	0.00	0.01	0.00	0.09	0.21	0.03	0.20	0.08	0.00	0.35	0.30	0.31	0.48	0.42	0.39	0.39	0.42	0.18	0.19	0.32	0.19	0.26	0.21	0.36	1.22	0.28	0.08
FI25	-0.04	0.04	0.00	0.00	0.00	0.35	0.00	-0.10	0.09	0.00	0.10	0.16	0.07	0.32	0.02	0.00	0.17	0.08	0.15	0.05	-0.02	0.01	-0.12	0.00	0.13	0.00	1.66	0.00
FI26	0.07	0.14	0.02	0.09	-0.10	0.14	0.00	0.87	0.16	0.12	0.31	0.29	0.43	0.36	0.15	0.38	0.57	0.39	0.82	0.76	0.24	0.08	0.18	0.10	0.20	0.15	0.13	1.42

SHARE: Survey of Health, Ageing and Retirement in Europe; CVD1: Heart problem; CVD2: Stroke; FI1: Hypertension; FI2: Diabetes; FI3: Cancer; FI4: Arthritis; FI5: Chronic lung; FI6: Memory; FI7: Eyesight; FI8: Hearing; FI9: Health; FI10: Dressing; FI11: Bathing; FI12: Eating; FI13: Getting in/out bed; FI14: Using toilet; FI15: Preparing meals; FI16: Shopping; FI17: Managing money; FI18: Taking medications; FI19: Walking; FI20: Getting up from chair; FI21: Climbing; FI22: Stooping; FI23: Reaching arms; FI24: Lifting; FI25: Picking up coin; FI26: Cognition. In the analysis, cognition was binary, assigning a value of 1 to those above the median and 0 to others. That was, all indicators were binary variables.

All analyses were adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, physical activity, and different country.

Supplementary Table 24. The edge weights matrices of the ELSA network.

	CVD1	CVD2	FI1	FI2	FI3	FI4	FI5	FI6	FI7	FI8	FI9	FI10	FI11	FI12	FI13	FI14	FI15	FI16	FI17	FI18	FI19	FI20	FI21	FI22	FI23	FI24	FI25	FI26	FI27
CVD1	2.43	0.00	0.06	0.62	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.01	0.00	0.00	-0.22	0.00	0.00	0.13	0.00	0.19	0.00	0.00	0.00	0.00	-0.11
CVD2	0.66	5.46	0.00	0.00	0.47	-0.18	0.33	0.09	0.00	0.00	-0.03	0.00	0.28	0.00	0.00	0.38	0.00	0.00	0.07	0.05	0.00	0.00	0.00	-0.20	0.00	0.00	0.00	-0.05	0.00
FI1	0.31	0.65	0.67	0.00	0.44	0.00	0.00	-0.38	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.01	0.00	0.00	0.01	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.09
FI2	-0.66	0.40	0.86	8.86	0.00	0.00	-0.38	-0.40	0.00	0.11	-0.15	-0.02	0.00	0.04	0.00	0.15	0.00	0.02	0.12	0.00	0.42	0.38	0.01	0.00	0.02	0.00	0.01	0.00	0.26
FI3	-0.16	0.39	0.00	0.00	7.89	0.00	0.00	0.00	0.00	-0.47	0.00	0.00	0.03	0.02	0.00	0.00	0.00	0.00	0.00	0.65	0.00	0.15	0.00	0.04	0.00	0.00	-0.31	-1.44	0.00
FI4	0.00	0.00	0.11	0.00	-0.11	5.94	0.00	0.27	0.00	0.14	0.00	0.00	0.37	0.22	0.00	0.18	0.00	0.08	0.20	0.00	0.00	0.25	0.44	0.26	0.72	0.41	0.25	0.58	-0.07
FI5	0.00	0.00	-0.28	0.00	-0.11	0.00	6.91	0.46	0.00	0.00	0.00	-0.11	0.13	0.25	0.11	0.09	0.00	-0.08	0.31	0.00	0.00	0.26	0.00	0.34	0.00	0.00	0.28	0.00	-0.05
FI6	0.03	0.00	0.00	0.00	0.00	0.24	0.00	6.65	0.00	-0.03	0.00	0.20	0.00	0.00	0.00	-0.18	0.00	0.13	0.00	0.00	0.00	0.06	0.00	0.00	0.03	0.21	0.00	0.00	0.10
FI7	0.00	0.00	0.00	0.00	0.00	0.00	0.93	0.00	0.00	0.00	0.00	-0.20	0.43	-0.62	0.00	0.00	0.00	0.02	-0.91	0.73	1.42	-2.73	0.00	-0.99	-0.65	-0.86	-0.90	0.00	0.20
FI8	0.00	0.05	0.00	0.00	0.14	0.00	0.00	0.00	0.00	1.94	0.05	0.29	0.12	0.04	0.19	0.00	0.19	0.23	0.26	0.37	0.27	0.00	0.00	0.11	0.00	0.24	0.26	0.09	0.11
FI9	0.00	0.00	0.02	0.00	0.26	0.00	0.35	0.00	0.00	0.42	2.60	0.43	0.11	0.01	0.00	0.00	0.00	0.16	0.05	0.04	0.19	0.07	0.11	0.21	0.07	0.11	0.02	0.18	0.07
FI10	0.58	0.37	0.43	0.29	0.83	0.09	0.78	0.95	0.00	0.38	0.18	0.46	0.41	0.45	0.20	0.55	0.22	0.54	0.75	0.26	0.28	0.72	0.22	0.52	0.33	0.16	0.67	0.14	0.25
FI11	0.00	0.02	0.02	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00	0.03	1.44	0.43	0.08	0.16	0.52	0.05	0.00	0.17	0.00	0.00	0.30	0.16	0.31	0.24	-0.10	0.21	0.06
FI12	-0.04	0.27	0.00	0.00	-0.06	0.01	0.00	0.00	0.00	0.03	0.00	0.05	0.10	1.54	0.08	0.01	0.68	0.00	0.28	0.07	0.40	0.15	0.09	0.09	0.14	0.13	0.18	0.10	0.20
FI13	0.00	0.64	0.00	0.00	0.00	0.00	0.59	-0.28	0.00	-0.08	0.00	-0.04	0.15	0.00	2.16	-0.17	0.00	0.65	0.03	0.00	0.05	-0.08	0.00	0.16	0.00	0.23	0.23	0.87	-0.55
FI14	0.00	0.00	0.00	0.00	0.00	0.00	-0.16	0.00	0.00	0.00	0.00	0.00	0.26	0.05	0.00	1.46	0.22	0.00	0.10	0.00	0.00	0.27	0.11	0.03	0.09	0.07	0.23	0.00	-0.09
FI15	-0.03	0.00	0.00	0.00	0.00	-0.22	0.00	0.24	0.00	0.00	0.00	0.20	0.08	0.42	0.00	0.19	1.13	0.06	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.05	0.15	0.01	-0.11
FI16	0.00	0.29	-0.06	0.00	0.00	0.00	0.02	0.00	0.00	0.23	0.00	0.04	0.30	0.43	0.76	0.52	0.00	1.92	0.67	0.42	0.73	0.63	0.00	0.00	0.00	0.00	0.43	0.12	-0.06
FI17	0.00	0.00	-0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.29	0.43	0.00	0.35	0.73	1.42	0.02	0.54	0.37	0.00	0.29	0.18	0.00	0.14	0.00	0.19
FI18	0.00	0.62	0.00	0.00	0.00	0.00	-0.73	1.04	0.00	0.22	0.00	0.18	0.36	0.27	0.03	0.17	0.00	0.39	0.53	2.19	0.26	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.49
FI19	0.00	0.00	0.00	0.00	0.00	0.26	0.23	0.87	0.00	0.34	0.00	0.00	0.12	0.00	0.00	-0.16	0.00	0.17	0.46	0.67	1.66	0.57	0.02	0.00	0.00	0.00	0.35	0.00	0.17
FI20	0.19	0.17	0.01	0.00	-0.41	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.21	0.30	0.31	0.48	0.14	0.89	0.29	0.46	0.12	2.10	0.12	0.38	0.09	0.20	0.37	0.22	0.16
FI21	0.00	0.00	0.01	0.00	0.00	0.58	-0.22	0.01	0.00	0.07	0.00	0.03	0.56	0.42	0.58	0.46	0.81	0.00	0.11	0.00	0.00	0.20	1.32	0.34	0.60	0.30	0.26	0.30	0.03
FI22	0.45	0.24	0.31	0.00	0.00	0.33	0.87	0.23	0.00	0.00	0.00	0.15	0.50	0.34	0.64	0.63	0.52	0.25	0.42	0.25	0.75	0.84	0.43	1.68	0.44	0.35	0.68	0.10	-0.03

FI23	-0.02	0.00	0.07	0.00	0.04	0.77	0.00	0.05	0.00	0.19	0.19	0.06	0.37	0.50	0.07	0.58	0.31	0.13	0.26	0.16	0.00	0.27	0.75	0.37	1.65	0.30	0.29	0.44	-0.12
FI24	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.21	0.09	0.00	0.07	0.36	0.07	0.09	0.11	0.00	0.00	0.04	0.11	0.03	0.00	1.78	0.26	0.17	0.04
FI25	0.13	0.00	0.02	0.00	0.10	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.13	0.17	0.22	0.25	0.11	0.21	0.79	0.23	0.00	0.27	0.23	0.42	0.17	0.41	1.57	0.31	0.00
FI26	0.00	0.24	-0.02	0.00	0.00	0.26	0.22	0.00	0.00	0.18	0.00	-0.02	0.47	0.00	0.54	0.09	0.21	0.19	0.24	0.31	0.48	0.09	0.23	0.14	0.12	0.00	0.29	2.54	0.06
FI27	-0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.20	0.01	0.00	0.04	0.27	0.00	0.00	0.28	0.19	0.42	0.26	0.14	0.03	-0.08	0.00	0.00	0.07	-0.14	1.33

ELSA: English Longitudinal Study of Ageing; CVD1: Heart problem; CVD2: Stroke; FI1: Hypertension; FI2: Diabetes; FI3: Cancer; FI4: Arthritis; FI5: Chronic lung; FI6: Psychiatric; FI7: Memory; FI8: Eyesight; FI9: Hearing; FI10: Health; FI11: Dressing; FI12: Bathing; FI13: Eating; FI14: Getting in/out bed; FI15: Using toilet; FI16: Preparing meals; FI17: Shopping; FI18: Managing money; FI19: Taking medications; FI20: Walking; FI21: Getting up from chair; FI22: Climbing; FI23: Stooping; FI24: Reaching arms; FI25: Lifting; FI26: Picking up coin; FI27: Cognition. In the analysis, cognition was binary, assigning a value of 1 to those above the median and 0 to others. That was, all indicators were binary variables.

All analyses were adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 25. The edge weights matrices of the MHAS network.

	CVD1	CVD2	FI1	FI2	FI3	FI4	FI5	FI6	FI7	FI8	FI9	FI10	FI11	FI12	FI13	FI14	FI15	FI16	FI17	FI18	FI19	FI20	FI21	FI22	FI23	FI24	FI25
CVD1	2.20	0.00	0.24	0.00	0.00	-0.12	0.33	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.04	0.00	0.00	0.00	0.06	0.00	0.13	0.13	0.00	-0.02
CVD2	-0.07	2.58	0.37	0.15	0.00	0.00	-0.35	0.06	0.00	0.32	0.48	0.84	0.67	0.30	0.00	0.50	0.68	0.64	0.47	0.60	0.00	0.50	0.23	0.27	0.37	0.18	0.10
FI1	0.55	0.11	2.18	0.19	0.00	0.01	0.00	0.02	0.04	0.22	0.21	0.14	0.01	0.16	0.17	0.00	0.00	0.23	0.24	0.21	0.05	0.22	0.12	0.12	0.09	0.14	-0.08
FI2	0.05	0.70	0.18	4.42	0.00	0.00	-0.01	0.15	0.04	0.63	0.23	0.40	0.49	0.20	0.21	0.13	0.18	0.46	0.03	0.24	0.23	0.27	0.27	0.00	0.19	0.10	-0.06
FI3	0.00	-0.01	-0.19	-0.14	3.19	0.00	0.00	-0.02	-0.04	0.18	0.00	-0.13	0.00	0.00	0.00	-0.40	0.00	0.00	0.00	0.28	0.06	-0.19	0.00	0.26	0.22	0.03	0.00
FI4	-0.12	0.00	0.00	0.00	0.00	1.76	-0.01	0.00	0.14	0.35	0.25	0.00	0.14	0.35	0.12	-0.06	0.00	0.00	-0.19	0.39	0.40	0.24	0.42	0.32	0.20	0.18	-0.07
FI5	0.00	0.00	0.20	0.00	0.00	0.15	2.68	0.03	0.10	0.17	0.06	0.00	0.00	0.09	0.00	-0.06	0.00	0.00	-0.11	0.16	0.05	0.19	0.15	0.23	0.24	0.11	-0.14
FI6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.89	0.00	0.24	0.23	0.14	0.21	0.23	0.16	0.19	0.19	0.29	0.16	0.14	0.13	0.00	0.09	0.20	0.00	0.21	0.13
FI7	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.13	1.30	0.18	-0.13	0.00	0.00	0.00	-0.03	0.06	0.00	0.00	0.00	-0.04	0.01	0.00	0.00	0.00	0.00	0.06	0.14
FI8	0.20	0.00	0.21	0.11	0.00	0.22	0.30	0.18	0.10	1.05	0.22	0.15	0.12	0.43	0.21	0.12	0.29	0.00	0.21	0.52	0.30	0.42	0.35	0.33	0.43	0.20	0.13
FI9	0.00	0.55	0.00	0.23	0.00	0.00	-0.06	0.00	0.00	0.15	0.41	0.25	0.00	0.14	0.23	0.00	0.00	0.13	0.00	0.00	0.07	0.11	0.23	0.02	0.05	0.02	0.00
FI10	0.00	0.60	0.05	-0.05	0.00	0.11	0.38	0.16	0.00	0.00	0.30	0.79	0.00	0.20	0.21	0.28	0.18	0.00	0.25	0.38	0.18	0.66	0.21	0.43	0.09	0.04	-0.09
FI11	0.21	0.00	0.00	0.00	0.00	0.27	-0.02	0.00	0.00	-0.06	0.11	0.20	0.86	0.03	0.27	0.69	0.32	0.26	0.52	0.00	0.00	-0.32	0.18	0.00	0.11	0.45	-0.01
FI12	0.00	-0.52	0.00	-0.20	0.00	0.00	0.19	0.01	-0.09	0.00	0.42	0.25	0.00	0.34	0.27	0.24	0.13	0.12	0.00	0.34	0.35	0.27	0.32	-0.12	0.33	0.00	0.00
FI13	0.35	0.00	0.00	0.00	0.00	0.00	-0.38	0.00	0.00	-0.05	-0.16	0.00	0.00	0.03	0.18	0.00	0.43	0.00	0.21	0.00	0.00	0.03	0.13	0.01	0.24	0.10	0.00
FI14	0.00	0.00	-0.09	0.00	0.00	0.13	0.03	0.00	0.00	0.02	0.00	0.25	0.57	0.14	0.22	0.64	0.00	0.47	0.37	0.00	-0.04	0.02	0.00	0.14	0.11	0.08	0.20
FI15	0.60	0.10	0.10	0.35	0.00	0.00	0.02	0.18	0.00	0.00	0.31	0.72	0.34	0.53	0.64	0.81	1.02	0.86	0.88	0.52	0.26	0.22	0.08	0.12	0.44	0.30	0.00
FI16	-0.23	-0.67	0.00	0.00	0.00	-0.28	-0.24	0.09	0.34	0.00	0.00	-0.10	0.00	0.00	0.00	0.06	0.00	0.18	0.23	-0.26	0.00	-0.25	0.00	0.00	0.00	0.40	0.09
FI17	-0.61	0.00	0.00	-0.02	0.00	0.00	0.13	0.00	0.00	-0.12	0.00	0.00	0.06	0.00	0.00	0.25	0.00	0.49	0.42	0.00	-0.37	0.00	-0.27	-0.20	-0.10	0.00	0.25
FI18	0.21	0.00	0.05	0.01	0.00	0.29	0.19	0.15	0.00	0.26	0.38	0.53	0.34	0.38	0.48	0.23	0.65	0.33	0.12	0.92	0.36	0.31	0.42	0.34	0.38	0.49	0.13
FI19	0.00	0.00	0.04	0.00	0.00	0.12	0.00	0.00	0.00	0.06	0.20	0.13	0.48	0.37	0.50	0.00	0.00	0.00	0.00	0.09	0.37	0.00	0.14	0.14	0.12	0.08	-0.10
FI20	0.17	0.00	0.05	0.10	0.00	0.00	0.03	0.00	0.06	0.13	0.24	0.10	0.00	0.07	0.12	-0.02	0.00	0.00	0.00	0.32	0.21	0.47	0.13	0.18	0.17	0.00	0.10
FI21	0.00	0.44	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.16	0.14	0.00	0.00	0.00	0.06	-0.09	0.00	0.00	0.00	0.21	0.21	0.17	0.62	0.00	0.08	0.30	-0.01
FI22	0.07	0.00	0.05	-0.05	0.00	0.00	0.11	0.09	0.09	0.25	0.35	0.00	0.17	0.00	0.00	0.00	0.00	0.12	0.01	-0.08	0.05	0.00	0.00	0.64	0.05	0.11	0.06

FI23	0.03	0.34	0.00	-0.16	0.00	0.01	0.00	0.00	0.11	0.02	0.00	0.42	0.00	0.32	0.18	0.02	0.20	0.21	0.08	0.09	0.06	0.08	0.04	0.18	0.46	0.16	0.04
FI24	0.00	0.58	0.00	-0.18	0.00	0.00	0.00	0.00	0.02	0.00	0.35	0.34	0.37	0.00	0.14	0.36	0.24	0.35	0.15	-0.10	0.07	0.14	0.00	0.00	0.00	0.50	0.00
FI25	0.04	0.00	0.00	0.06	0.00	0.00	0.00	0.07	-0.01	0.07	0.00	0.00	0.00	0.02	0.00	0.11	0.17	0.06	0.19	0.08	0.05	0.02	0.00	0.15	0.12	0.06	0.85

MHAS: Mexican Health and Aging Study; CVD1: Heart problem; CVD2: Stroke; FI1: Hypertension; FI2: Diabetes; FI3: Cancer; FI4: Arthritis; FI5: Chronic lung; FI6: Eyesight; FI7: Hearing; FI8: Health; FI9: Dressing; FI10: Bathing; FI11: Eating; FI12: Getting in/out bed; FI13: Using toilet; FI14: Preparing meals; FI15: Shopping; FI16: Managing money; FI17: Taking medications; FI18: Walking; FI19: Getting up from chair; FI20: Climbing; FI21: Stooping; FI22: Reaching arms; FI23: Lifting; FI24: Picking up coin; FI25: Cognition. In the analysis, cognition was binary, assigning a value of 1 to those above the median and 0 to others. That was, all indicators were binary variables.

All analyses were adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity.

Supplementary Table 26. The association of baseline frailty status with risks of incident CVD after exclusion of chronic comorbidities.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.45 (1.22, 1.72)	<0.001	1.37 (1.19, 1.57)	<0.001	1.61 (1.46, 1.77)	<0.001	1.91 (1.64, 2.23)	<0.001	1.42 (1.23, 1.65)	<0.001	1.49 (1.40, 1.58)	<0.001
Model 2	1.46 (1.23, 1.74)	<0.001	1.39 (1.21, 1.60)	<0.001	1.59 (1.44, 1.75)	<0.001	1.90 (1.63, 2.22)	<0.001	1.41 (1.21, 1.63)	<0.001	1.50 (1.41, 1.59)	<0.001
Model 3	1.45 (1.22, 1.73)	<0.001	1.41 (1.22, 1.61)	<0.001	1.58 (1.43, 1.74)	<0.001	1.89 (1.62, 2.21)	<0.001	1.41 (1.22, 1.63)	<0.001	1.50 (1.41, 1.59)	<0.001
Model 4	1.35 (1.13, 1.61)	0.001	1.40 (1.22, 1.61)	<0.001	1.48 (1.35, 1.64)	<0.001	1.84 (1.57, 2.16)	<0.001	1.40 (1.21, 1.62)	<0.001	1.45 (1.36, 1.54)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Chronic comorbidities referred to two or more of hypertension, diabetes, cancer, arthritis, lung disease, psychiatric disease, memory disease.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 27. The association of changes in frailty status with risks of incident CVD after exclusion of chronic comorbidities.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.51 (1.16, 1.97)	0.002	1.80 (1.38, 2.35)	<0.001	1.32 (1.08, 1.62)	0.006	1.89 (1.24, 2.86)	0.003	1.49 (1.17, 1.89)	0.001	1.50 (1.34, 1.69)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.53 (0.32, 0.88)	0.015	0.57 (0.40, 0.82)	0.002	0.58 (0.41, 0.83)	0.003	0.25 (0.09, 0.70)	0.008	0.62 (0.44, 0.87)	0.005	0.55 (0.46, 0.66)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 28. The association of mean FI, FI change with risks of incident CVD after exclusion of chronic comorbidities.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.15 (0.99, 1.34)	0.075	1.97 (1.44, 2.68)	<0.001	1.17 (1.00, 1.36)	0.049	1.32 (1.01, 1.72)	0.041	1.31 (1.04, 1.65)	0.022	1.25 (1.14, 1.36)	<0.001
T3	1.31 (1.13, 1.52)	<0.001	2.82 (2.09, 3.81)	<0.001	1.59 (1.37, 1.84)	<0.001	1.58 (1.21, 2.06)	0.001	1.70 (1.36, 2.13)	<0.001	1.58 (1.45, 1.72)	<0.001
T4	1.45 (1.25, 1.68)	<0.001	3.72 (2.75, 5.01)	<0.001	1.88 (1.62, 2.18)	<0.001	1.96 (1.50, 2.55)	<0.001	2.11 (1.69, 2.64)	<0.001	1.88 (1.72, 2.04)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.10 (0.95, 1.27)	0.203	1.16 (0.90, 1.49)	0.241	0.94 (0.82, 1.07)	0.338	1.02 (0.80, 1.30)	0.852	0.86 (0.69, 1.06)	0.146	1.01 (0.93, 1.09)	0.881
T3	1.02 (0.88, 1.18)	0.789	1.03 (0.79, 1.33)	0.839	0.98 (0.86, 1.12)	0.821	1.00 (0.79, 1.27)	0.996	0.93 (0.76, 1.15)	0.517	0.99 (0.92, 1.07)	0.856
T4	1.21 (1.05, 1.39)	0.008	1.49 (1.18, 1.88)	0.001	1.19 (1.06, 1.34)	0.004	1.34 (1.08, 1.68)	0.009	1.27 (1.05, 1.54)	0.013	1.26 (1.17, 1.36)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 29. The association of baseline frailty status with risks of incident CVD after considering the use of medications for chronic diseases.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.59 (1.49, 1.71)	<0.001	1.54 (1.38, 1.71)	<0.001	1.79 (1.68, 1.91)	<0.001	1.83 (1.65, 2.03)	<0.001	1.63 (1.46, 1.81)	<0.001	1.65 (1.59, 1.71)	<0.001
Model 2	1.64 (1.52, 1.77)	<0.001	1.56 (1.40, 1.74)	<0.001	1.76 (1.66, 1.88)	<0.001	1.82 (1.64, 2.02)	<0.001	1.62 (1.45, 1.81)	<0.001	1.66 (1.60, 1.73)	<0.001
Model 3	1.64 (1.52, 1.76)	<0.001	1.57 (1.41, 1.74)	<0.001	1.76 (1.65, 1.87)	<0.001	1.81 (1.63, 2.02)	<0.001	1.62 (1.45, 1.81)	<0.001	1.67 (1.61, 1.73)	<0.001
Model 4	1.51 (1.40, 1.63)	<0.001	1.55 (1.40, 1.73)	<0.001	1.65 (1.55, 1.76)	<0.001	1.77 (1.59, 1.98)	<0.001	1.61 (1.44, 1.80)	<0.001	1.60 (1.54, 1.66)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

For chronic diseases such as hypertension, diabetes, cancer, arthritis, lung disease, psychiatric disease, memory disease, in addition to the doctor's diagnosis data, we further considered the use of medications corresponding to the condition.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 30. The association of changes in frailty status with risks of incident CVD after considering the use of medications for chronic diseases.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.14 (1.01, 1.29)	0.041	1.85 (1.49, 2.30)	<0.001	1.31 (1.13, 1.50)	<0.001	1.57 (1.18, 2.08)	0.002	1.46 (1.21, 1.77)	<0.001	1.32 (1.23, 1.43)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.75 (0.62, 0.90)	0.003	0.52 (0.38, 0.72)	<0.001	0.78 (0.65, 0.93)	0.007	0.58 (0.39, 0.85)	0.006	0.72 (0.58, 0.89)	0.003	0.72 (0.65, 0.79)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 31. The association of mean FI, FI change with risks of incident CVD after considering the use of medications for chronic diseases.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.38 (1.24, 1.52)	<0.001	2.16 (1.64, 2.84)	<0.001	1.22 (1.08, 1.37)	0.002	1.50 (1.20, 1.86)	<0.001	1.27 (1.05, 1.53)	0.014	1.36 (1.28, 1.46)	<0.001
T3	1.72 (1.56, 1.90)	<0.001	2.85 (2.17, 3.73)	<0.001	1.45 (1.29, 1.62)	<0.001	1.80 (1.45, 2.25)	<0.001	1.73 (1.44, 2.08)	<0.001	1.69 (1.58, 1.80)	<0.001
T4	2.12 (1.91, 2.35)	<0.001	4.50 (3.45, 5.87)	<0.001	1.94 (1.73, 2.18)	<0.001	2.60 (2.08, 3.24)	<0.001	2.30 (1.92, 2.75)	<0.001	2.25 (2.11, 2.40)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.90 (0.82, 0.99)	0.035	1.05 (0.84, 1.30)	0.682	0.92 (0.82, 1.02)	0.101	0.90 (0.74, 1.09)	0.273	0.78 (0.65, 0.92)	0.004	0.89 (0.84, 0.95)	<0.001
T3	0.94 (0.86, 1.03)	0.184	1.03 (0.82, 1.28)	0.821	0.92 (0.83, 1.02)	0.098	0.94 (0.77, 1.14)	0.520	0.92 (0.78, 1.09)	0.351	0.93 (0.87, 0.98)	0.011
T4	1.17 (1.07, 1.28)	0.001	1.57 (1.29, 1.92)	<0.001	1.15 (1.05, 1.27)	0.003	1.25 (1.05, 1.49)	0.012	1.23 (1.05, 1.43)	0.009	1.20 (1.14, 1.27)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 32. The association of baseline frailty status with risks of incident CVD after excluding hypertension, diabetes, and arthritis.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.62 (1.50, 1.75)	<0.001	1.43 (1.28, 1.59)	<0.001	1.76 (1.64, 1.88)	<0.001	1.87 (1.68, 2.08)	<0.001	1.56 (1.39, 1.74)	<0.001	1.61 (1.55, 1.68)	<0.001
Model 2	1.67 (1.54, 1.81)	<0.001	1.45 (1.30, 1.62)	<0.001	1.74 (1.62, 1.86)	<0.001	1.85 (1.66, 2.07)	<0.001	1.55 (1.38, 1.73)	<0.001	1.63 (1.57, 1.70)	<0.001
Model 3	1.66 (1.54, 1.80)	<0.001	1.45 (1.30, 1.62)	<0.001	1.73 (1.61, 1.85)	<0.001	1.85 (1.66, 2.07)	<0.001	1.55 (1.38, 1.73)	<0.001	1.64 (1.57, 1.70)	<0.001
Model 4	1.53 (1.41, 1.66)	<0.001	1.44 (1.29, 1.61)	<0.001	1.61 (1.50, 1.73)	<0.001	1.81 (1.62, 2.03)	<0.001	1.54 (1.38, 1.73)	<0.001	1.56 (1.50, 1.63)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 33. The association of changes in frailty status with risks of incident CVD after excluding hypertension, diabetes, and arthritis.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.40 (1.22, 1.60)	<0.001	1.87 (1.51, 2.31)	<0.001	1.18 (1.02, 1.37)	0.025	1.50 (1.13, 1.99)	0.005	1.42 (1.17, 1.72)	<0.001	1.38 (1.28, 1.49)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.81 (0.67, 0.98)	0.029	0.56 (0.41, 0.77)	<0.001	0.75 (0.61, 0.92)	0.006	0.57 (0.38, 0.85)	0.006	0.74 (0.59, 0.93)	0.009	0.72 (0.65, 0.80)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 34. The association of mean FI, FI change with risks of incident CVD after excluding hypertension, diabetes, and arthritis.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.27 (1.15, 1.40)	<0.001	1.75 (1.35, 2.28)	<0.001	1.22 (1.08, 1.38)	0.001	1.26 (1.02, 1.55)	0.034	1.21 (1.01, 1.46)	0.043	1.28 (1.20, 1.37)	<0.001
T3	1.54 (1.39, 1.70)	<0.001	2.25 (1.74, 2.90)	<0.001	1.42 (1.26, 1.59)	<0.001	1.49 (1.21, 1.84)	<0.001	1.64 (1.37, 1.96)	<0.001	1.55 (1.45, 1.65)	<0.001
T4	1.87 (1.69, 2.08)	<0.001	3.58 (2.79, 4.60)	<0.001	1.97 (1.75, 2.22)	<0.001	2.21 (1.79, 2.73)	<0.001	1.99 (1.66, 2.38)	<0.001	2.06 (1.93, 2.20)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.90 (0.82, 0.99)	0.034	1.05 (0.84, 1.30)	0.684	0.86 (0.78, 0.96)	0.008	0.98 (0.81, 1.18)	0.797	0.85 (0.71, 1.01)	0.061	0.89 (0.84, 0.95)	<0.001
T3	0.96 (0.88, 1.05)	0.407	0.92 (0.73, 1.15)	0.452	0.91 (0.82, 1.00)	0.059	0.87 (0.72, 1.06)	0.172	1.04 (0.88, 1.23)	0.641	0.93 (0.88, 0.99)	0.020
T4	1.16 (1.06, 1.27)	0.001	1.46 (1.20, 1.78)	<0.001	1.15 (1.04, 1.26)	0.005	1.27 (1.06, 1.51)	0.009	1.31 (1.12, 1.53)	0.001	1.20 (1.14, 1.27)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 35. The association of baseline frailty status with risks of incident CVD after excluding samples lost to follow-up en route.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.70 (1.58, 1.83)	<0.001	1.51 (1.35, 1.68)	<0.001	1.84 (1.72, 1.98)	<0.001	1.81 (1.63, 2.02)	<0.001	1.67 (1.49, 1.87)	<0.001	1.69 (1.63, 1.76)	<0.001
Model 2	1.67 (1.55, 1.80)	<0.001	1.53 (1.37, 1.71)	<0.001	1.80 (1.68, 1.93)	<0.001	1.77 (1.59, 1.97)	<0.001	1.66 (1.48, 1.86)	<0.001	1.68 (1.61, 1.75)	<0.001
Model 3	1.66 (1.53, 1.79)	<0.001	1.54 (1.38, 1.72)	<0.001	1.79 (1.66, 1.92)	<0.001	1.75 (1.57, 1.96)	<0.001	1.66 (1.48, 1.86)	<0.001	1.68 (1.61, 1.75)	<0.001
Model 4	1.51 (1.40, 1.64)	<0.001	1.53 (1.37, 1.71)	<0.001	1.66 (1.54, 1.79)	<0.001	1.67 (1.50, 1.87)	<0.001	1.65 (1.47, 1.85)	<0.001	1.60 (1.53, 1.67)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

The death data collection period for each cohort included HRS 2002-2018, CHARLS 2013-2018, SHARE 2013-2019, ELSA 2006-2012, and MHAS 2003-2018. It was important to note that ELSA's death data was only updated until 2012.

A sample lost during follow-up specifically referred to a sample that was non-CVD in the previous surveys, and no new surveys were available in the follow-up surveys (for example, a sample that was non-CVD during the HRS 2000-2010 survey was eliminated at the time of the 2012 survey when follow-up was lost).

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 36. The association of changes in frailty status with risks of incident CVD after excluding samples lost to follow-up en route.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.24 (1.09, 1.42)	0.001	1.93 (1.55, 2.41)	<0.001	1.40 (1.21, 1.62)	<0.001	1.42 (1.05, 1.91)	0.021	1.44 (1.19, 1.75)	<0.001	1.38 (1.28, 1.50)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.72 (0.59, 0.88)	0.001	0.55 (0.40, 0.75)	<0.001	0.76 (0.63, 0.92)	0.005	0.57 (0.37, 0.87)	0.010	0.72 (0.58, 0.89)	0.003	0.71 (0.64, 0.79)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

The death data collection period for each cohort included HRS 2002-2018, CHARLS 2013-2018, SHARE 2013-2019, ELSA 2006-2012, and MHAS 2003-2018. It was important to note that ELSA's death data was only updated until 2012.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 37. The association of mean FI, FI change with risks of incident CVD after excluding samples lost to follow-up en route.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.28 (1.15, 1.43)	<0.001	2.01 (1.51, 2.67)	<0.001	1.31 (1.15, 1.50)	<0.001	1.31 (1.02, 1.67)	0.032	1.28 (1.06, 1.56)	0.012	1.34 (1.25, 1.44)	<0.001
T3	1.62 (1.46, 1.80)	<0.001	3.04 (2.31, 4.00)	<0.001	1.58 (1.39, 1.80)	<0.001	1.66 (1.31, 2.11)	<0.001	1.72 (1.42, 2.07)	<0.001	1.69 (1.57, 1.81)	<0.001
T4	2.05 (1.84, 2.29)	<0.001	4.44 (3.39, 5.81)	<0.001	2.36 (2.07, 2.69)	<0.001	2.40 (1.90, 3.03)	<0.001	2.36 (1.96, 2.84)	<0.001	2.34 (2.18, 2.50)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.92 (0.83, 1.01)	0.092	1.04 (0.84, 1.29)	0.713	0.87 (0.78, 0.97)	0.013	0.89 (0.73, 1.09)	0.249	0.84 (0.70, 1.00)	0.047	0.89 (0.84, 0.95)	<0.001
T3	0.96 (0.87, 1.06)	0.391	0.90 (0.72, 1.12)	0.333	0.88 (0.79, 0.98)	0.024	0.98 (0.81, 1.18)	0.810	0.97 (0.82, 1.15)	0.745	0.93 (0.87, 0.98)	0.013
T4	1.19 (1.08, 1.30)	<0.001	1.44 (1.18, 1.75)	<0.001	1.15 (1.04, 1.27)	0.006	1.21 (1.01, 1.46)	0.035	1.31 (1.12, 1.54)	0.001	1.21 (1.14, 1.28)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

The death data collection period for each cohort included HRS 2002-2018, CHARLS 2013-2018, SHARE 2013-2019, ELSA 2006-2012, and MHAS 2003-2018. It was important to note that ELSA's death data was only updated until 2012.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 38. The association of baseline frailty status with risks of incident CVD after considering death as a competitive risk.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.16 (1.07, 1.25)	<0.001	1.42 (1.28, 1.57)	<0.001	1.48 (1.39, 1.58)	<0.001	1.82 (1.65, 2.01)	<0.001	1.59 (1.43, 1.77)	<0.001	1.39 (1.34, 1.45)	<0.001
Model 2	1.17 (1.09, 1.27)	<0.001	1.44 (1.30, 1.60)	<0.001	1.47 (1.38, 1.57)	<0.001	1.81 (1.63, 2.00)	<0.001	1.59 (1.42, 1.76)	<0.001	1.41 (1.36, 1.47)	<0.001
Model 3	1.18 (1.09, 1.28)	<0.001	1.45 (1.31, 1.61)	<0.001	1.47 (1.37, 1.56)	<0.001	1.80 (1.63, 1.99)	<0.001	1.58 (1.42, 1.76)	<0.001	1.42 (1.37, 1.48)	<0.001
Model 4	1.16 (1.07, 1.26)	<0.001	1.44 (1.30, 1.60)	<0.001	1.40 (1.31, 1.50)	<0.001	1.76 (1.59, 1.95)	<0.001	1.57 (1.41, 1.75)	<0.001	1.39 (1.33, 1.44)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 39. The association of changes in frailty status with risks of incident CVD after considering death as a competitive risk.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.17 (1.03, 1.32)	0.016	1.75 (1.40, 2.19)	<0.001	1.25 (1.09, 1.44)	0.002	1.64 (1.24, 2.17)	0.001	1.44 (1.20, 1.72)	<0.001	1.30 (1.20, 1.40)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.78 (0.66, 0.94)	0.008	0.59 (0.44, 0.80)	0.001	0.82 (0.69, 0.98)	0.024	0.53 (0.36, 0.78)	0.001	0.79 (0.64, 0.96)	0.021	0.76 (0.69, 0.83)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 40. The association of mean FI, FI change with risks of incident CVD after considering death as a competitive risk.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.35 (1.23, 1.50)	<0.001	2.11 (1.61, 2.78)	<0.001	1.29 (1.14, 1.46)	<0.001	1.50 (1.21, 1.85)	<0.001	1.28 (1.07, 1.54)	0.008	1.39 (1.30, 1.48)	<0.001
T3	1.63 (1.48, 1.80)	<0.001	2.90 (2.23, 3.77)	<0.001	1.56 (1.38, 1.75)	<0.001	1.84 (1.49, 2.27)	<0.001	1.73 (1.45, 2.07)	<0.001	1.71 (1.60, 1.82)	<0.001
T4	1.81 (1.63, 2.01)	<0.001	3.93 (3.02, 5.10)	<0.001	2.15 (1.91, 2.42)	<0.001	2.49 (2.01, 3.09)	<0.001	2.24 (1.87, 2.67)	<0.001	2.17 (2.03, 2.32)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.95 (0.86, 1.05)	0.293	1.09 (0.88, 1.35)	0.448	0.90 (0.81, 0.99)	0.040	0.97 (0.80, 1.17)	0.765	0.84 (0.71, 1.00)	0.044	0.92 (0.87, 0.98)	0.008
T3	0.99 (0.90, 1.08)	0.832	0.92 (0.73, 1.14)	0.435	0.91 (0.82, 1.01)	0.064	0.95 (0.78, 1.14)	0.561	0.97 (0.83, 1.14)	0.723	0.94 (0.89, 1.00)	0.035
T4	1.14 (1.05, 1.25)	0.003	1.44 (1.18, 1.75)	<0.001	1.13 (1.03, 1.24)	0.007	1.28 (1.07, 1.52)	0.006	1.33 (1.15, 1.55)	<0.001	1.19 (1.13, 1.26)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 41. The association of baseline frailty status with risks of incident CVD after PSM treatment.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Model 1	1.53 (1.40, 1.66)	<0.001	1.50 (1.34, 1.68)	<0.001	1.74 (1.62, 1.86)	<0.001	1.84 (1.63, 2.08)	<0.001	1.61 (1.44, 1.81)	<0.001	1.49 (1.40, 1.58)	<0.001
Model 2	1.55 (1.43, 1.69)	<0.001	1.50 (1.34, 1.68)	<0.001	1.73 (1.61, 1.85)	<0.001	1.84 (1.63, 2.07)	<0.001	1.61 (1.43, 1.81)	<0.001	1.50 (1.41, 1.59)	<0.001
Model 3	1.55 (1.43, 1.69)	<0.001	1.51 (1.35, 1.69)	<0.001	1.71 (1.60, 1.83)	<0.001	1.84 (1.63, 2.08)	<0.001	1.61 (1.43, 1.81)	<0.001	1.50 (1.41, 1.59)	<0.001
Model 4	1.52 (1.39, 1.65)	<0.001	1.51 (1.35, 1.69)	<0.001	1.67 (1.56, 1.79)	<0.001	1.84 (1.63, 2.08)	<0.001	1.61 (1.43, 1.81)	<0.001	1.45 (1.36, 1.54)	<0.001

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Model 1 adjusted for age and sex; Model 2 further adjusted education, employment; Model 3 further adjusted marital status and co-residence with children; Model 4 was fully adjusted, further controlling smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country.

Supplementary Table 42. The association of changes in frailty status with risks of incident CVD after PSM treatment.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Stable Non-frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Non-frailty to Frailty	1.25 (1.07, 1.47)	0.004	2.12 (1.63, 2.74)	<0.001	1.31 (1.11, 1.55)	0.001	1.68 (1.14, 2.46)	0.008	1.47 (1.19, 1.81)	<0.001	1.44 (1.32, 1.58)	<0.001
Stable Frailty	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
Frailty to Non-frailty	0.67 (0.55, 0.82)	<0.001	0.53 (0.38, 0.75)	<0.001	0.79 (0.65, 0.96)	0.016	0.47 (0.30, 0.72)	0.001	0.74 (0.59, 0.93)	0.009	0.69 (0.62, 0.77)	<0.001

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. In addition, we added the baseline frailty index to the models for control.

Supplementary Table 43. The association of mean FI, FI change with risks of incident CVD after PSM treatment.

	HRS		CHARLS		SHARE		ELSA		MHAS		Pooled	
	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>	HR (95%CI)	<i>P</i>
Mean FI												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	1.56 (1.26, 1.93)	<0.001	2.60 (1.64, 4.15)	<0.001	1.40 (1.07, 1.83)	0.015	1.82 (1.03, 3.21)	0.041	1.33 (0.99, 1.79)	0.059	1.38 (1.23, 1.56)	<0.001
T3	1.76 (1.43, 2.15)	<0.001	3.42 (2.20, 5.31)	<0.001	1.42 (1.10, 1.85)	0.008	2.27 (1.30, 3.95)	0.004	1.75 (1.33, 2.30)	<0.001	1.70 (1.52, 1.91)	<0.001
T4	2.19 (1.82, 2.64)	<0.001	5.03 (3.29, 7.69)	<0.001	2.17 (1.71, 2.75)	<0.001	2.48 (1.49, 4.13)	<0.001	2.40 (1.86, 3.10)	<0.001	2.36 (2.12, 2.62)	<0.001
FI change												
T1	1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.		1 Ref.	
T2	0.87 (0.74, 1.02)	0.089	1.09 (0.82, 1.45)	0.566	0.93 (0.79, 1.11)	0.426	1.20 (0.84, 1.71)	0.318	0.84 (0.68, 1.06)	0.138	0.86 (0.79, 0.94)	0.001
T3	0.92 (0.79, 1.07)	0.263	0.80 (0.59, 1.09)	0.156	0.89 (0.75, 1.05)	0.169	1.06 (0.75, 1.52)	0.735	1.05 (0.85, 1.30)	0.656	0.85 (0.78, 0.93)	<0.001
T4	1.16 (1.02, 1.31)	0.024	1.60 (1.27, 2.03)	<0.001	1.17 (1.02, 1.33)	0.025	1.38 (1.04, 1.84)	0.025	1.35 (1.13, 1.63)	0.001	1.22 (1.13, 1.31)	<0.001

FI: frailty index; CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Mean FI was calculated by the FI at baseline and the FI in the second survey. FI change was calculated by the FI in the second survey minus the FI at baseline. T1 was the lower quarter, T2 was the two quarters, T3 was the three quarters, and T4 was the upper quarter. All analyses had been adjusted for age, sex, education, employment, marital status, co-residence with children, smoking, drinking, social activity, and physical activity. In the SHARE and Pooled cohorts, we controlled the different country. Since mean FI and FI change were calculated from baseline FI, baseline FI was not included as a control variable in the analysis to avoid collinearity.

Supplementary Table 44. Characteristics of the sample included in the final analysis compared with those excluded because of younger age, CVD at baseline, and missing data in HRS.

Characteristics	Total (N=19,580)	Included (N=12,624)	Excluded (N=6,956)	<i>P</i>
Age, mean (S.D.)	67.09 (10.84)	65.72 (9.46)	69.57 (12.61)	<0.001
Sex, n (%)				<0.001
Male	11,468 (58.57)	7,630 (60.44)	3,838 (55.18)	
Female	8,112 (41.43)	4,994 (39.56)	3,118 (44.82)	
Education, n (%)				<0.001
Below high school	5,719 (29.21)	3,244 (25.70)	2,475 (35.58)	
High school	6,566 (33.53)	4,410 (34.93)	2,156 (30.99)	
Above high school	7,258 (37.07)	4,970 (39.37)	2,288 (32.89)	
Missing	37 (0.19)	0 (0.00)	37 (0.53)	
Employment, n (%)				<0.001
Unemployed	4,896 (25.01)	2,804 (22.21)	2,092 (30.07)	
Working or retired	14,650 (74.82)	9,820 (77.79)	4,830 (69.44)	
Missing	34 (0.17)	0 (0.00)	34 (0.49)	
Marital status, n (%)				<0.001
Unmarried and others	7,056 (36.04)	4,220 (33.43)	2,836 (40.77)	
Married and partnered	12,520 (63.94)	8,404 (66.57)	4,116 (59.17)	
Missing	4 (0.02)	0 (0.00)	4 (0.06)	
Co-residence with children, n (%)				<0.001

No	10,611 (54.19)	6,913 (54.76)	3,698 (53.16)	
Yes	8,936 (45.64)	5,711 (45.24)	3,225 (46.36)	
Missing	33 (0.17)	0 (0.00)	33 (0.47)	
Smoking, n (%)				<0.001
No	16,493 (84.23)	10,667 (84.50)	5,826 (83.76)	
Yes	2,971 (15.17)	1,957 (15.50)	1,014 (14.58)	
Missing	116 (0.59)	0 (0.00)	116 (1.67)	
Drinking, n (%)				<0.001
No	10,769 (55.00)	6,416 (50.82)	4,353 (62.58)	
Yes	8,807 (44.98)	6,208 (49.18)	2,599 (37.36)	
Missing	4 (0.02)	0 (0.00)	4 (0.06)	
Social activity, n (%)				<0.001
No	13,593 (69.42)	8,366 (66.27)	5,227 (75.14)	
Yes	5,949 (30.38)	4,258 (33.73)	1,691 (24.31)	
Missing	38 (0.19)	0 (0.00)	38 (0.55)	
Physical activity, n (%)				<0.001
Others	11,369 (58.06)	6,658 (52.74)	4,711 (67.73)	
Vigorous	8,205 (41.91)	5,966 (47.26)	2,239 (32.19)	
Missing	6 (0.03)	0 (0.00)	6 (0.09)	
Frailty index, mean (S.D.)	0.19 (0.16)	0.15 (0.13)	0.26 (0.18)	<0.001

S.D.: standard deviation. The differences of categorical variables were assessed by χ^2 tests, and the differences of continuous variables were compared by t tests (two-tailed independent t-test).

Supplementary Table 45. Characteristics of the sample included in the final analysis compared with those excluded because of younger age, CVD at baseline, and missing data in CHARLS.

Characteristics	Total (N=17,596)	Included (N=10,288)	Excluded (N=7,308)	<i>P</i>
Age, mean (S.D.)	60.06 (10.15)	61.72 (8.32)	57.70 (11.90)	<0.001
Sex, n (%)				<0.001
Male	8,419 (47.85)	5,174 (50.30)	3,245 (44.40)	
Female	9,157 (52.04)	5,113 (49.70)	4,044 (55.34)	
Missing	19 (0.11)	0 (0.00)	19 (0.26)	
Education, n (%)				<0.001
Below high school	15,332 (87.14)	9,153 (88.98)	6,179 (84.55)	
High school	1,801 (10.24)	967 (9.40)	834 (11.41)	
Above high school	426 (2.42)	167 (1.62)	259 (3.54)	
Missing	36 (0.20)	0 (0.00)	36 (0.49)	
Employment, n (%)				<0.001
Unemployed	7,373 (41.90)	4,171 (40.55)	3,202 (43.81)	
Working or retired	10,152 (57.70)	6,116 (59.45)	4,036 (55.23)	
Missing	70 (0.40)	0 (0.00)	70 (0.96)	
Marital status, n (%)				<0.001
Unmarried and others	2,234 (12.70)	1,296 (12.60)	938 (12.84)	
Married and partnered	15,348 (87.23)	8,991 (87.40)	6,357 (86.99)	
Missing	13 (0.07)	0 (0.00)	13 (0.18)	
Co-residence with children, n (%)				<0.001
No	7,420 (42.17)	4,932 (47.94)	2,488 (34.04)	
Yes	10,098 (57.39)	5,355 (52.06)	4,743 (64.90)	
Missing	77 (0.44)	0 (0.00)	77 (1.05)	
Smoking, n (%)				<0.001
No	10,628 (60.40)	6,019 (58.51)	4,609 (63.07)	
Yes	6,930 (39.39)	4,268 (41.49)	2,662 (36.43)	

Missing	37 (0.21)	0 (0.00)	37 (0.51)	
Drinking, n (%)				<0.001
No	11,784 (66.97)	6,678 (64.92)	5,106 (69.87)	
Yes	5,767 (32.78)	3,609 (35.08)	2,158 (29.53)	
Missing	44 (0.25)	0 (0.00)	44 (0.60)	
Social activity, n (%)				0.967
No	9,647 (54.83)	5,642 (54.85)	4,005 (54.80)	
Yes	7,948 (45.17)	4,645 (45.15)	3,303 (45.20)	
Physical activity, n (%)				<0.001
Others	15,232 (86.57)	8,727 (84.84)	6,505 (89.01)	
Vigorous	2,361 (13.42)	1,560 (15.16)	801 (10.96)	
Missing	2 (0.01)	0 (0.00)	2 (0.03)	
Frailty index, mean (S.D.)	0.19 (0.14)	0.18 (0.13)	0.20 (0.16)	<0.001

S.D.: standard deviation. The differences of categorical variables were assessed by χ^2 tests, and the differences of continuous variables were compared by t tests (two-tailed independent t-test).

Supplementary Table 46. Characteristics of the sample included in the final analysis compared with those excluded because of younger age, CVD at baseline, and missing data in SHARE.

Characteristics	Total (N=57,982)	Included (N=36,954)	Excluded (N=21,028)	<i>P</i>
Age, mean (S.D.)	65.96 (10.39)	64.96 (9.29)	67.71 (11.87)	<0.001
Sex, n (%)				<0.001
Male	25,073 (43.24)	15,491 (41.92)	9,582 (45.57)	
Female	32,909 (56.76)	21,463 (58.08)	11,446 (54.43)	
Education, n (%)				<0.001
Below high school	23,442 (40.43)	14,573 (39.44)	8,869 (42.18)	
High school	16,772 (28.93)	11,122 (30.10)	5,650 (26.87)	
Above high school	16,787 (29.14)	11,259 (30.47)	5,639 (26.82)	
Missing	870 (1.50)	0 (0.00)	870 (4.14)	
Employment, n (%)				<0.001
Unemployed	26,597 (45.87)	17,913 (48.47)	8,684 (41.30)	
Working or retired	30,702 (52.95)	19,041 (51.53)	11,661 (55.45)	
Missing	683 (1.18)	0 (0.00)	683 (3.25)	
Marital status, n (%)				<0.001
Unmarried and others	16,538 (28.52)	10,191 (27.58)	6,347 (30.18)	
Married and partnered	41,428 (71.45)	26,763 (72.42)	14,665 (69.74)	
Missing	16 (0.03)	0 (0.00)	16 (0.08)	
Co-residence with children, n (%)				<0.001
No	45,937 (79.23)	29,061 (78.64)	16,876 (80.25)	

Yes	11,996 (20.69)	7,892 (21.36)	4,103 (19.51)	
Missing	49 (0.08)	0 (0.00)	49 (0.23)	
Smoking, n (%)				<0.001
No	46,524 (80.24)	29,837 (80.74)	16,687 (79.36)	
Yes	10,753 (18.55)	7,117 (19.26)	3,636 (17.29)	
Missing	705 (1.22)	0 (0.00)	705 (3.35)	
Drinking, n (%)				<0.001
No	19,284 (33.26)	10,581 (28.63)	8,703 (41.39)	
Yes	38,450 (66.31)	26,373 (71.37)	12,077 (57.43)	
Missing	248 (0.43)	0 (0.00)	248 (1.18)	
Social activity, n (%)				<0.001
No	38,503 (66.41)	22,871 (61.89)	15,632 (74.34)	
Yes	19,475 (33.59)	14,083 (38.11)	5,392 (25.64)	
Missing	4 (0.01)	0 (0.00)	4 (0.02)	
Physical activity, n (%)				<0.001
Others	38,480 (66.37)	23,481 (63.54)	14,999 (71.33)	
Vigorous	18,771 (32.37)	13,473 (36.46)	5,298 (25.19)	
Missing	731 (1.26)	0 (0.00)	731 (3.48)	
Frailty index, mean (S.D.)	0.15 (0.15)	0.13 (0.12)	0.20 (0.18)	<0.001

S.D.: standard deviation. The differences of categorical variables were assessed by χ^2 tests, and the differences of continuous variables were compared by t tests (two-tailed independent t-test).

Supplementary Table 47. Characteristics of the sample included in the final analysis compared with those excluded because of younger age, CVD at baseline, and missing data in ELSA.

Characteristics	Total (N=9,432)	Included (N=7,173)	Excluded (N=2,259)	<i>P</i>
Age, mean (S.D.)	65.41 (10.20)	65.35 (9.41)	65.60 (12.46)	0.381
Sex, n (%)				0.857
Male	4,126 (43.74)	3,142 (43.80)	984 (43.56)	
Female	5,306 (56.26)	4,031 (56.20)	1,275 (56.44)	
Education, n (%)				<0.001
Below high school	2,897 (30.71)	2,203 (30.71)	694 (30.72)	
High school	3,418 (36.24)	2,665 (37.15)	753 (33.33)	
Above high school	3,057 (32.41)	2,305 (32.13)	752 (33.29)	
Missing	60 (0.64)	0 (0.00)	60 (2.66)	
Employment, n (%)				0.001
Unemployed	2,203 (23.36)	1,630 (22.72)	573 (25.37)	
Working or retired	7,227 (76.62)	5,543 (77.28)	1,684 (74.55)	
Missing	2 (0.02)	0 (0.00)	2 (0.09)	
Marital status, n (%)				0.022
Unmarried and others	3,053 (32.37)	2,281 (31.80)	772 (34.17)	
Married and partnered	6,378 (67.62)	4,892 (68.20)	1,486 (65.78)	
Missing	1 (0.01)	0 (0.00)	1 (0.04)	
Co-residence with children, n (%)				<0.001
No	7,912 (83.88)	6,008 (83.76)	1,904 (84.29)	

Yes	1,501 (15.91)	1,165 (16.24)	336 (14.87)	
Missing	19 (0.20)	0 (0.00)	19 (0.84)	
Smoking, n (%)				0.001
No	7,953 (84.32)	6,067 (84.58)	1,886 (83.49)	
Yes	1,475 (15.64)	1,106 (15.42)	369 (16.33)	
Missing	4 (0.04)	0 (0.00)	4 (0.18)	
Drinking, n (%)				<0.001
No	2,171 (23.02)	1,373 (19.14)	798 (35.33)	
Yes	7,261 (76.98)	5,800 (80.86)	1,461 (64.67)	
Social activity, n (%)				<0.001
No	7,314 (77.54)	5,415 (75.49)	1,899 (84.06)	
Yes	2,112 (22.39)	1,758 (24.51)	354 (15.67)	
Missing	6 (0.06)	0 (0.00)	6 (0.27)	
Physical activity, n (%)				<0.001
Others	7,638 (80.98)	5,788 (80.69)	1,850 (81.89)	
Vigorous	1,661 (17.61)	1,385 (19.31)	276 (12.22)	
Missing	133 (1.41)	0 (0.00)	133 (5.89)	
Frailty index, mean (S.D.)	0.15 (0.15)	0.14 (0.13)	0.19 (0.17)	<0.001

S.D.: standard deviation. The differences of categorical variables were assessed by χ^2 tests, and the differences of continuous variables were compared by t tests (two-tailed independent t-test).

Supplementary Table 48. Characteristics of the sample included in the final analysis compared with those excluded because of younger age, CVD at baseline, and missing data in MHAS.

Characteristics	Total (N=15,182)	Included (N=9,855)	Excluded (N=5,327)	<i>P</i>
Age, mean (S.D.)	60.26 (10.84)	61.67 (9.12)	57.66 (13.06)	<0.001
Sex, n (%)				<0.001
Male	6,503 (42.83)	4,413 (44.78)	2,090 (39.23)	
Female	8,679 (57.17)	5,442 (55.22)	3,237 (60.77)	
Education, n (%)				<0.001
Below high school	13,664 (90.00)	8,913 (90.44)	4,751 (89.19)	
High school	749 (4.93)	478 (4.85)	271 (5.09)	
Above high school	750 (4.94)	464 (4.71)	286 (5.37)	
Missing	19 (0.13)	0 (0.00)	19 (0.36)	
Employment, n (%)				<0.001
Unemployed	8,844 (58.25)	5,607 (56.89)	3,237 (60.77)	
Working or retired	6,300 (41.50)	4,248 (43.11)	2,052 (38.52)	
Missing	38 (0.25)	0 (0.00)	38 (0.71)	
Marital status, n (%)				<0.001
Unmarried and others	4,218 (27.78)	2,989 (30.33)	1,229 (23.07)	
Married and partnered	10,508 (69.21)	6,866 (69.67)	3,642 (68.37)	
Missing	456 (3.00)	0 (0.00)	456 (8.56)	
Co-residence with children, n (%)				<0.001
No	4,447 (29.29)	2,902 (29.45)	1,545 (29.00)	

Yes	10,552 (69.50)	6,953 (70.55)	3,599 (67.56)	
Missing	183 (1.21)	0 (0.00)	183 (3.44)	
Smoking, n (%)				<0.001
No	12,522 (82.48)	8,150 (82.70)	4,372 (82.07)	
Yes	2,651 (17.46)	1,705 (17.30)	946 (17.76)	
Missing	9 (0.06)	0 (0.00)	9 (0.17)	
Drinking, n (%)				<0.001
No	10,441 (68.77)	6,733 (68.32)	3,708 (69.61)	
Yes	4,734 (31.18)	3,122 (31.68)	1,612 (30.26)	
Missing	7 (0.05)	0 (0.00)	7 (0.13)	
Social activity, n (%)				<0.001
No	12,116 (79.81)	8,441 (85.65)	3,675 (68.99)	
Yes	1,989 (13.10)	1,414 (14.35)	575 (10.79)	
Missing	1,077 (7.09)	0 (0.00)	1,077 (20.22)	
Physical activity, n (%)				<0.001
Others	9,268 (61.05)	6,490 (65.85)	2,778 (52.15)	
Vigorous	4,768 (31.41)	3,365 (34.15)	1,403 (26.34)	
Missing	1,146 (7.55)	0 (0.00)	1,146 (21.51)	
Frailty index, mean (S.D.)	0.18 (0.15)	0.19 (0.14)	0.16 (0.16)	<0.001

S.D.: standard deviation. The differences of categorical variables were assessed by χ^2 tests, and the differences of continuous variables were compared by t tests (two-tailed independent t-test).

Supplementary Table 49. Detailed sample size of Fig.1a-f.

Cohort/country		Follow year	Total, n	CVD, n (%)	Non-CVD, n (%)
Fig.1a HRS		2000	13,446	4,959 (36.88)	8,487 (63.12)
		2002	11,802	3,975 (33.68)	7,827 (66.32)
		2004	10,419	3,243 (31.13)	7,176 (68.87)
		2006	9,179	2,582 (28.13)	6,597 (71.87)
		2008	7,984	2,058 (25.77)	5,926 (74.23)
		2010	6,838	1,441 (21.07)	5,897 (78.93)
		2012	5,790	989 (17.08)	4,801 (82.92)
		2014	4,751	621 (13.07)	4,130 (86.93)
		2016	3,554	253 (7.12)	3,301 (92.88)
Fig.1b CHARLS		2011	14,092	1,823 (12.94)	12,269 (87.06)
		2013	13,055	1,698 (13.01)	11,357 (86.99)
		2015	10,580	1,342 (12.68)	9,238 (87.32)
Fig.1c SHARE		2011	39,056	6,400 (16.39)	32,656 (83.61)
		2013	32,007	4,257 (13.30)	27,750 (86.70)
		2015	26,163	2,516 (9.62)	23,647 (90.38)
		2017	14,867	980 (6.60)	13,887 (93.40)
Fig.1d ELSA		2004	7,597	2,037 (26.81)	5,560 (73.19)
		2006	5,914	1,013 (17.13)	4,901 (82.87)
		2008	5,185	775 (14.95)	4,410 (85.05)
		2010	4,585	607 (13.24)	3,978 (86.76)
		2012	3,920	444 (11.33)	3,476 (88.67)
		2014	3,362	319 (9.49)	3,043 (90.51)
		2016	2,824	207 (7.33)	2,617 (92.67)
Fig.1e MHAS		2001	13,169	2,002 (15.20)	11,067 (84.80)
		2003	9,584	1,709 (17.83)	7,875 (82.17)
		2012	8,096	1,233 (15.23)	6,863 (84.77)
		2015	6,017	505 (8.39)	5,512 (91.61)
Fig.1f United States of America		2000	13,446	4,959 (36.88)	8,487 (63.12)
Fig.1f China		2011	14,092	1,823 (12.94)	12,269 (87.06)
Fig.1f Estonia		2011	4,382	933 (21.29)	3,449 (78.71)
Fig.1f France		2011	3,744	565 (15.09)	3,179 (84.91)
Fig.1f Belgium		2011	3,715	534 (14.37)	3,181 (85.63)
Fig.1f Czech Republic		2011	3,665	678 (18.50)	2,987 (81.50)
Fig.1f Austria		2011	3,601	603 (16.75)	2,998 (83.25)

Fig.1f Switzerland	2011	2,866	325 (11.34)	2,541 (88.66)
Fig.1f Spain	2011	2,808	468 (16.67)	2,340 (83.33)
Fig.1f Italy	2011	2,528	440 (17.40)	2,088 (82.60)
Fig.1f Netherlands	2011	2,019	184 (9.11)	1,835 (90.89)
Fig.1f Slovenia	2011	1,909	361 (18.91)	1,548 (81.09)
Fig.1f Denmark	2011	1,820	285 (15.66)	1,535 (84.34)
Fig.1f Portugal	2011	1,355	189 (13.95)	1,166 (86.05)
Fig.1f Sweden	2011	1,354	188 (13.89)	1,166 (86.11)
Fig.1f Hungary	2011	1,210	164 (13.55)	1,046 (86.45)
Fig.1f Poland	2011	1,112	291 (26.17)	821 (73.83)
Fig.1f Germany	2011	968	192 (19.83)	776 (80.17)
Fig.1f United Kingdom	2004	7,597	2,037 (26.81)	5,560 (73.19)
Fig.1f Mexico	2001	13,169	2,002 (15.20)	11,067 (84.80)

CVD: cardiovascular disease; HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Supplementary Table 50. Detailed sample size of Supplementary Figure.11a-f.

Cohort/country		Follow year	Total, n	Heart disease, n (%)	Non-heart disease, n (%)
Supplementary Figure.11a HRS		2000	13,999	4,493 (32.10)	9,506 (67.90)
		2002	18,321	9,587 (52.33)	8,734 (47.67)
		2004	11,407	3,405 (29.85)	8,002 (70.15)
		2006	10,506	3,168 (30.16)	7,338 (69.84)
		2008	9,429	2,863 (30.37)	6,566 (69.63)
		2010	8,542	2,579 (30.19)	5,963 (69.81)
		2012	7,525	2,260 (30.03)	5,265 (69.97)
		2014	6,301	1,857 (29.47)	4,444 (70.53)
		2016	3,738	218 (5.83)	3,520 (94.17)
Supplementary Figure.11b CHARLS		2011	14,364	510 (3.55)	13,854 (96.45)
		2013	13,291	396 (2.98)	12,895 (97.02)
		2015	10,810	100 (0.93)	10,710 (99.07)
Supplementary Figure.11c SHARE		2011	40,315	5,502 (13.65)	34,813 (86.35)
		2013	33,336	3,726 (11.18)	29,610 (88.82)
		2015	27,392	2,189 (8.00)	25,203 (92.00)
		2017	15,594	828 (5.31)	14,766 (94.69)
Supplementary Figure.11d ELSA		2004	7,668	1,797 (23.44)	5,871 (76.56)
		2006	6,084	916 (15.06)	5,168 (84.94)
		2008	5,334	685 (12.84)	4,649 (87.16)
		2010	4,735	543 (11.47)	4,192 (88.53)
		2012	4,066	410 (10.08)	3,656 (89.92)
		2014	3,497	307 (8.78)	3,190 (91.22)
		2016	2,928	204 (6.97)	2,724 (93.03)
Supplementary Figure.11e MHAS		2001	12,943	1,625 (12.55)	11,318 (87.45)
		2003	9,477	1,413 (14.91)	8,064 (85.09)
		2012	14,117	7,097 (50.27)	7,020 (49.73)
		2015	6,059	438 (7.23)	5,621 (92.77)
Supplementary Figure.11f United States of America		2000	13,999	4,493 (32.10)	9,506 (67.90)
Supplementary Figure.11f China		2011	14,364	510 (3.55)	13,854 (96.45)
Supplementary Figure.11f Estonia		2011	4,611	885 (19.19)	3,726 (80.81)
Supplementary Figure.11f France		2011	3,840	504 (13.12)	3,336 (86.88)
Supplementary Figure.11f Belgium		2011	3,817	454 (11.89)	3,363 (88.11)
Supplementary Figure.11f Czech Republic		2011	3,797	554 (14.59)	3,243 (85.41)

Supplementary Figure.11f Austria	2011	3,743	479 (12.80)	3,264 (87.20)
Supplementary Figure.11f Switzerland	2011	2,917	274 (9.40)	2,643 (90.60)
Supplementary Figure.11f Spain	2011	2,867	419 (14.61)	2,448 (85.39)
Supplementary Figure.11f Italy	2011	2,582	380 (14.72)	2,202 (85.28)
Supplementary Figure.11f Netherlands	2011	2,083	138 (6.63)	1,945 (93.37)
Supplementary Figure.11f Slovenia	2011	1,955	309 (15.80)	1,646 (84.20)
Supplementary Figure.11f Denmark	2011	1,871	245 (13.09)	1,626 (86.91)
Supplementary Figure.11f Portugal	2011	1,154	264 (22.88)	890 (77.12)
Supplementary Figure.11f Sweden	2011	1,388	152 (10.95)	1,236 (89.05)
Supplementary Figure.11f Hungary	2011	1,281	133 (10.38)	1,148 (89.62)
Supplementary Figure.11f Poland	2011	1,410	160 (11.35)	1,250 (88.65)
Supplementary Figure.11f Germany	2011	999	152 (15.22)	847 (84.78)
Supplementary Figure.11f United Kingdom	2004	7,668	1,797 (23.44)	5,871 (76.56)
Supplementary Figure.11f Mexico	2001	12,943	1,625 (12.55)	11,318 (87.45)

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.

Supplementary Table 51. Detailed sample size of Supplementary Figure.12a-f.

Cohort/country	Follow year	Total, n	Stroke, n (%)	Non-stroke, n (%)
Supplementary Figure.12a HRS	2000	16,694	2,017 (12.08)	14,677 (87.92)
	2002	15,241	1,724 (11.31)	13,517 (88.69)
	2004	13,874	1,467 (10.57)	12,407 (89.43)
	2006	12,537	1,220 (9.73)	11,317 (90.27)
	2008	11,064	991 (8.96)	10,073 (91.04)
	2010	9,828	700 (7.12)	9,128 (92.88)
	2012	8,538	478 (5.60)	8,060 (94.40)
	2014	7,115	313 (4.40)	6,802 (95.60)
	2016	5,495	152 (2.77)	5,343 (97.23)
Supplementary Figure.12b CHARLS	2011	15,901	2,832 (17.81)	13,069 (82.19)
	2013	14,763	2,752 (18.64)	12,011 (81.36)
	2015	12,176	2,654 (21.80)	9,522 (78.20)
Supplementary Figure.12c SHARE	2011	44,547	2,549 (5.72)	41,998 (94.28)
	2013	37,711	1,724 (4.57)	35,987 (95.43)
	2015	31,685	1,039 (3.28)	30,646 (96.72)
	2017	18,438	409 (2.22)	18,029 (97.78)
Supplementary Figure.12d ELSA	2004	8,037	534 (6.64)	7,503 (93.36)
	2006	6,910	276 (4.00)	6,634 (96.00)
	2008	6,231	225 (3.61)	6,006 (96.39)
	2010	5,599	164 (2.93)	5,435 (97.07)
	2012	4,867	116 (2.38)	4,751 (97.62)
	2014	4,222	73 (1.73)	4,149 (98.27)
	2016	3,583	38 (1.06)	3,545 (98.94)
Supplementary Figure.12e MHAS	2001	13,042	576 (4.42)	12,466 (95.58)
	2003	9,597	473 (4.93)	9,124 (95.07)
	2012	8,288	257 (3.10)	8,031 (96.90)
	2015	6,633	130 (1.96)	6,503 (98.04)
Supplementary Figure.12f United States of America	2000	16,694	2,017 (12.08)	14,677 (87.92)
Supplementary Figure.12f China	2011	15,901	2,832 (17.81)	13,069 (82.19)
Supplementary Figure.12f Estonia	2011	5,587	395 (7.07)	5,192 (92.93)
Supplementary Figure.12f France	2011	4,261	207 (4.86)	4,054 (95.14)
Supplementary Figure.12f Belgium	2011	4,123	215 (5.22)	3,908 (94.78)
Supplementary Figure.12f Czech Republic	2011	4,251	293 (6.89)	3,958 (93.11)
Supplementary Figure.12f Austria	2011	4,015	340 (8.47)	3,675 (91.53)
Supplementary Figure.12f Switzerland	2011	3,060	89 (2.91)	2,971 (97.09)

Supplementary Figure.12f Spain	2011	3,157	159 (5.04)	2,998 (94.96)
Supplementary Figure.12f Italy	2011	2,787	141 (5.06)	2,646 (94.94)
Supplementary Figure.12f Netherlands	2011	2,238	68 (3.04)	2,170 (96.96)
Supplementary Figure.12f Slovenia	2011	2,209	161 (7.29)	2,048 (92.71)
Supplementary Figure.12f Denmark	2011	1,946	96 (4.93)	1,850 (95.07)
Supplementary Figure.12f Portugal	2011	1,488	77 (5.17)	1,411 (94.83)
Supplementary Figure.12f Sweden	2011	1,580	79 (5.00)	1,501 (95.00)
Supplementary Figure.12f Hungary	2011	1,465	63 (4.30)	1,402 (95.70)
Supplementary Figure.12f Poland	2011	1,315	95 (7.23)	1,220 (92.77)
Supplementary Figure.12f Germany	2011	1,065	71 (6.67)	994 (93.33)
Supplementary Figure.12f United Kingdom	2004	8,037	534 (6.64)	7,503 (93.36)
Supplementary Figure.12f Mexico	2001	13,042	576 (4.42)	12,466 (95.58)

HRS: Health and Retirement Study; CHARLS: China Health and Retirement Longitudinal Study; SHARE: Survey of Health, Ageing and Retirement in Europe; ELSA: English Longitudinal Study of Ageing; MHAS: Mexican Health and Aging Study.