

Dynamic frailty and incident cardiometabolic multimorbidity in Chinese adults

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Supplementary Table SI. Components and coding of the original 32-item frailty index and the modified 29-item frailty index

No.	Domain	Deficit/item	Coding of deficit score	Included in the modified 29-item FI	Reason for exclusion
1	Chronic condition	Self-reported physician-diagnosed hypertension	Yes = 1; No = 0	Yes	—
2	Chronic condition	Self-reported physician-diagnosed cancer	Yes = 1; No = 0	Yes	—
3	Chronic condition	Self-reported physician-diagnosed arthritis	Yes = 1; No = 0	Yes	—
4	Chronic condition	Self-reported physician-diagnosed lung disease	Yes = 1; No = 0	Yes	—
5	Chronic condition	Self-reported physician-diagnosed asthma	Yes = 1; No = 0	Yes	—
6	Chronic condition	Self-reported physician-diagnosed memory-related disease	Yes = 1; No = 0	Yes	—
7	Chronic condition	Self-reported physician-diagnosed psychological problem	Yes = 1; No = 0	Yes	—
8	Sensory function	Self-reported vision problems	Yes = 1; No = 0	Yes	—
9	Sensory function	Self-reported hearing status	Very good = 0; good = 0.25; fair = 0.50; poor = 0.75; very poor = 1	Yes	—
10	General health	Self-reported general health status	Very good = 0; good = 0.25; fair = 0.50; poor = 0.75; very poor = 1	Yes	—
11	Activities of daily living	Difficulty with dressing	Yes = 1; No = 0	Yes	—
12	Activities of daily living	Difficulty with bathing or showering	Yes = 1; No = 0	Yes	—
13	Activities of daily living	Difficulty with eating	Yes = 1; No = 0	Yes	—
14	Activities of daily living	Difficulty with getting in and out of bed	Yes = 1; No = 0	Yes	—
15	Activities of daily living	Difficulty with using the toilet	Yes = 1; No = 0	Yes	—

No.	Domain	Deficit/item	Coding of deficit score	Included in the modified 29-item FI	Reason for exclusion
16	Instrumental activities of daily living	Difficulty with managing money	Yes = 1; No = 0	Yes	—
17	Instrumental activities of daily living	Difficulty with taking medication	Yes = 1; No = 0	Yes	—
18	Instrumental activities of daily living	Difficulty with shopping for groceries	Yes = 1; No = 0	Yes	—
19	Instrumental activities of daily living	Difficulty with cleaning the house	Yes = 1; No = 0	Yes	—
20	Instrumental activities of daily living	Difficulty with preparing meals	Yes = 1; No = 0	Yes	—
21	Mobility and physical function	Difficulty with walking 100 yards or one block	Yes = 1; No = 0	Yes	—
22	Mobility and physical function	Difficulty with getting up from a chair after sitting for a long period	Yes = 1; No = 0	Yes	—
23	Mobility and physical function	Difficulty with climbing several flights of stairs without resting	Yes = 1; No = 0	Yes	—
24	Mobility and physical function	Difficulty with lifting or carrying weights over 10 pounds/jin	Yes = 1; No = 0	Yes	—
25	Mobility and physical function	Difficulty with picking up a coin from a table	Yes = 1; No = 0	Yes	—
26	Mobility and physical function	Difficulty with stooping, kneeling, or crouching	Yes = 1; No = 0	Yes	—
27	Mobility and physical function	Difficulty with reaching the arms above shoulder level	Yes = 1; No = 0	Yes	—
28	Depressive symptoms	Depression assessed using the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10)	CESD-10 score >10 = 1; score ≤10 = 0	Yes	—

No.	Domain	Deficit/item	Coding of deficit score	Included in the modified 29-item FI	Reason for exclusion
29	Cognitive function	Cognitive deficit: (memory deficit score + orientation deficit score) / 14	Continuous score ranging from 0 to 1	Yes	—
30	Chronic condition	<i>Self-reported physician-diagnosed diabetes</i>	Yes = 1; No = 0	No	<i>Overlap with the CMM outcome</i>
31	Chronic condition	<i>Self-reported physician-diagnosed heart disease</i>	Yes = 1; No = 0	No	<i>Overlap with the CMM outcome</i>
32	Chronic condition	<i>Self-reported physician-diagnosed stroke</i>	Yes = 1; No = 0	No	<i>Overlap with the CMM outcome</i>

Notes: The original frailty index comprised 32 health deficits. Diabetes, heart disease, and stroke were excluded from the modified index to avoid conceptual overlap with the definition of cardiometabolic multimorbidity, leaving 29 deficits for the primary analyses. Each deficit was coded on a scale from 0 to 1, with higher values indicating greater impairment. Binary deficits were coded as 0 or 1. Self-reported hearing and general health were coded as follows: very good = 0, good = 0.25, fair = 0.50, poor = 0.75, and very poor = 1. Depressive symptoms were assessed using the CESD-10, with scores >10 coded as 1 and scores ≤10 coded as 0. The memory deficit score (range, 0-10) was calculated as the average number of words not recalled across immediate and delayed recall tasks. The orientation deficit score (range, 0-4) was based on the number of incorrect responses to four temporal-orientation questions (day of the week, month, date, and year). The cognitive deficit score was calculated as the sum of the memory and orientation deficit scores divided by 14. The modified FI was calculated as the sum of the 29 retained deficit scores divided by 29, yielding a score from 0 to 1; higher scores indicated greater frailty.

Abbreviations: CESD-10, 10-item Center for Epidemiologic Studies Depression Scale; CMM, cardiometabolic multimorbidity; FI, frailty index.

Supplementary Table SII. Distribution of the Cumulative FI score tertiles and incident CMM events

Tertile	Definition	N	Incident CMM events	Event proportion, %	Mean (SD)	Median	Range
T1	≤ 0.145	3819	317	8.3	0.084 (0.038)	0.089	0.000-0.145
T2	>0.145 to ≤0.304	3800	589	15.5	0.217 (0.044)	0.211	0.145-0.304
T3	> 0.304	3791	934	24.6	0.507 (0.199)	0.446	0.304-1.511

Notes: Total FI was calculated as the sum of the FI scores assessed in 2011 and 2013. Tertile boundaries were derived from the 33.3rd and 66.7th percentiles of Total FI in the Table I analysis cohort. Because two wave-specific FI values were summed, Total FI29 values could exceed 1. CMM, cardiometabolic multimorbidity; FI, frailty index; SD, standard deviation.

Supplementary Table SIII. Baseline characteristics of participants in the baseline frailty analysis according to frailty status in 2011

Characteristic	Overall (N=13,835)	Robust (N=7,261)	Pre-frail (N=4,707)	Frail (N=1,867)	P value	Missing, %
Age, years	57.0 [51.0, 64.0]	55.0 [49.0, 61.0]	58.0 [53.0, 66.0]	64.0 [57.0, 71.0]	<0.001	0.0
Sex, n (%)					<0.001	0.0
Female	7036 (50.9)	3249 (44.7)	2644 (56.2)	1143 (61.2)		
Male	6799 (49.1)	4012 (55.3)	2063 (43.8)	724 (38.8)		
Education, n (%)					<0.001	0.0
College or above	560 (4.0)	431 (5.9)	109 (2.3)	20 (1.1)		
High school	4043 (29.2)	2717 (37.4)	1099 (23.3)	227 (12.2)		
Primary school or below	9232 (66.7)	4113 (56.6)	3499 (74.3)	1620 (86.8)		
Residence, n (%)					<0.001	0.1
City/town	2733 (19.8)	1755 (24.2)	765 (16.3)	213 (11.4)		
Village	11093 (80.2)	5501 (75.8)	3939 (83.7)	1653 (88.5)		
Marital status, n (%)					<0.001	0.0
Married	12201 (88.2)	6683 (92.0)	4070 (86.5)	1448 (77.6)		
Never married/separated/widowed	1634 (11.8)	578 (8.0)	637 (13.5)	419 (22.4)		
Smoking status, n (%)					<0.001	3.6
Current smoker	4077 (29.5)	2321 (32.0)	1311 (27.9)	445 (23.8)		
Ex-smoker	1035 (7.5)	487 (6.7)	365 (7.8)	183 (9.8)		

Characteristic	Overall (N=13,835)	Robust (N=7,261)	Pre-frail (N=4,707)	Frail (N=1,867)	P value	Missing, %
Non-smoker	8220 (59.4)	4124 (56.8)	2897 (61.5)	1199 (64.2)		
Alcohol consumption, n (%)					<0.001	7.2
Drink but less than once a month	1124 (8.1)	654 (9.0)	358 (7.6)	112 (6.0)		
Drink more than once a month	2677 (19.3)	1539 (21.2)	869 (18.5)	269 (14.4)		
Never	9043 (65.4)	4471 (61.6)	3176 (67.5)	1396 (74.8)		
Sleep duration, h/night	6.5 [5.0, 8.0]	7.0 [6.0, 8.0]	6.0 [5.0, 8.0]	6.0 [4.0, 7.0]	<0.001	7.7
Physical activity, n (%)					<0.001	64.4
Light	1248 (9.0)	598 (8.2)	446 (9.5)	204 (10.9)		
Moderate	1659 (12.0)	875 (12.1)	583 (12.4)	201 (10.8)		
Vigorous	2025 (14.6)	1128 (15.5)	692 (14.7)	205 (11.0)		
Body mass index, kg/m ²	22.9 [20.7, 25.4]	23.0 [20.9, 25.3]	23.0 [20.6, 25.6]	22.5 [20.1, 25.4]	0.001	20.1
Waist circumference, cm	84.0 [77.0, 91.0]	83.3 [77.1, 90.3]	84.3 [77.0, 91.4]	84.2 [77.0, 92.2]	0.015	19.5
Triglycerides	103.5 [74.3, 152.2]	101.8 [73.5, 152.2]	105.3 [74.3, 150.4]	106.2 [77.9, 151.8]	0.090	31.5
High-density lipoprotein cholesterol	49.9 [40.6, 60.3]	49.5 [40.2, 59.9]	49.9 [41.4, 60.3]	50.6 [41.0, 61.5]	0.019	31.5
C-reactive protein	1.0 [0.5, 2.1]	0.9 [0.5, 1.9]	1.0 [0.6, 2.2]	1.1 [0.6, 2.5]	<0.001	31.5
Glycated hemoglobin	5.1 [4.9, 5.4]	5.1 [4.8, 5.4]	5.1 [4.9, 5.4]	5.1 [4.9, 5.5]	0.031	31.2

Note: Data are presented as median (interquartile range) for continuous variables and n (%) for categorical variables. Continuous variables were compared using the Kruskal-Wallis test; categorical variables were compared using the chi-square test or Fisher exact test, as appropriate. Missing observations are not displayed as separate categories. Percentages for categorical variables were calculated using the full analytic cohort as the denominator and may therefore not sum to 100%. Continuous-variable summaries were calculated from available observations. BMI, body mass index; CRP, C-reactive protein; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; TG, triglycerides; WC, waist circumference.

Supplementary Table SIV. Baseline characteristics of participants included in the frailty transition analysis according to frailty status in 2011

Characteristic	Overall (N=11,410)	Robust (N=6,024)	Pre-frail (N=3,899)	Frail (N=1,487)	P value	Missing, %
Age, years	57.0 [51.0, 64.0]	55.0 [49.0, 61.0]	58.0 [52.0, 65.0]	63.0 [57.0, 70.0]	<0.001	0.0
Sex, n (%)					<0.001	0.0
Female	5843 (51.2)	2725 (45.2)	2202 (56.5)	916 (61.6)		
Male	5567 (48.8)	3299 (54.8)	1697 (43.5)	571 (38.4)		
Education, n (%)					<0.001	0.0
College or above	400 (3.5)	319 (5.3)	69 (1.8)	12 (0.8)		
High school	3289 (28.8)	2199 (36.5)	908 (23.3)	182 (12.2)		
Primary school or below	7721 (67.7)	3506 (58.2)	2922 (74.9)	1293 (87.0)		
Residence, n (%)					<0.001	0.1
City/town	2040 (17.9)	1331 (22.1)	558 (14.3)	151 (10.2)		
Village	9364 (82.1)	4690 (77.9)	3338 (85.6)	1336 (89.8)		
Marital status, n (%)					<0.001	0.0
Married	10158 (89.0)	5573 (92.5)	3393 (87.0)	1192 (80.2)		
Never married/separated/widowed	1252 (11.0)	451 (7.5)	506 (13.0)	295 (19.8)		
Smoking status, n (%)					<0.001	3.1
Current smoker	3435 (30.1)	1961 (32.6)	1104 (28.3)	370 (24.9)		
Ex-smoker	839 (7.4)	410 (6.8)	285 (7.3)	144 (9.7)		
Non-smoker	6785 (59.5)	3416 (56.7)	2419 (62.0)	950 (63.9)		
Alcohol consumption, n (%)					<0.001	6.9
Drink but less than once a month	916 (8.0)	526 (8.7)	299 (7.7)	91 (6.1)		
Drink more than once a month	2252 (19.7)	1297 (21.5)	726 (18.6)	229 (15.4)		
Never	7451 (65.3)	3723 (61.8)	2627 (67.4)	1101 (74.0)		
Sleep duration, h/night	7.0 [5.0, 8.0]	7.0 [6.0, 8.0]	6.0 [5.0, 8.0]	6.0 [4.0, 7.0]	<0.001	6.5
Physical activity, n (%)					<0.001	63.6
Light	1011 (8.9)	492 (8.2)	351 (9.0)	168 (11.3)		
Moderate	1401 (12.3)	752 (12.5)	480 (12.3)	169 (11.4)		
Vigorous	1744 (15.3)	965 (16.0)	594 (15.2)	185 (12.4)		

Characteristic	Overall (N=11,410)	Robust (N=6,024)	Pre-frail (N=3,899)	Frail (N=1,487)	P value	Missing, %
Body mass index, kg/m ²	22.9 [20.7, 25.4]	22.9 [20.9, 25.3]	22.9 [20.5, 25.6]	22.4 [20.2, 25.4]	0.001	17.8
Waist circumference, cm	84.0 [77.0, 91.0]	83.2 [77.2, 90.4]	84.1 [77.0, 91.2]	84.0 [76.5, 92.0]	0.146	17.3
Triglycerides	102.7 [74.3, 149.6]	100.9 [73.5, 149.6]	104.4 [74.3, 150.4]	106.2 [77.9, 148.7]	0.122	29.2
High-density lipoprotein cholesterol	49.9 [41.0, 60.3]	49.5 [40.2, 59.9]	50.3 [41.4, 60.7]	51.0 [41.4, 61.5]	0.017	29.2
C-reactive protein	1.0 [0.5, 2.0]	0.9 [0.5, 1.8]	1.0 [0.6, 2.1]	1.1 [0.6, 2.4]	<0.001	29.2
Glycated hemoglobin	5.1 [4.9, 5.4]	5.1 [4.8, 5.4]	5.1 [4.9, 5.4]	5.1 [4.8, 5.4]	0.182	28.8

Note: Table IV describes the 2011 baseline characteristics of participants included in the frailty transition analysis. Data are presented as median (interquartile range) for continuous variables and n (%) for categorical variables. Continuous variables were compared using the Kruskal-Wallis test; categorical variables were compared using the chi-square test or Fisher exact test, as appropriate. Missing observations are not displayed as separate categories. Percentages for categorical variables were calculated using the full transition-analysis cohort as the denominator and may therefore not sum to 100%. Continuous-variable summaries were calculated from available observations. BMI, body mass index; CRP, C-reactive protein; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; TG, triglycerides; WC, waist circumference.

Supplementary Table SV. Baseline characteristics of participants included in and excluded from the baseline frailty analysis

Variable	Level	Included (n=13,835)	Excluded (n=3,096)	P value	Absolute SMD	Overall missing, %
Age, years		57.0 [51.0, 64.0]	61.0 [54.0, 69.0]	<0.001	0.350	0.0
Sex	Female	7036 (50.9)	1627 (52.6)	0.092	0.034	0.0
	Male	6799 (49.1)	1469 (47.4)			
Education	College or above	560 (4.0)	226 (7.3)	<0.001	0.156	0.0
	High school	4043 (29.2)	843 (27.2)			
	Primary school or below	9232 (66.7)	2021 (65.3)			
	Missing	0 (0.0)	6 (0.2)			
Residence	City/town	2733 (19.8)	1088 (35.1)	<0.001	0.370	0.2
	Village	11093 (80.2)	1986 (64.1)			
	Missing	9 (0.1)	22 (0.7)			
Marital status	Married	12201 (88.2)	2504 (80.9)	<0.001	0.224	0.1
	Never married/separated/widowed	1634 (11.8)	570 (18.4)			
	Missing	0 (0.0)	22 (0.7)			
Smoking status	Current smoker	4077 (29.5)	676 (21.8)	<0.001	0.285	4.5
	Ex-smoker	1035 (7.5)	356 (11.5)			
	Non-smoker	8220 (59.4)	1800 (58.1)			
	Missing	503 (3.6)	264 (8.5)			
Alcohol consumption	Drink but less than once a month	1124 (8.1)	199 (6.4)	<0.001	0.205	7.7
	Drink more than once a month	2677 (19.3)	410 (13.2)			
	Never	9043 (65.4)	2167 (70.0)			
	Missing	991 (7.2)	320 (10.3)			
Sleep duration, hours		6.5 [5.0, 8.0]	6.0 [5.0, 8.0]	<0.001	0.093	8.9
Physical activity	Light	1248 (9.0)	404 (13.0)	<0.001	0.279	65.3
	Moderate	1659 (12.0)	320 (10.3)			
	Vigorous	2025 (14.6)	215 (6.9)			

Variable	Level	Included (n=13,835)	Excluded (n=3,096)	P value	Absolute SMD	Overall missing, %
	<i>Missing</i>	8903 (64.4)	2157 (69.7)			
Body mass index		22.9 [20.7, 25.4]	24.2 [21.5, 26.9]	<0.001	0.039	22.6
Waist circumference		84.0 [77.0, 91.0]	87.9 [80.0, 96.0]	<0.001	0.256	21.8
Triglycerides		103.5 [74.3, 152.2]	121.2 [85.0, 183.6]	<0.001	0.199	33.7
High-density lipoprotein cholesterol		49.9 [40.6, 60.3]	45.6 [37.5, 56.1]	<0.001	0.252	33.6
C-reactive protein		1.0 [0.5, 2.1]	1.4 [0.7, 3.1]	<0.001	0.147	33.6
Glycated hemoglobin		5.1 [4.9, 5.4]	5.2 [4.9, 5.7]	<0.001	0.344	33.4

Notes: Data are presented as median [interquartile range] for continuous variables and n (%) for categorical variables. P values were calculated using the Kruskal-Wallis test for continuous variables and the Pearson chi-square test for categorical variables. Absolute standardized mean differences quantify between-group imbalance. Missing observations are shown as a separate category for categorical variables. Overall missing (%) is the proportion of missing observations in the combined included and excluded sample. IQR, interquartile range; SMD, standardized mean difference.

Supplementary Table SVI. Baseline characteristics of participants included in and excluded from the frailty transition analysis

Variable	Level	Included (n=11,410)	Excluded (n=2,425)	P value	Absolute SMD	Overall missing, %
Age, years		57.0 [51.0, 64.0]	57.0 [50.0, 66.0]	0.034	0.102	0.0
Sex	Female	5843 (51.2)	1193 (49.2)	0.075	0.040	0.0
	Male	5567 (48.8)	1232 (50.8)			
Education	College or above	400 (3.5)	160 (6.6)	<0.001	0.159	0.0
	High school	3289 (28.8)	754 (31.1)			
	Primary school or below	7721 (67.7)	1511 (62.3)			
Residence	City/town	2040 (17.9)	693 (28.6)	<0.001	0.257	0.1
	Village	9364 (82.1)	1729 (71.3)			
	<i>Missing</i>	6 (0.1)	3 (0.1)			
Marital status	Married	10158 (89.0)	2043 (84.2)	<0.001	0.141	0.0

Variable	Level	Included (n=11,410)	Excluded (n=2,425)	P value	Absolute SMD	Overall missing, %
Smoking status	Never married/separated/widowed	1252 (11.0)	382 (15.8)	<0.001	0.165	3.6
	Current smoker	3435 (30.1)	642 (26.5)			
	Ex-smoker	839 (7.4)	196 (8.1)			
	Non-smoker	6785 (59.5)	1435 (59.2)			
	<i>Missing</i>	351 (3.1)	152 (6.3)			
Alcohol consumption	Drink but less than once a month	916 (8.0)	208 (8.6)	0.014	0.073	7.2
	Drink more than once a month	2252 (19.7)	425 (17.5)			
	Never	7451 (65.3)	1592 (65.6)			
	<i>Missing</i>	791 (6.9)	200 (8.2)			
Sleep duration, hours		7.0 [5.0, 8.0]	6.0 [5.0, 8.0]	0.054	0.040	7.7
Physical activity	Light	1011 (8.9)	237 (9.8)	<0.001	0.128	64.4
	Moderate	1401 (12.3)	258 (10.6)			
	Vigorous	1744 (15.3)	281 (11.6)			
	<i>Missing</i>	7254 (63.6)	1649 (68.0)			
Body mass index		22.9 [20.7, 25.4]	23.2 [20.7, 25.6]	0.080	0.024	20.1
Waist circumference		84.0 [77.0, 91.0]	84.4 [77.6, 92.0]	0.009	0.049	19.5
Triglycerides		102.7 [74.3, 149.6]	108.0 [75.2, 158.4]	0.012	0.034	31.5
High-density lipoprotein cholesterol		49.9 [41.0, 60.3]	48.3 [39.8, 59.1]	0.002	0.074	31.5
C-reactive protein		1.0 [0.5, 2.0]	1.1 [0.6, 2.5]	<0.001	0.076	31.5
Glycated hemoglobin		5.1 [4.9, 5.4]	5.1 [4.9, 5.5]	0.007	0.110	31.2

Notes: Data are presented as median [interquartile range] for continuous variables and n (%) for categorical variables. P values were calculated using the Kruskal-Wallis test for continuous variables and the Pearson chi-square test for categorical variables. Absolute standardized mean differences quantify between-group imbalance. Missing observations are shown as a separate category for categorical variables. Overall missing (%) is the proportion of missing observations in the combined included and excluded sample. IQR, interquartile range; SMD, standardized mean difference.

Supplementary Table SVII. Schoenfeld residual tests for the proportional hazards assumption in the baseline frailty Cox models

Model	Tested term	Chi-square	df	P value
Model 1	Baseline frailty status	5.50	2	0.064
	Global test	6.84	4	0.145
Model 2 (primary)	Baseline frailty status	6.25	2	0.044
	Global test	21.18	17	0.219
Model 3 (biomarker-adjusted)	Baseline frailty status	8.98	2	0.011
	Global test	25.11	21	0.242

Note: The proportional hazards assumption was evaluated using scaled Schoenfeld residuals with the Kaplan-Meier transformation of time. Exposure-specific tests evaluated baseline FI status as a 2-df term. P values <0.05 indicate potential non-proportional hazards. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. Model 1 included 13,835 participants/2,333 events; Model 2, 3,955/660; and Model 3, 2,919/518. FI, frailty index.

Supplementary Table SVIII. Time-varying associations between baseline frailty status and incident CMM estimated using frailty-by-log-time interaction models

Model	Frailty status	HR (95% CI) at 2 years	HR (95% CI) at 4 years	HR (95% CI) at 7 years	Joint chi-square	df	P for interaction
Model 2 (primary)	Pre-frail	2.84 (1.86–4.34)	1.98 (1.61–2.44)	1.48 (1.19–1.84)	6.24	2	0.044
	Frail	2.99 (1.79–5.01)	2.43 (1.87–3.14)	2.05 (1.56–2.69)			
Model 3 (biomarker-adjusted)	Pre-frail	3.29 (2.02–5.37)	2.03 (1.60–2.58)	1.38 (1.07–1.77)	8.57	2	0.014
	Frail	3.96 (2.24–6.99)	2.89 (2.17–3.85)	2.25 (1.66–3.05)			

Note: Hazard ratios are relative to the robust group. Time-varying effects were modeled by including interactions between the pre-frail and frail indicators and log(t/4); therefore, the main exposure coefficients represent the estimated associations at 4 years. The joint P value was obtained from a 2-df Wald test of the pre-frail-by-log-time and frail-by-log-time interaction terms. Model 2 included 3,955 participants and 660 incident CMM events; Model 3 included 2,919 participants and 518 events. Model adjustment sets were identical to those defined in Table III. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SIX. Piecewise time-varying associations between baseline frailty status and incident CMM

Model	Frailty status	HR (95% CI), 0-4 years	HR (95% CI), >4-7 years	Joint chi-square	df	P for interaction
Model 2 (primary)	Pre-frail	2.24 (1.69–2.98)	1.48 (1.18–1.86)	5.80	2	0.055
	Frail	2.83 (2.01–3.98)	1.91 (1.43–2.57)			
Model 3 (biomarker-adjusted)	Pre-frail	2.44 (1.75–3.39)	1.37 (1.06–1.78)	8.48	2	0.014
	Frail	3.57 (2.44–5.22)	2.06 (1.49–2.85)			

Note: Hazard ratios are relative to the robust group. Follow-up was divided into 0-4 years and >4-7 years. Piecewise time-varying coefficient Cox models were fitted using a counting-process formulation with participant-level clustered robust standard errors. The joint P value was obtained from a 2-df Wald test of the pre-frail-by-period and frail-by-period interaction terms. Model 2 included 3,955 participants and 660 incident CMM events; Model 3 included 2,919 participants and 518 events. Model adjustment sets were identical to those defined in Table III. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SX. Schoenfeld residual tests for the proportional hazards assumption in the frailty-transition Cox models

Baseline frailty status	Model	Tested term	Chi-square	df	P value	Global chi-square	Global df	Global P value
Robust	Model 1	Frailty transition	0.79	2	0.673	2.12	4	0.714
	Model 2 (primary)	Frailty transition	6.02	2	0.049	19.78	17	0.286
	Model 3 (biomarker-adjusted)	Frailty transition	1.91	2	0.384	17.33	21	0.691
Pre-frail	Model 1	Frailty transition	3.13	2	0.210	5.74	4	0.220
	Model 2 (primary)	Frailty transition	0.99	2	0.611	21.23	17	0.216

Baseline frailty status	Model	Tested term	Chi-square	df	P value	Global chi-square	Global df	Global P value
Frail	Model 3 (biomarker-adjusted)	Frailty transition	1.54	2	0.464	20.82	21	0.470
	Model 1	Frailty transition	1.33	2	0.514	3.96	4	0.412
	Model 2 (primary)	Frailty transition	1.93	2	0.380	14.36	17	0.642
	Model 3 (biomarker-adjusted)	Frailty transition	1.12	2	0.571	13.13	21	0.904

Note: The proportional hazards assumption was evaluated using scaled Schoenfeld residuals with the Kaplan-Meier transformation of time. Exposure-specific tests evaluated frailty transition as a 2-df term within each baseline frailty stratum. P values <0.05 indicate potential non-proportional hazards. Within the robust, pre-frail, and frail baseline strata, the reference categories were remaining robust, remaining pre-frail, and remaining frail, respectively. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. Model-specific sample sizes and events were identical to those reported in Table II.

Supplementary Table SXI. Piecewise time-varying associations between frailty transitions and incident CMM among participants who were robust at baseline

Baseline frailty status	Model	Reference transition	Frailty transition	HR (95% CI), 0-2 years	HR (95% CI), >2-5 years	Joint chi-square	df	P for interaction
Robust	Model 2 (primary)	Remained robust	Progressed to pre-frail	3.35 (1.88–5.97)	1.47 (1.03–2.09)	5.91	2	0.052
			Progressed to frail	2.49 (0.71–8.66)	1.72 (0.82–3.58)			

Note: Hazard ratios are relative to participants who remained robust. Follow-up was divided into 0-2 years and >2-5 years. Piecewise time-varying coefficient Cox models were fitted using a counting-process formulation with participant-level clustered robust standard errors. The joint P value was obtained from a 2-df Wald test of the two frailty-transition-by-period interaction terms. The analysis included 1,750 participants and 201 incident CMM events. Model 2 was adjusted for age, sex, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXII. Schoenfeld residual tests for the proportional hazards assumption in the total FI tertile models

Model	Tested term	Chi-square	df	P value
Model 1	Total FI tertile	8.867	2	0.012
Model 1	GLOBAL	9.090	4	0.059
Model 2	Total FI tertile	10.260	2	0.006
Model 2	GLOBAL	25.835	17	0.078
Model 3	Total FI tertile	12.164	2	0.002
Model 3	GLOBAL	30.503	21	0.082

Notes: The proportional hazards assumption was assessed using scaled Schoenfeld residuals with the Kaplan-Meier transformation of time. The term-specific tests for Total FI tertile were statistically significant in all three models, whereas the GLOBAL tests were not statistically significant. These findings motivated the piecewise time-varying coefficient analyses shown in Supplementary Table SXIII. FI, frailty index.

Supplementary Table SXIII. Piecewise time-varying associations between total FI tertiles and incident CMM

Model	Follow-up period	T1 HR (95% CI)	T2 HR (95% CI)	P value	T3 HR (95% CI)	P value	P for interaction
Model 1	0–2 years	1.00 (reference)	2.52 (1.93–3.30)	<0.001	4.25 (3.30–5.48)	<0.001	0.012
Model 1	>2–5 years	1.00 (reference)	1.72 (1.47–2.02)	<0.001	2.74 (2.35–3.19)	<0.001	
Model 2	0–2 years	1.00 (reference)	3.37 (1.94–5.87)	<0.001	5.64 (3.30–9.63)	<0.001	0.007
Model 2	>2–5 years	1.00 (reference)	1.55 (1.16–2.08)	0.003	2.18 (1.63–2.92)	<0.001	
Model 3	0–2 years	1.00 (reference)	4.00 (2.06–7.75)	<0.001	6.87 (3.62–13.04)	<0.001	0.004
Model 3	>2–5 years	1.00 (reference)	1.52 (1.09–2.11)	0.013	2.07 (1.49–2.87)	<0.001	

Notes: T1 was the reference category. Follow-up was divided into 0-2 years and >2-5 years because incident CMM was assessed at the 2015 and 2018 survey waves after Total FI was defined in 2013. Piecewise time-varying coefficient Cox models were fitted using a counting-process formulation with participant-level clustered robust standard errors. P for interaction was obtained from a 2-df joint Wald test of the T2-by-period and T3-by-period interaction terms. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference and was considered the primary model. Model 3 further adjusted for triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. CMM, cardiometabolic multimorbidity; FI, frailty index; HR, hazard ratio; CI, confidence interval.

Supplementary Table SXIV. Multiple-imputation analysis of baseline FI status and incident CMM

Baseline FI status	N/events	Model 1		Model 2		Model 3	
		HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Robust	7261/857	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Pre-frail	4707/965	1.75 (1.59–1.92)	<0.001	1.77 (1.61–1.95)	<0.001	1.78 (1.62–1.96)	<0.001
Frail	1867/511	2.40 (2.14–2.70)	<0.001	2.43 (2.15–2.74)	<0.001	2.44 (2.16–2.76)	<0.001

Notes: Missing covariate data were handled using multiple imputation by chained equations with 50 imputed datasets and 20 iterations. Predictive mean matching was used for continuous variables, logistic regression for binary categorical variables, and multinomial logistic regression for multicategory variables. Frailty exposures, event indicators, and follow-up times were not imputed. The event indicator and Nelson-Aalen cumulative hazard were included in the imputation models. Cox models were fitted in each imputed dataset, and estimates were combined using Rubin's rules. N/events refer to the full analytic cohort before imputation. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference and was considered the primary model. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin and was considered a secondary biomarker-adjusted model. CMM, cardiometabolic multimorbidity; FI, frailty index; HR, hazard ratio; CI, confidence interval.

Supplementary Table SXV. Multiple-imputation analysis of changes in FI status and incident cardiometabolic multimorbidity

Baseline FI status	FI transition	N/events	Model 1		Model 2		Model 3	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Robust	Remained robust	4238/383	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Robust	Progressed to pre-frail	1569/250	1.83 (1.56–2.16)	<0.001	1.86 (1.58–2.19)	<0.001	1.84 (1.55–2.17)	<0.001
Robust	Progressed to frail	217/51	2.62 (1.94–3.53)	<0.001	2.56 (1.89–3.48)	<0.001	2.42 (1.76–3.31)	<0.001
Pre-frail	Remained pre-frail	2131/423	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Pre-frail	Recovered to robust	1044/126	0.59 (0.48–0.72)	<0.001	0.60 (0.49–0.73)	<0.001	0.59 (0.48–0.72)	<0.001
Pre-frail	Progressed to frail	724/204	1.45 (1.23–1.72)	<0.001	1.42 (1.19–1.69)	<0.001	1.42 (1.19–1.69)	<0.001
Frail	Remained frail	743/235	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Frail	Recovered to pre-frail	610/143	0.67 (0.54–0.83)	<0.001	0.71 (0.57–0.88)	0.002	0.71 (0.57–0.88)	0.002
Frail	Recovered to robust	134/25	0.51 (0.34–0.77)	0.002	0.56 (0.37–0.85)	0.007	0.57 (0.37–0.87)	0.009

Notes: Missing covariate data were handled using multiple imputation by chained equations with 50 imputed datasets and 20 iterations. Predictive mean matching was used for continuous variables, logistic regression for binary categorical variables, and multinomial logistic regression for multicategory variables. Frailty exposures, event indicators, and follow-up times were not imputed. The event indicator and Nelson-Aalen cumulative hazard were included in the imputation models. Cox models were fitted in each imputed dataset, and estimates were combined using Rubin's rules. N/events refer to the full analytic cohort before imputation. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference

and was considered the primary model. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin and was considered a secondary biomarker-adjusted model. CMM, cardiometabolic multimorbidity; FI, frailty index; HR, hazard ratio; CI, confidence interval. Within each baseline FI category, participants who remained robust, remained pre-frail, and remained frail were used as the respective reference groups.

Supplementary Table SXVI. Multiple-imputation analysis of total FI tertiles and incident CMM

Total FI tertile	N/events	Model 1		Model 2		Model 3	
		HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
T1	3819/317	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
T2	3800/589	1.91 (1.66–2.19)	<0.001	1.96 (1.71–2.25)	<0.001	1.95 (1.70–2.24)	<0.001
T3	3791/934	3.10 (2.72–3.54)	<0.001	3.15 (2.75–3.62)	<0.001	3.18 (2.77–3.66)	<0.001
P for trend			<0.001		<0.001		<0.001

Notes: Missing covariate data were handled using multiple imputation by chained equations with 50 imputed datasets and 20 iterations. Predictive mean matching was used for continuous variables, logistic regression for binary categorical variables, and multinomial logistic regression for multicategory variables. Frailty exposures, event indicators, and follow-up times were not imputed. The event indicator and Nelson-Aalen cumulative hazard were included in the imputation models. Cox models were fitted in each imputed dataset, and estimates were combined using Rubin's rules. N/events refer to the full analytic cohort before imputation. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference and was considered the primary model. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin and was considered a secondary biomarker-adjusted model. CMM, cardiometabolic multimorbidity; FI, frailty index; HR, hazard ratio; CI, confidence interval. Total FI was calculated as the sum of the FI scores assessed in 2011 and 2013. T1 was defined as Total FI ≤ 0.145 , T2 as >0.145 to ≤ 0.304 , and T3 as >0.304 ; T1 was the reference category. P for trend was calculated by assigning each participant the median Total FI value of their tertile and modeling this value continuously.

Supplementary Table SXVII. Associations between baseline FI status and incident CMM using alternative frailty cutoffs

Cut-off scheme	Frailty status	N/events	Model 1		Model 2		Model 3	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Cut-off 1	Robust	7261/857	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Pre-frail	4056/799	1.68 (1.52–1.85)	<0.001	1.60 (1.33–1.93)	<0.001	1.55 (1.25–1.92)	<0.001
	Frail	2518/677	2.36 (2.12–2.62)	<0.001	2.39 (1.95–2.93)	<0.001	2.67 (2.12–3.36)	<0.001

Cut-off scheme	Frailty status	N/events	Model 1		Model 2		Model 3	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Cut-off 2	Robust	5539/589	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
	Pre-frail	6429/1233	1.81 (1.64–2.00)	<0.001	1.83 (1.51–2.22)	<0.001	1.83 (1.47–2.29)	<0.001
	Frail	1867/511	2.66 (2.35–3.01)	<0.001	2.50 (1.96–3.20)	<0.001	2.90 (2.20–3.83)	<0.001

Notes: FI was categorized using two alternative definitions: cut-off 1 (robust, FI ≤ 0.10 ; pre-frail, >0.10 to ≤ 0.21 ; frail, >0.21) and cut-off 2 (robust, FI ≤ 0.08 ; pre-frail, >0.08 to <0.25 ; frail, ≥ 0.25). N/events are presented for the full baseline frailty cohort, and robust participants were the reference group. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. Model-specific N/events for Models 1, 2, and 3 were 13,835/2,333, 3,955/660, and 2,919/518, respectively. Model-specific sample sizes differed because complete-case analyses were performed. CMM, cardiometabolic multimorbidity; CI, confidence interval; FI, frailty index; HR, hazard ratio.

Supplementary Table SXVIII. Associations between frailty transitions and incident CMM using alternative FI cutoffs

Cut-off scheme	Baseline status	Frailty transition	N/events	Model 1		Model 2		Model 3	
				HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Cut-off 1	Robust	Remained robust	4238/383	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Progressed to pre-frail	1427/226	1.83 (1.55–2.16)	<0.001	1.74 (1.28–2.38)	<0.001	1.84 (1.28–2.65)	<0.001
		Progressed to frail	359/75	2.33 (1.81–3.00)	<0.001	2.21 (1.36–3.57)	0.001	2.25 (1.29–3.93)	0.004
	Pre-frail	Remained pre-frail	1580/284	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Recovered to robust	976/118	0.65 (0.52–0.80)	<0.001	0.58 (0.39–0.87)	0.008	0.50 (0.31–0.80)	0.004
		Progressed to frail	812/226	1.61 (1.35–1.92)	<0.001	1.12 (0.78–1.62)	0.527	1.08 (0.71–1.64)	0.709
	Frail	Remained frail	1130/337	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Recovered to pre-frail	686/158	0.72 (0.60–0.87)	<0.001	0.76 (0.54–1.08)	0.125	0.74 (0.51–1.08)	0.118
		Recovered to robust	202/33	0.50 (0.35–0.71)	<0.001	0.44 (0.23–0.85)	0.015	0.37 (0.17–0.82)	0.014
Cut-off 2	Robust	Remained robust	2738/205	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Progressed to pre-frail	1706/230	1.85 (1.53–2.24)	<0.001	1.89 (1.31–2.74)	<0.001	1.97 (1.27–3.06)	0.002
		Progressed to frail	131/33	3.42 (2.34–4.99)	<0.001	2.85 (1.31–6.18)	0.008	3.13 (1.33–7.39)	0.009
	Pre-frail	Remained pre-frail	3462/630	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Recovered to robust	1076/117	0.57 (0.47–0.70)	<0.001	0.63 (0.45–0.89)	0.009	0.60 (0.40–0.89)	0.011
		Progressed to frail	810/222	1.54 (1.31–1.79)	<0.001	1.16 (0.84–1.59)	0.360	1.15 (0.81–1.63)	0.449
	Frail	Remained frail	743/235	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
		Recovered to pre-frail	661/152	0.66 (0.53–0.80)	<0.001	0.70 (0.47–1.05)	0.082	0.63 (0.41–0.98)	0.042
		Recovered to robust	83/16	0.53 (0.32–0.88)	0.015	0.48 (0.19–1.22)	0.125	0.47 (0.14–1.55)	0.213

Notes: Frailty status in 2011 and 2013 was classified using the same two alternative FI definitions described in Supplementary Table SXVII. N/events are shown for the full frailty-transition cohort. Within the robust, pre-frail, and frail baseline strata, participants who remained robust, remained pre-frail, and remained frail were the respective reference groups. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. For cut-off 1, model-specific N/events for Models 1, 2, and 3 were 6,024/684, 1,750/201, and 1,289/154 among robust participants; 3,368/628, 1,025/169,

and 789/131 among pre-frail participants; and 2,018/528, 607/158, and 467/133 among frail participants. For cut-off 2, the corresponding N/events were 4,575/468, 1,267/131, and 925/100; 5,348/969, 1,677/283, and 1,281/222; and 1,487/403, 438/114, and 339/96, respectively. Model-specific sample sizes differed because complete-case analyses were performed. CMM, cardiometabolic multimorbidity; CI, confidence interval; FI, frailty index; HR, hazard ratio.

Supplementary Table SXIX. Associations between baseline frailty status and incident CMM after exclusion of events occurring within the first 2 years

Frailty status	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Robust	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Pre-frail	1.71 (1.54–1.90)	<0.001	1.56 (1.28–1.90)	<0.001	1.54 (1.23–1.93)	<0.001
Frail	2.43 (2.14–2.77)	<0.001	2.21 (1.73–2.83)	<0.001	2.45 (1.86–3.23)	<0.001

Note: Participants who developed cardiometabolic multimorbidity during the first 2 years of follow-up were excluded to reduce potential reverse causation. Robust participants were used as the reference group. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXX. Associations between frailty transitions and incident CMM in the 2-year landmark analysis

Baseline frailty status	Frailty transition	N/events	Model 1		Model 2		Model 3	
			RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Robust	Remained robust	3518/235	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Robust	Progressed to pre-frail	1228/141	1.66 (1.36–2.03)	<0.001	1.38 (0.95–2.01)	0.093	1.48 (0.97–2.27)	0.072
Robust	Progressed to frail	167/27	2.19 (1.50–3.19)	<0.001	1.71 (0.79–3.70)	0.175	2.09 (0.98–4.48)	0.057
Pre-frail	Remained pre-frail	1637/227	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Pre-frail	Recovered to robust	854/69	0.59 (0.46–0.76)	<0.001	0.69 (0.44–1.08)	0.102	0.58 (0.34–0.99)	0.048
Pre-frail	Progressed to frail	525/115	1.53 (1.25–1.88)	<0.001	1.00 (0.63–1.59)	0.996	0.97 (0.58–1.61)	0.907

Baseline frailty status	Frailty transition	N/events	Model 1		Model 2		Model 3	
			RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Frail	Remained frail	476/105	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Frail	Recovered to pre-frail	446/74	0.74 (0.57–0.97)	0.031	0.58 (0.34–0.99)	0.045	0.51 (0.29–0.88)	0.015
Frail	Recovered to robust	108/15	0.63 (0.38–1.03)	0.067	0.64 (0.29–1.44)	0.280	0.61 (0.23–1.63)	0.329

Note: Participants who developed CMM by the 2015 survey were excluded, and only those who remained CMM-free in 2015 and had valid outcome data in 2018 were included. Risk ratios were estimated using modified Poisson regression with robust sandwich standard errors because all participants were assessed for the outcome at the same post-landmark survey wave. N/events are shown for the full landmark cohort. Within the robust, pre-frail, and frail baseline strata, the reference categories were remaining robust, remaining pre-frail, and remaining frail, respectively. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Model 3 further included triglycerides, high-density lipoprotein cholesterol, C-reactive protein, and glycated hemoglobin. Model-specific N/events for Models 1, 2, and 3 were 4,913/403, 1,468/120, and 1,101/97 among participants who were robust at baseline; 3,016/411, 950/112, and 728/85 among those who were pre-frail; and 1,030/194, 322/57, and 249/49 among those who were frail, respectively. Model-specific sample sizes differed because complete-case analyses were performed. CMM, cardiometabolic multimorbidity; CI, confidence interval; RR, risk ratio.

Supplementary Table SXXI. Association between baseline FI status and incident CMM stratified by age

Subgroup	Frailty status	N/events	HR (95% CI)	P value	P for interaction
<60 years	Robust	1365/135	1.00 (reference)	—	0.045
	Pre-frail	807/138	1.75 (1.37–2.23)	<0.001	
	Frail	214/56	2.80 (2.02–3.89)	<0.001	
≥60 years	Robust	656/104	1.00 (reference)	—	<0.001
	Pre-frail	619/147	1.70 (1.31–2.21)	<0.001	
	Frail	294/80	1.94 (1.42–2.64)	<0.001	

Note: Hazard ratios were estimated using the primary model, adjusted for age, sex, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Age was retained as a continuous covariate within each age stratum. Robust participants were used as the reference

group. The P value for interaction was obtained from a likelihood-ratio test comparing models with and without the frailty status-by-age group interaction terms. FI, frailty index; CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXXII. Association between baseline FI status and incident CMM stratified by sex

Subgroup	Frailty status	N/events	HR (95% CI)	P value	P for interaction
Female	Robust	987/115	1.00 (reference)	—	0.884
	Pre-frail	839/169	1.70 (1.34–2.17)	<0.001	
	Frail	305/88	2.19 (1.63–2.95)	<0.001	
Male	Robust	1034/124	1.00 (reference)	—	
	Pre-frail	587/116	1.84 (1.41–2.39)	<0.001	
	Frail	203/48	2.30 (1.61–3.29)	<0.001	

Note: Hazard ratios were estimated using the primary model, adjusted for age, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Sex was omitted from the sex-stratified models because it was constant within each stratum. Robust participants were used as the reference group. The P value for interaction was obtained from a likelihood-ratio test comparing models with and without the frailty status-by-sex interaction terms. FI, frailty index; CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXXIII. Associations between frailty transitions and incident CMM stratified by age

Baseline frailty status	Age group	Frailty transition	N/events	HR (95% CI)	P value	P for interaction
Robust	<60 years	Remained robust	850/69	1.00 (reference)	—	0.639
		Progressed to pre-frail	293/39	1.81 (1.21–2.72)	0.004	
		Progressed to frail	34/6	2.15 (0.90–5.13)	0.083	
	≥60 years	Remained robust	378/45	1.00 (reference)	—	
		Progressed to pre-frail	168/36	1.86 (1.18–2.93)	0.007	
		Progressed to frail	27/6	1.49 (0.61–3.65)	0.381	

Baseline frailty status	Age group	Frailty transition	N/events	HR (95% CI)	P value	P for interaction
Pre-frail	<60 years	Remained pre-frail	380/63	1.00 (reference)	—	0.773
		Recovered to robust	204/22	0.65 (0.40–1.07)	0.089	
		Progressed to frail	109/21	1.21 (0.72–2.03)	0.475	
	≥60 years	Remained pre-frail	275/66	1.00 (reference)	—	
		Recovered to robust	116/15	0.42 (0.24–0.76)	0.004	
		Progressed to frail	110/26	0.93 (0.58–1.49)	0.759	
Frail	<60 years	Remained frail	77/23	1.00 (reference)	—	0.440
		Recovered to pre-frail	96/22	0.85 (0.45–1.61)	0.613	
		Recovered to robust	20/1	0.17 (0.02–1.36)	0.096	
	≥60 years	Remained frail	115/37	1.00 (reference)	—	
		Recovered to pre-frail	102/25	0.65 (0.38–1.11)	0.114	
		Recovered to robust	28/6	0.49 (0.20–1.24)	0.131	

Note: Hazard ratios were estimated using the primary multivariable-adjusted model. The model included age as a continuous variable, sex, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. Within each baseline frailty stratum, participants who remained in the same frailty category were used as the reference group. P values for interaction were obtained from likelihood-ratio tests comparing models with and without all frailty-transition-by-age-group interaction terms. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXXIV. Associations between frailty transitions and incident CMM stratified by sex

Baseline frailty status	Sex	Frailty transition	N/events	HR (95% CI)	P value	P for interaction
Robust	Female	Remained robust	558/55	1.00 (reference)	—	0.184
		Progressed to pre-frail	268/36	1.35 (0.88–2.08)	0.168	
		Progressed to frail	36/6	1.56 (0.65–3.71)	0.319	
	Male	Remained robust	670/59	1.00 (reference)	—	
		Progressed to pre-frail	193/39	2.61 (1.72–3.96)	<0.001	
		Progressed to frail	25/6	2.58 (1.09–6.10)	0.031	
Pre-frail	Female	Remained pre-frail	388/86	1.00 (reference)	—	0.003
		Recovered to robust	168/12	0.31 (0.17–0.58)	<0.001	
		Progressed to frail	156/31	0.82 (0.54–1.26)	0.368	
	Male	Remained pre-frail	267/43	1.00 (reference)	—	
		Recovered to robust	152/25	0.93 (0.57–1.55)	0.793	
		Progressed to frail	63/16	2.12 (1.14–3.93)	0.017	
Frail	Female	Remained frail	115/37	1.00 (reference)	—	0.165
		Recovered to pre-frail	119/32	0.89 (0.53–1.50)	0.657	
		Recovered to robust	27/3	0.39 (0.12–1.31)	0.129	
	Male	Remained frail	77/23	1.00 (reference)	—	
		Recovered to pre-frail	79/15	0.28 (0.13–0.62)	0.002	
		Recovered to robust	21/4	0.38 (0.12–1.17)	0.091	

Note: Hazard ratios were estimated using the primary multivariable-adjusted model. The sex-stratified models included age, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference; sex was omitted because it was constant within each subgroup. Within each baseline frailty stratum, participants who remained in the same frailty category were used as the reference group. P values for interaction were obtained from likelihood-ratio tests comparing models with and without all frailty-transition-by-sex interaction terms. CMM, cardiometabolic multimorbidity; CI, confidence interval; HR, hazard ratio.

Supplementary Table SXXV. Associations between cumulative FI tertiles and incident CMM stratified by age

Age group	Cumulative FI29 tertile	N/events	HR (95% CI)	P value	P for trend	P for interaction
<60 years	T1	760/56	1.00 (reference)	—	<0.001	0.771
	T2	730/98	1.91 (1.37–2.67)	<0.001		
	T3	573/112	2.78 (1.97–3.92)	<0.001		
≥60 years	T1	323/37	1.00 (reference)	—	<0.001	
	T2	428/77	1.78 (1.20–2.65)	0.005		
	T3	568/148	2.75 (1.88–4.01)	<0.001		

Note: Hazard ratios were estimated using the primary multivariable-adjusted model, which included continuous age, sex, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference. The cumulative FI was calculated as the sum of FI values measured in 2011 and 2013 and categorized into tertiles: T1 (≤ 0.145), T2 (> 0.145 to ≤ 0.304), and T3 (> 0.304). T1 was used as the reference category. P values for trend were calculated using the median cumulative FI29 value within each tertile. P for interaction was obtained using a likelihood-ratio test comparing models with and without all cumulative-FI29-tertile-by-age-group interaction terms. CMM, cardiometabolic multimorbidity; CI, confidence interval; FI, frailty index; HR, hazard ratio.

Supplementary Table SXXVI. Associations between cumulative FI tertiles and incident CMM stratified by sex

Sex	Cumulative FI tertiles	N/events	HR (95% CI)	P value	P for trend	P for interaction
Female	T1	500/45	1.00 (reference)	—	<0.001	0.024
	T2	617/77	1.40 (0.97–2.04)	0.076		
	T3	718/176	2.60 (1.84–3.68)	<0.001		
Male	T1	583/48	1.00 (reference)	—	<0.001	
	T2	541/98	2.49 (1.76–3.54)	<0.001		
	T3	423/84	2.88 (1.97–4.22)	<0.001		

Note: Hazard ratios were estimated using the primary multivariable-adjusted model, which included age, education, residence, marital status, smoking status, alcohol consumption, sleep duration, physical activity, body mass index, and waist circumference; sex was omitted because it was constant within each subgroup. The cumulative FI

was calculated as the sum of FI values measured in 2011 and 2013 and categorized into tertiles: T1 (≤ 0.145), T2 (> 0.145 to ≤ 0.304), and T3 (> 0.304). T1 was used as the reference category. P values for trend were calculated using the median cumulative FI value within each tertile. P for interaction was obtained using a likelihood-ratio test comparing models with and without all cumulative-FI-tertile-by-sex interaction terms. CMM, cardiometabolic multimorbidity; CI, confidence interval; FI, frailty index; HR, hazard ratio.