

## **Supplementary appendix**

### **Sex-specific transitions of frailty states and modifiable determinants in community-dwelling older adults: a nationwide Chinese cohort**

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**eTable 1 Items included in the frailty index**

Type of deficit	No.	Variables	Cut-off points
<b>Mental health</b>	1	Look on the bright side of things	Always=0; often=0.25; sometimes=0.5; seldom=0.75; never=1
	2	Keep my belongings neat and clean	Always=0; often=0.25; sometimes=0.5; seldom=0.75; never=1
	3	Make own decisions	Always=0; often=0.25; sometimes=0.5; seldom=0.75; never=1
	4	Feel fearful or anxious	Always=1; often=0.75; sometimes=0.5; seldom=0.25; never=0
	5	Feel useless because of age	Always=1; often=0.75; sometimes=0.5; seldom=0.25; never=0
<b>Activities of daily living</b>	6	Bathing	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
	7	Dressing	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
	8	Use of toilet	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
	9	Indoor transferring	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
	10	Continence	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
	11	Eating	Without assistance=0; need some assistance=0.5; unable to do so without assistance=1
<b>Instrumental activities of daily living</b>	12	Visiting neighbors by oneself	Yes=0; need some assistance=0.5; unable to do so=1
	13	Shopping by oneself if necessary	Yes=0; need some assistance=0.5; unable to do so=1
	14	Cooking	Yes=0; need some assistance=0.5; unable to do so=1
	15	Washing clothes	Yes=0; need some assistance=0.5; unable to do so=1
	16	Walking 1 km	Yes=0; need some assistance=0.5; unable to do so=1
	17	Lift a weight of 5 kg	Yes=0; need some assistance=0.5; unable to do so=1
	18	Continuously crouch and stand up three times	Yes=0; need some assistance=0.5; unable to do so=1
<b>Physical functional</b>	19	Use public transportation	Yes=0; need some assistance=0.5; unable to do so=1
	20	Able to use chopsticks to eat	yes=0; no=1
	21	Hand behind neck	Right hand=0.5; left hand=0.5; both hands=0; neither hand=1
	22	Hand behind lower back	Right hand=0.5; left hand=0.5; both hands=0; neither hand=1

<b>limitations</b>	23	Able to raise arm upright	Right hand=0.5; left hand=0.5; both hands=0; neither hand=1
	24	Able to stand up from sitting	Yes =0; need some assistance=0.5; unable to do so =1
	25	Able to pick up a book from the floor	Yes =0; need some assistance=0.5; unable to do so =1
<b>Sensory functioning</b>	26	Visual function	Can see=0; can see but not distinguish the break in the circle=0.5; cannot see=1; blind=1
	27	Hearing ability	Can hear without a hearing aid=0; can hear with a hearing aid=0.33; partly deaf, despite using a hearing aid=0.67; deaf=1
<b>Cognitive function</b>	28	China-Modified Mini-Mental State Examination score	severe impairment (0-17) =1, mild impairment (18-23) =0.5, normal (24-30) =0
	29	Hypertension	Yes=1; no=0
	30	Diabetes	Yes=1; no=0
	31	Heart disease	Yes=1; no=0
	32	Stroke or cerebrovascular disease	Yes=1; no=0
<b>Chronic disease</b>	33	Bronchitis, emphysema, pneumonia, asthma	Yes=1; no=0
	34	Tuberculosis	Yes=1; no=0
	35	Cancer	Yes=1; no=0
	36	Gastric or duodenal ulcer	Yes=1; no=0
	37	Parkinson's disease	Yes=1; no=0
	38	Bedsore	Yes=1; no=0
<b>Subjective and objective functioning</b>	39	Self-reported health	Very good=0; good=0.25; fair=0.5; bad=0.75; very bad=1
	40	Interviewer rated-health	Surprisingly healthy=0; relatively healthy=0.33; moderately unhealthy=0.67; very unhealthy=1

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**eTable 2 Observed numbers of frailty states transition from one follow-up to next follow-up**

Sex	Pre-transition, n (%)	Post-transition, n (%)				
		Robust	Pre-frail	Frail	Death	Total
Men	Robust	2361 (48.17)	1216 (24.81)	341 (6.96)	983 (20.06)	4910 (100)
	Pre-frail	549 (15.44)	945 (26.58)	608 (17.10)	1453 (40.87)	3555 (100)
	Frail	19 (2.19)	65 (7.49)	174 (20.05)	610 (70.28)	610 (100)
Women	Robust	1444 (42.62)	1146 (33.83)	301 (8.88)	497 (14.67)	3388 (100)
	Pre-frail	609 (13.00)	1471 (31.41)	986 (21.05)	1617 (34.53)	4683 (100)
	Frail	18 (1.46)	119 (9.64)	303 (24.52)	795 (64.37)	1235 (100)

**eTable 3 Possible transition states of frailty and corresponding transition probabilities at 1-6, 9, 12, and 16 years, stratified by sex**

Sex	States transition	Transition probabilities (%)								
		Time (years)								
		1	2	3	4	5	6	9	12	16
Men	Maintain robustness	76.3	59.9	48	39.1	32.2	26.8	15.8	9.5	4.9
Men	Maintain pre-frailty	59.5	38.1	26.2	19.2	14.8	11.7	6.6	3.9	2
Men	Maintain frailty	61.8	39.1	25.4	16.9	11.5	7.9	3	1.4	0.6
Men	Robust → pre-frail	15.2	20.8	21.8	20.8	18.9	16.7	10.9	6.9	3.6
Men	Pre-frail → frail	12	14.7	13.9	12	9.9	8.1	4.4	2.5	1.2
Men	Pre-frail → robust	11.3	15.4	16.2	15.4	14	12.4	8.1	5.1	2.7
Men	Frail → pre-frail	8.2	10.1	9.5	8.2	6.8	5.6	3	1.7	0.8
Men	Robust → deceased	7	15.5	24.2	33.2	41.5	49.2	67.6	79.7	89.3
Men	Pre-frail → deceased	17.2	31.7	43.7	53.4	61.3	67.7	80.9	88.5	94.1
Men	Frail → deceased	29.3	48.8	62.1	71.4	78	82.8	91.1	95	97.5
Women	Maintain robustness	73.2	55.5	43.2	34.3	27.8	22.8	13.1	7.9	4.1
Women	Maintain pre-frailty	63.7	43.5	31.7	24.3	19.3	15.8	9.3	5.8	3.1
Women	Maintain frailty	66	44.6	30.9	21.8	15.8	11.6	5.2	2.6	1.2
Women	Robust → pre-frail	20	27.5	29.1	27.8	25.4	22.7	15	9.6	5.2
Women	Pre-frail → frail	13	17	17.1	15.7	13.8	11.8	7.2	4.4	2.3
Women	Pre-frail → robust	9.2	12.7	13.4	12.9	11.7	10.5	6.9	4.4	2.4
Women	Frail → pre-frail	8.3	10.9	11	10	8.8	7.6	4.6	2.8	1.5
Women	Robust → deceased	4.8	11.6	19.5	27.8	35.9	43.5	62.7	76	87
Women	Pre-frail → deceased	14.1	26.8	37.8	47.2	55.2	61.9	76.5	85.4	92.2
Women	Frail → deceased	25.1	42.9	55.7	65.1	72.2	77.5	87.5	92.7	96.2

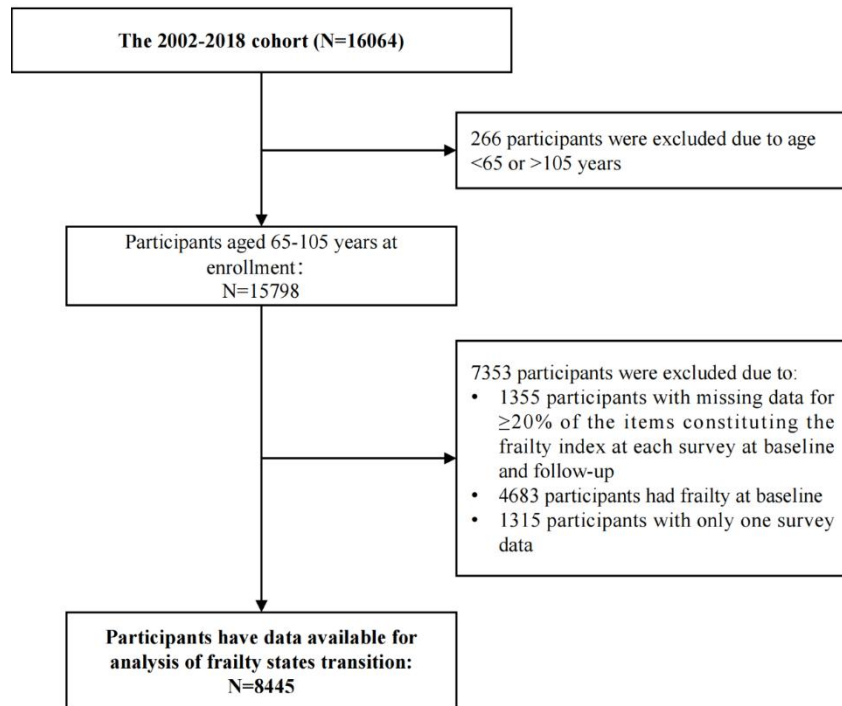
**eTable 4 Effects of covariates on transitions among frailty states**

Covariates	Level	HR (95% CI)
		Death transition
		Robust → Deceased
Age		
Men	—	1.069 (1.056, 1.081)
Women	—	1.081 (1.060, 1.102)
Education level		
Men	None (0)	1.145 (0.910, 1.440)
Women	None (0)	0.837 (0.585, 1.196)
Residence		
Men	Rural	1.196 (0.956, 1.496)
Women	Rural	1.054(0.744, 1.493)
Marital status		
Men	Other	1.351 (1.084, 1.683)
Women	Other	0.779 (0.549, 1.107)
Social participation		
Men	No	1.057 (0.681, 1.640)
Women	No	0.381 (0.123, 1.176)
Smoking status		
Men	Current	1.316 (1.060, 1.635)
Women	Current	0.959 (0.586, 1.570)
Current drinking		
Men	Yes	1.051 (0.857, 1.288)
Women	Yes	0.846 (0.503, 1.424)
Exercise		
Men	No	0.996 (0.795, 1.249)
Women	No	1.011 (0.713, 1.434)
Dietary pattern		
Men	Intermediate/ Unfavorable	0.940 (0.760, 1.162)
Women	Intermediate/ Unfavorable	0.962 (0.681, 1.358)
BMI		
Men	<18.5 or ≥28 kg/m²	1.174 (0.953, 1.447)
Women	<18.5 or ≥28 kg/m2	0.819 (0.582, 1.151)

Reference of covariates: education level, ref= ever (≥1); residence, ref=city and town; marital status, ref=married; smoking status, ref=never; current drinking, ref= no; dietary pattern, ref=favorable; exercise, ref=yes; social participation, ref=yes; BMI, ref=18.5~28 kg/m<sup>2</sup>.

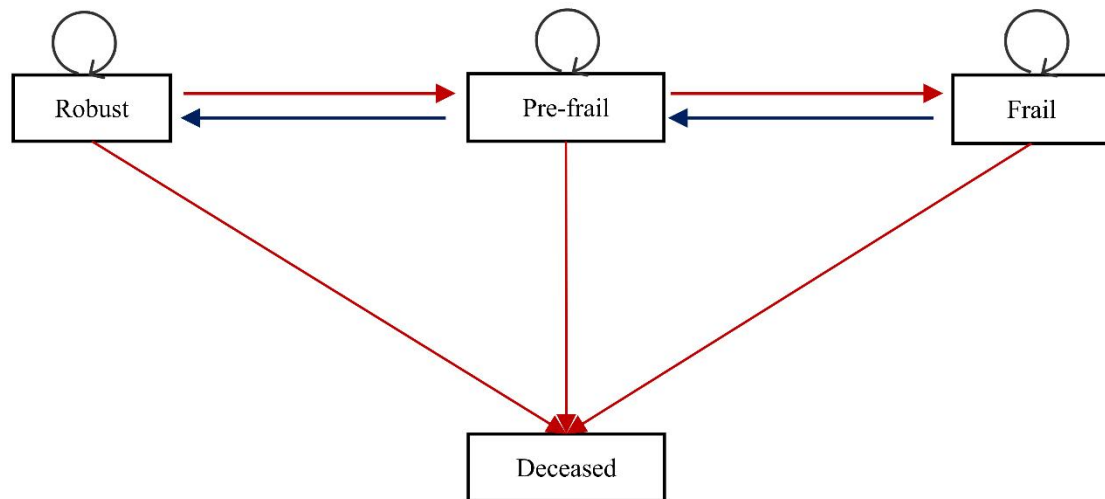
Boldface indicates statistical significance ( $P<0.05$ ).





**eFigure 1 Flowchart of participants selection**

This figure illustrates the participant selection process for the study. Participants were excluded based on the following criteria: missing age information (n=266), missing frailty index data (n=1,355), being frail at baseline (n=4,683), and participation in only one survey round (n=1,315). Consequently, the final analytical sample comprised 8,445 participants.



**eFigure 2 Multi-state Markov model**

This diagram shows the transitions among the robust, pre-frail, frail, and deceased states. The robust, pre-frail, and frail states are modeled as transient states, while the deceased state is considered an absorbing state in the multi-state Markov model. The arrows show which transitions are possible between states.

## **Supplementary Appendix**

### **1 eAppendix 1:**

#### **1.1 Assessment of covariate**

##### **1.1.1 Social participation**

In this study, social participation was defined as engagement in activities involving interaction with others within social or community settings. This was assessed based on responses to Chinese Longitudinal Healthy Longevity Survey (CLHLS) questionnaire items regarding "participation in outdoor activities, card games, or organized social activities during the past month" <sup>1</sup>. Responses were dichotomized into "yes" or "no" categories.

##### **1.1.2 Smoking status**

Smoking status was determined based on responses to the following CLHLS questionnaire items: "Do you currently smoke?", "Did you smoke in the past?", and "If you do not smoke now, at what age did you quit smoking?". Responses were categorized into two groups: current smoking (including smoking cessation <30 years ago) and never smoking (including smoking cessation ≥30 years ago) <sup>2</sup>.

##### **1.1.3 Current Drinking**

Current drinking status was determined based on the response to the CLHLS questionnaire item "Do you currently drink alcohol?". Responses were categorized as "yes" or "no".

##### **1.1.4 Dietary pattern**

Previous studies have shown that consumption of plant-based foods or adherence to a Mediterranean diet can reduce the risk of frailty <sup>3-7</sup>. Therefore, this study assessed dietary patterns based on the frequency of consumption of five food categories: fish, fruits, vegetables, legumes, and tea. Consumption frequency was classified into three levels: "often or almost daily" (assigned 2 points), "sometimes or occasionally"

(assigned 1 point), and "rarely or never" (assigned 0 points). The scores for the five food categories were summed to obtain a total score (range: 0–10). Based on the total score, dietary patterns were categorized into two groups: unfavorable (0–4 points) and moderate or favorable (5–10 points).

#### 1.1.5 Exercise

In this study, "exercise" was defined as purposeful physical fitness activities and was assessed based on the response to the CLHLS questionnaire item "Do you currently engage in regular purposeful exercise, such as walking or playing ball games?"<sup>8</sup>.

#### 1.1.6 BMI

BMI was calculated by dividing weight (kg) by the square of height (m). Studies have found that the relationship between BMI and risk of frailty is a U-shaped nonlinear association, with higher or lower BMI being associated with an increased risk of frailty in community-dwelling older adults.<sup>9,10</sup> Therefore, this study categorized BMI as  $<18.5$  or  $\text{BMI} \geq 28 \text{ kg/m}^2$ , and  $\geq 18.5$  to  $<28 \text{ kg/m}^2$ .

### 1.2 Multi-state Markov model

The multi-state Markov model is employed to describe the process by which individuals transition through a series of states over continuous time, under the assumption that future state changes depend only on the current state. Transition intensities are assumed to remain constant over time. The BFGS quasi-Newton optimization algorithm was used for parameter estimation<sup>11</sup>.

Figure 1 illustrates the possible transitions among the robust, pre-frail, frail, and deceased states. The four states are coded as follows: robust as 1, pre-frail as 2, frail as 3, and deceased as 4. States 1–3 are transient states, while state 4 is an absorbing state. Individuals in transient states may move between adjacent states, but no further transitions occur once the absorbing state is reached.

Assuming an individual is in state  $S(t)$  at time  $t$ , the transition between states is determined

by the transition intensity  $q_{rs}(t, z(t))$ , calculated as:

$$q_{rs}(t, z(t)) = \lim_{\delta t \rightarrow 0} P(S(t + \delta t) = s | S(t) = r) / \delta t$$

Here,  $q_{rs}$  represents the instantaneous rate of transition from state  $r$  to state  $s$ .

All  $q_{rs}$  values form the transition intensity matrix  $Q$ , defined as:

$$Q = \begin{pmatrix} -(q_{12} + q_{14}) & q_{12} & 0 & q_{14} \\ q_{21} & -(q_{21} + q_{23} + q_{24}) & q_{23} & q_{24} \\ 0 & q_{32} & -(q_{32} + q_{34}) & q_{34} \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

In this matrix,  $q_{13}$  and  $q_{31}$  are set to 0, as direct transitions between robust and frail states are not considered. The term  $-(q_{12} + q_{14})$  represents the instantaneous rate of remaining in the robust state, while  $q_{12}$  denotes the instantaneous transition rate from robust to pre-frail. Since death is an absorbing state, all elements  $q_{41}$  to  $q_{44}$  are assigned a value of 0. Other elements are defined similarly. Each row of matrix  $Q$  sums to 0, so the diagonal elements are defined as  $q_{rr} = -\sum_{s \neq r} q_{rs}$

The probability that an individual in state  $r$  will transition next to state  $s$  is given by  $-q_{rs}/q_{rr}$ . The mean sojourn time represents the expected average duration an individual remains continuously in a specific state before transitioning out, calculated as  $-1/\hat{q}_{rr}$ , where  $\hat{q}_{rr}$  is the estimated  $r$ -th diagonal element of the transition intensity matrix. In this study, the estimated mean sojourn time for each transient state  $r$  was derived based on a given set of covariate values (age, education level, residential area, marital status, social participation, smoking, drinking, exercise, dietary pattern, and BMI).

A proportional intensity model was used to model the effect of explanatory variables  $\mathbf{z}_{ij}$  on transition rates. The effect of explanatory variables on the transition intensity for individual  $i$  at observation  $j$  is calculated as:

$$q_{rs}(z_{ij}) = q_{rs}^{(0)} \exp(\boldsymbol{\beta}_{rs}^T \mathbf{z}_{ij})$$

where  $q_{rs}$  denotes the baseline transition intensity from state  $r$  to state  $s$ , and  $\exp(\boldsymbol{\beta}_{rs})$  represents the hazard ratio of the covariates for the transition intensity from state  $r$  to state  $s$ .

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