

NUTRITIONAL AND FRAILTY STATE TRANSITIONS IN THE SINGAPORE LONGITUDINAL AGING STUDY

K. WEI^{1,2,*}, F.S. THEIN^{1,*}, M.S.Z. NYUNT³, Q. GAO³, S.L. WEE^{1,4}, T.P. NG^{1,3}

1. Geriatric Education and Research Institute, Singapore; 2. Key Laboratory of Systems Biomedicine (Ministry of Education), Shanghai Center for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai, China; 3. Gerontology Research Programme, Department of Psychological Medicine, National University of Singapore, Singapore; 4. Faculty of Health and Social Sciences, Singapore Institute of Technology, Singapore. *Co-first authors for this work. Corresponding author: A/P Tze-Pin Ng, Gerontology Research Programme, National University of Singapore, Department of Psychological Medicine, NUHS Tower Block, 9th Floor, 1E Kent Ridge Road, Singapore 119228 Fax: 65-67772191, Tel: 65-67723478, Email: pcmngtp@nus.edu.sg

Abstract: *Background:* Malnutrition is a major determinant of the physical frailty syndrome. Dynamic transitions in frailty states over time is well documented, but few studies have documented temporal changes in nutritional states and whether they influence frailty outcomes. *Design:* Longitudinal cohort study. *Setting and Participants:* Community-dwelling older Singaporeans aged ≥ 55 with a 5-year follow-up (n=1162) in the Singapore Longitudinal Ageing Study 2 (SLAS-2). *Measurements:* The Mini Nutritional Assessment Short-Form (MNA-SF) was used to determine nutritional status, and the Fried's criteria (shrinking, weakness, slowness, exhaustion and inactivity) was used to assess physical frailty phenotype at both baseline and follow-up. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were adjusted for multiple baseline co-variables. *Results:* At baseline, being at risk of malnutrition/malnourished was associated with increased odds of prevalent pre-frailty (OR=2.76, 95% CI=1.86-4.10) and frailty (OR=4.10, 95% CI=1.41-11.9). Baseline robust individuals who were persistently at risk of malnutrition/malnourished showed an increased odds of conversion to being pre-frail/frail at follow-up (OR=3.45, 95% CI=1.00-11.9). Among baseline pre-frail/frail individuals, reversion to being robust were significantly less likely among those who were persistently at risk of malnutrition/malnourished (OR=0.26, 95% CI=0.10-0.67) and those whose baseline normal nutrition worsened at follow-up (OR=0.20, 95% CI=0.06-0.74). *Conclusion:* Changes in nutritional states are associated with frailty state transitions, and monitoring changes in nutritional status is recommended for the prevention and severity reduction of frailty among older people in the community.

Key words: Malnutrition, frailty, transition, association.

Introduction

Frailty is a state of increased vulnerability to stressors due to progressive multisystem physiological decline leading to increased risks of adverse health outcomes including functional decline, poor quality of life, loss of independence, hospitalization and institutionalizations, and mortality (1). Frailty is widely characterized as a physical phenotype including features of body mass loss, muscle weakness, slow gait, exhaustion and physical inactivity (2). Studies show that (protein-calorie) macronutrient and micronutrient deficiencies, malnutrition and poor quality of diet are associated with the development and severity of frailty in older people (3-6). Frailty and malnutrition are equally very common among older persons. Studies reported community prevalence of 50% pre-frailty and 5% frailty (using the physical phenotype criteria) (7), and Mini Nutritional Assessment (MNA) estimates of malnutrition at 6% in the community, and 50% in the clinical and long-term care settings (8).

Frailty is a dynamic process characterized by transitions between adjacent frailty states (9, 10). Though progression typically favours a more deteriorated state of frailty, studies show that a sizeable proportion of pre-frail/frail individuals

revert back to lesser frailty states (11, 12). Identifying key factors influencing frailty transitions thus has significant therapeutic implications. In contrast, little is known of the long-term changes in nutritional status over years among free-living older persons in the community (13), and there are no studies that show whether deterioration or improvement in nutritional status over time is associated with changes in frailty status.

In this study, we investigated the association between changes in nutritional states and frailty state transitions in a population-based older adult cohort in the Singapore Longitudinal Ageing Study 2 (SLAS-2) with a 5-year follow-up, using the Mini Nutritional Assessment Short-Form (MNA-SF) and the Fried's frailty criteria to assess nutritional and frailty status at baseline and follow-up.

Methods

Study design and participants

The Singapore Longitudinal Ageing Study (SLAS) is a long-term observational prospective cohort study of ageing and health of older persons aged 55 and above in Singapore. Two cohorts were recruited from community-living older adults aged 55 and above in separate recruitment waves in 2003-2005

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(SLAS-1) and 2008-2013 (SLAS-2) in different geographical areas. An extensive range of demographic, psychosocial, life style, behavioural, biomedical, physical, cognitive, functional and blood biomarkers data were collected at baseline interviews. The participants in SLAS-1 had completed two follow-ups approximately 3 years apart, and participants in SLAS-2 started the first follow-up in 2013, and is ongoing. Details of the methodology of the SLAS-1 and SLAS-2 cohorts have been described in previous papers (14). The study was approved by the National University of Singapore Institutional Review Board (NUS IRB) with informed consent collected for all participants.

The participants in this study were selected from the total 3270 participants recruited at SLAS-2 baseline and involved 1162 participants who had been re-assessed at follow-up to date as of February 2017 (flow chart detailed in Supplementary Figure 1).

Measurements

Frailty

Participants were assessed for frailty in accordance to the Fried's frailty criteria employed in the Cardiovascular Health Study: shrinking (unintentional weight loss), weakness, slowness, physical inactivity and exhaustion (2). Participants who presented none of the components were defined as robust, 1 to 2 components as pre-frail, and 3 or more components as frail.

Shrinking

Body mass index (BMI) of less than 18.5 kg/m² and/or unintentional weight loss of 4.5 kg (10 pounds) or more within the past 6 months.

Weakness

Dominant knee extensions were used to evaluate leg muscle strength, with an average value from 3 trials used (in kilograms), standardized based on gender. Knee extension strength in the lowest quintile was categorized as weakness.

Slowness was determined with a 6-meter fast gait speed test, using an average of 2 measurements. A gait speed of less than 0.8 m/s was categorized as slowness.

Physical inactivity

Physical activities were determined based on time in hours (self-reported) used to conduct light (such as office work, strolling, driving a car, personal care or standing with minute motion), moderate, and vigorous activities (such as strenuous sports dancing, gardening, jogging, brisk walking or swimming) throughout the week (both weekdays and weekends). Physical inactivity was denoted using the overall amount of time used to perform moderate and vigorous activities weekly and activity time falling below the gender-specific lowest quintile.

Exhaustion was evaluated using 3 questions from the vitality domain in the Medical Outcomes Study 12-Item Short Form Healthy Survey (SF-12): "Did you feel tired?" "Did you feel worn out?" "Did you have a lot of energy?". The total summed scores ranged from 3 to 15 with a higher score corresponding to more energy. Exhaustion was denoted with a score of less than 10.

Nutritional status

MNA-SF was used to evaluate nutritional status. The MNA-SF is a commonly employed nutritional screening tool for the elderly population, comprising 6 questions relating to health, cognition, mobility and nutrition (14). Total scores range between 0-14, with 12-14 indicating normal nutritional status, 8-11 indicating at risk of malnutrition and 7 or less indicating malnourished.

Baseline Covariates

Sociodemographic data included age, gender, race, marital status, education, living arrangements and housing type (an indicator of socioeconomic status). Central obesity was determined by waist circumference ≥ 90 cm. Medical comorbidities were evaluated based on responses to a self-reported checklist of whether participants were diagnosed and treated by a medical practitioner for 22 medical illnesses for the past year. Cognitive function was determined using the locally validated Mini-Mental State Examination (MMSE) (15). Normal cognition was denoted by a score of 24 or more, and cognitive impairment was denoted by a score of less than 24. Depressive symptoms were evaluated using the Geriatric Depression Scale (GDS), previously validated in local Singaporean populations (16). Clinically significant depression was identified as a score of 5 or more. Polypharmacy was identified as self-reported use of 5 or more medications. Hospitalization was identified as self-reported new hospitalization events for any medical conditions within the past year. The instrumental/basic activities of daily living (IADL/ADL) disability was determined by self-reported difficulty and/or requiring assistance in at least one IADL and/or ADL activity from the Lawton Instrumental Activity of Daily Living and Barthel Basic Activities of Daily Living instruments. Quality of life (QOL) was measured using the SF-12 physical component score (PCS) and mental component score (MCS), and poor QOL was determined by values below the lowest quartile of PCS score.

Statistical Analysis

The data were analysed using Stata Version 12.0 (Stata Corp LP, Texas, USA). Categorical variables were represented as count and percentage (n, %) while continuous variables were represented as mean \pm standard deviation. Differences in the distribution of categorical variables and continuous variables among different groups were evaluated using Chi-Square test and Kruskal-Wallis test respectively. Statistical

Table 1
Characteristics of SLAS-2 Participants with Follow-up by Baseline Frailty and Nutritional Status

Characteristics	Total	Frailty Status			P	Nutritional Status		P
		Robust	Pre-frailty	Frailty		Normal nutrition	At risk/Malnourished *	
N	1162	570 (52.1)	487 (44.6)	36 (3.29)		897 (79.8)	227 (20.2)	
<i>Socio-demographic</i>								
Age (years)	65.3 ± 6.9	64.8 ± 6.3	65.4 ± 7.2	69.7 ± 8.1	0.002	65.1 ± 6.9	65.7 ± 6.8	0.182
Male gender	398 (36.4)	215 (37.7)	171 (35.1)	12 (33.3)	0.630	326 (36.3)	81 (35.7)	0.853
No education	151 (13.8)	78 (13.7)	65 (13.4)	8 (22.2)	0.300	128 (14.3)	28 (12.4)	0.760
Primary education	438 (40.2)	221 (38.8)	200 (41.1)	17 (47.2)		362 (40.4)	94 (41.6)	
Secondary/ higher education	502 (46.0)	270 (47.5)	221 (45.5)	11 (30.6)		406 (45.3)	104 (46.0)	
1-2 room public housing	134 (12.3)	59 (10.4)	67 (13.9)	8 (22.2)	0.165	106 (11.9)	33 (14.6)	0.542
3-5 room public housing	865 (79.5)	462 (81.2)	377 (78.0)	26 (72.2)		713 (79.9)	175 (77.4)	
High end public/private housing	89 (8.2)	48 (8.4)	39 (8.1)	2 (5.6)		73 (8.2)	18 (8.0)	
Non-Chinese ethnicity	78 (7.2)	36 (6.3)	40 (8.3)	2 (5.6)	0.446	67 (7.5)	15 (6.6)	0.650
Widowed, divorced or single	330 (30.2)	155 (27.2)	164 (33.7)	11 (30.6)	0.076	253 (28.2)	87 (38.3)	0.003
Living alone	148 (13.6)	69 (12.1)	73 (15.1)	6 (16.7)	0.331	115 (12.9)	34 (15.0)	0.402
<i>Life style and behavior</i>								
Physical activity score (point)	12.7 ± 1.8	12.8 ± 1.7	12.6 ± 1.8	11.6 ± 1.6	0.001	12.6 ± 1.8	12.7 ± 1.8	0.954
Social activity score (point)	11.5 ± 2.8	11.7 ± 2.9	11.5 ± 2.7	10.4 ± 2.2	0.020	11.6 ± 2.8	11.3 ± 2.7	0.232
Productive activity score (point)	10.1 ± 1.8	10.2 ± 1.9	10.0 ± 1.7	9.5 ± 2.0	0.044	10.1 ± 1.8	10.1 ± 1.9	0.896
Lifestyle activity score (point)	6.5 ± 1.6	6.7 ± 1.7	6.3 ± 1.6	5.6 ± 1.2	<0.001	6.5 ± 1.6	6.4 ± 1.7	0.144
<i>Morbidities and physical health</i>								
BMI (kg/m ²)	24.1 ± 4.0	24.5 ± 3.5	23.6 ± 4.3	22.9 ± 4.5	<0.001	25.0 ± 3.6	20.5 ± 3.3	<0.001
Central obesity	594 (54.5)	324 (56.9)	247 (50.9)	23 (63.9)	0.076	559 (62.4)	58 (25.8)	<0.001
Hypertension	720 (65.9)	370 (64.9)	324 (66.5)	26 (72.2)	0.615	608 (67.8)	133 (58.6)	0.009
Dyslipidemia	352 (33.9)	302 (37.1)	143 (31.2)	7 (19.4)	0.025	317 (36.9)	46 (21.7)	<0.001
Multi-morbidity (≥3 illnesses)	339 (31.0)	153 (26.8)	167 (34.3)	19 (52.8)	0.001	269 (30.0)	84 (37.0)	0.042
Diabetes/IFG	189 (17.3)	91 (16.0)	84 (17.3)	14 (38.9)	0.002	149 (16.6)	47 (20.7)	0.146
Metabolic syndrome	265 (25.5)	149 (27.3)	105 (22.9)	11 (30.6)	0.210	248 (28.9)	27 (12.7)	<0.001
Cardiac disease	76 (7.0)	29 (5.1)	40 (8.2)	7 (19.4)	0.002	58 (6.5)	21 (9.3)	0.143
History of stroke	28 (2.6)	8 (1.4)	17 (3.5)	3 (8.3)	0.008	19 (2.1)	12 (5.3)	0.009
Cancer	31 (2.8)	18 (3.2)	10 (2.1)	3 (8.3)	0.073	24 (2.7)	9 (4.0)	0.304
Arthritis	159 (14.6)	64 (11.2)	85 (17.5)	10 (27.8)	0.001	126 (14.1)	37 (16.3)	0.389
Asthma	46 (4.2)	20 (3.5)	22 (4.5)	4 (11.1)	0.080	36 (4.0)	10 (4.4)	0.790
Kidney failure	14 (1.3)	7 (1.2)	6 (1.2)	1 (2.8)	0.719	10 (1.1)	4 (1.8)	0.432
Hearing loss	18 (1.7)	1 (0.2)	17 (3.5)	0 (0)	<0.001	11 (1.2)	8 (3.5)	0.017
Visual impairment	68 (6.22)	27 (4.7)	38 (7.8)	3 (8.3)	0.105	107 (12.2)	29 (13.4)	0.650
Anemia	151 (14.5)	67 (12.3)	75 (16.3)	9 (25.0)	0.041	107 (12.5)	51 (23.8)	<0.001
Low albumin (<40 g/L)	92 (8.7)	41 (7.5)	43 (9.2)	8 (22.2)	0.009	71 (8.2)	21 (9.8)	0.461
Low cholesterol (<4.14 mmol/L)	143 (13.7)	64 (11.7)	72 (15.7)	7 (19.4)	0.120	109 (12.7)	39 (18.3)	0.033
<i>Mental health status</i>								
Mental and sleep disorders	258 (23.6)	110 (19.3)	132 (27.1)	16 (44.4)	<0.001	193 (21.5)	71 (31.3)	0.002
Depressive symptoms (GDS≥5)	10 (0.9)	4 (0.7)	6 (1.2)	0 (0)	0.560	0 (0)	10 (4.4)	<0.001
MMSE score (point)	28.5 ± 2.0	28.7 ± 1.7	28.4 ± 2.1	27.4 ± 3.40	0.009	28.6 ± 1.9	28.4 ± 2.3	0.538
Cognitive impairment (MMSE<24)	28 (2.6)	9 (1.6)	16 (3.3)	3 (8.3)	0.018	20 (2.2)	10 (4.4)	0.069
<i>Adverse outcomes</i>								
Hospitalization in the past year	72 (6.9)	24 (4.4)	43 (9.4)	5 (15.2)	0.001	58 (6.8)	19 (8.8)	0.300
Fall in the past year	96 (8.8)	45 (7.9)	44 (9.1)	7 (19.4)	0.058	80 (8.9)	21 (9.3)	0.868
Polypharmacy (≥5 medications)	157 (14.6)	73 (13.0)	74 (15.4)	10 (29.4)	0.024	126 (14.2)	40 (17.9)	0.173
IADL/ADL disability	97 (8.8)	28 (4.9)	64 (13.1)	5 (13.9)	<0.001	70 (7.8)	34 (15.0)	0.001
SF-12 PCS score (point)	69.8 ± 6.0	70.8 ± 4.8	69.2 ± 6.3	61.4 ± 10.0	<0.001	70.1 ± 5.6	68.5 ± 7.1	0.004
SF-12 MCS score (point)	73.8 ± 5.9	74.9 ± 4.5	73.0 ± 6.6	67.0 ± 10.1	<0.001	74.2 ± 5.5	72.1 ± 7.2	<0.001
Poor quality of life	202 (19.1)	69 (12.3)	111 (23.9)	22 (64.7)	<0.001	149 (17.3)	58 (26.6)	0.002

Variables are indicated as Mean (SD) or n (%). As some participants had missing variables such as frailty or nutritional status, the sample sizes of the different categories may not add up to the total sample; IFG: impaired fasting glucose; GDS: Geriatric Depression Scale; MMSE: Mini-mental State Examination; IADL/ADL: instrumental and basic activities of daily living; PCS: Physical Component Score, MCS: Mental Component Score. * As only 5 participants were determined as being malnourished using MNA-SF, we combined the categories of "At risk of malnutrition" and "Malnourished".

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Table 2
Associations of Baseline Nutritional Status with Prevalent Pre-frailty and Frailty

Cross-sectional analysis	Pre-frailty			Frailty		
	n (%)	OR (95% CI)	P	n (%)	OR (95% CI)	P
<i>MNA-SF Nutritional Status</i>						
Normal nutrition	341 (39.5)	1 (reference)		18 (2.08)	1 (reference)	
At risk/Malnourished	142 (63.7)	2.76 (1.86-4.10)	<0.001	18 (8.07)	4.10 (1.41-11.9)	0.010

Multinomial logistic regression was used. Estimates were adjusted for age, gender, education levels, race, house type, marital status, live alone, cognitive impairment, physical activity score, social activity score, productive activity score, lifestyle activity score, PCS score, MCS score, low albumin, low cholesterol, hospitalization, ADL/IADL disability, type 2 diabetes, arthritis, dyslipidaemia, mental and sleep disorders, stroke, cardiac disease, anaemia, multi-morbidity, polypharmacy, hearing loss. MNA-SF: Mini Nutritional Assessment Short-Form.

Table 3
Nutritional and Frailty State Transitions between Baseline and Follow-up

Baseline Status	SLAS-2 1st Follow-up			
	Normal nutrition	At risk of malnutrition	Malnourished	N
<i>MNA-SF Nutritional Status</i>				
Normal nutrition	780 (89.5)	90 (10.3)	2 (0.2)	872
At risk/Malnourished	115 (53.5)	96 (44.7)	4 (1.9)	215
N	895	186	6	1087
	Robust	Pre-frailty	Frailty	N
<i>Frailty Status</i>				
Robust	280 (53.2)	228 (43.4)	18 (3.4)	526
Pre-frailty	150 (33.9)	244 (55.2)	48 (10.9)	442
Frailty	6 (18.8)	17 (53.1)	9 (28.1)	32
N	436	489	75	1000

Data presenting n (%). MNA-SF: Mini Nutritional Assessment Short-Form.

significance was specified by a P-value of <0.05. Multinomial logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of associations. OR estimates were adjusted for baseline age, gender, education levels, race, house type, marital status, living alone, cognitive impairment, physical activity score, social activity score, productive activity score, lifestyle activity score, PCS score, MCS score, low albumin, low cholesterol, hospitalization, IADL/ADL disability, type 2 diabetes, arthritis, dyslipidaemia, mental and sleep disorders, stroke, cardiac disease, anaemia, multi-morbidity, polypharmacy, and hearing loss.

Results

Baseline characteristics of participants according to nutritional and frailty status are summarized in Table 1. As expected, pre-frailty and frailty compared to robust, and being at risk of malnutrition/malnourished compared to normal nutrition in common were significantly associated with many baseline covariate measures of adverse sociodemographic and lifestyle variables related to social deprivation, chronic

medical illnesses and multiple morbidities, and poorer physical and mental health and function. Compared to participants who successfully completed follow-up in our analysis, those who were not included were more malnourished, more frail at baseline, and had worse profiles on baseline characteristics shown in Table 1 (data not shown).

Cross-sectional associations at baseline

The associations between baseline nutritional states and prevalence of pre-frailty and frailty were reported in Table 2. As there were only 3 malnourished individuals who were also pre-frail or frail, data for both “at risk of malnutrition” and “malnourished” was presented as one group. At baseline, individuals who were at risk of malnutrition/malnourished had a higher prevalence of pre-frailty (adjusted OR=2.76, 95% CI=1.86-4.10) and frailty (adjusted OR=4.10, 95% CI=1.41-11.9), in comparison to their “normal nutrition” counterparts.

Nutritional and frailty state transitions

As shown in Table 3, 89.5% of participants with normal nutrition at baseline remained unchanged with normal

Table 4
Associations between Nutritional and Frailty State Transitions from Baseline to Follow-up

At baseline	MNA-SF Nutritional Status		Baseline Robust Conversion to Pre-frailty/Frailty		
	At follow-up	N	n (%)	OR (95% CI) *	P
Normal nutrition	Normal unchanged	447	193 (45.1)	1 (reference)	
	Nutrition status worsen	46	21 (50.0)	1.09 (0.53-2.23)	0.815
At risk/Malnourished	Malnutrition improved	37	16 (47.1)	1.22 (0.52-2.87)	0.647
	Malnutrition unchanged	18	12 (70.6)	3.45 (1.00-11.9)	0.050
At baseline	MNA-SF Nutritional Status		Baseline Pre-frailty/Frailty Reversion to Robust		
	At follow-up	N	n (%)	OR (95% CI) *	P
Normal nutrition	Normal unchanged	302	113 (39.8)	1 (reference)	
	Nutrition status worsen	47	7 (16.3)	0.20 (0.06-0.74)	0.015
At risk/Malnourished	Malnutrition improved	80	27 (38.0)	1.74 (0.85-3.57)	0.129
	Malnutrition unchanged	73	7 (10.8)	0.26 (0.10-0.67)	0.005

* Estimates were adjusted for age, gender, education levels, race, house type, marital status, live alone, cognitive impairment, physical activity score, social activity score, productive activity score, lifestyle activity score, PCS score, MCS score, low albumin, low cholesterol, hospitalization, ADL/IADL disability, type 2 diabetes, arthritis, dyslipidaemia, mental and sleep disorders, stroke, cardiac disease, anaemia, multi-morbidity, polypharmacy, hearing loss. MNA-SF: Mini Nutritional Assessment Short-Form.

nutrition at follow-up, but 10.5% converted to being at risk of malnutrition/malnourished. Among participants who were at risk of malnutrition/malnourished at baseline, 46.5% remained being at risk of malnutrition/malnourished, while 53.5% reverted to normal nutrition.

Frailty state transitions among the robust at baseline were 53.2% who remained robust, while the others either progressed to pre-frailty (43.4%) or frailty (3.4%) at follow-up. Amongst individuals who were already pre-frail at baseline, 33.9% displayed improvement to being robust, while 10.9% deteriorated to being frail. Among frail individuals at baseline, 53.1% showed improvements to being pre-frail and 18.8% to being robust.

Associations between nutritional and frailty state transitions

At baseline and follow-up, robust individuals who were persistently at risk of malnutrition/malnourished showed an increased odds of conversion to being pre-frail/frail (adjusted OR=3.45, 95% CI=1.00-11.9) (Table 4). Among pre-frail/frail individuals, reversion to being robust were significantly less likely among those who were persistently at risk of malnutrition/malnourished (adjusted OR=0.26, 95% CI=0.10-0.67) and those whose baseline normal nutrition worsened at follow-up (adjusted OR=0.20, 95% CI=0.06-0.74) (Table 4).

Discussion

Our study showed that 46.8% of robust individuals transitioned to poorer states of pre-frailty and frailty upon follow-up. These results reiterated previous findings of the dynamic transitions

in frailty (8, 9). Interestingly, reversion to improved states of frailty was observed, which was higher than those observed in other studies. In this population, 33.9% of pre-frail individuals reverted to robust state compared to the 11.9% observed in a prior study (8), and more than half of frail individuals (53.1%) converted to pre-frailty state at follow-up. This may be attributed to the relatively younger age and longer duration of follow-up of our cohort.

We showed at the same time that there were changes in nutritional states of older people over time that were dynamically associated with corresponding frailty state transitions. Nutrition has been shown in previous studies and systematic reviews to be an important determinant of frailty development and severity. Studies show that low intake of protein, vitamins A, B6, D, E and C, folate, and polyphenols, low serum levels of carotenoids, α -tocopherol, 25-hydroxyvitamin D, and vitamin B6, and poor nutritional status were positively associated, and dietary patterns rich in milk, meat and fish, fresh fruits and vegetables, and Mediterranean-like or high quality balanced diet were inversely associated with the development and severity of frailty in older people (3-6). However, most studies were based on cross-sectional design, and the few longitudinal studies have all determined nutritional status only once at baseline. Our baseline prevalence data showed the same: individuals at risk of malnutrition or malnourished were more than 2 times likely to be pre-frail and more than 4 times likely to be frail. Notably, however, the longitudinal analysis in this study showed that changes in nutritional status strongly influenced frailty outcomes. Older persons who were persistently at risk of malnutrition or malnourished over time were 3-4 times more

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likely to convert from being robust to pre-frailty or frailty. Older persons who were already pre-frail or frail were less likely to revert to being robust when their normal nutritional status worsened or when they remained at risk of malnutrition or malnourished.

Although systematic reviews suggest that a high-quality diet with satisfactory energy intake, optimally high intake of quality protein (evenly distributed throughout all meals), and meals that are rich in micronutrients and antioxidants are likely important factors for preventing and delaying the onset of frailty in older adults, there are presently still very limited evidence from randomized controlled trials in support of the efficacy of nutritional interventions in reversing frailty (17, 18) and even less still in improving physical performance and functional ability (19-24).

More randomized controlled trials are needed, but despite this, interventions to improve nutrition among older persons is arguably most certain to be effective for preventing and reducing frailty and improving functional wellbeing in older adults. Malnutrition is evidently a modifiable risk factor for frailty. This longitudinal study indicated that in the naturalistic real-world setting, certain positive changes in dietary, life style or health states had evidently helped to improve the nutritional and frailty status in some study participants. On the other hand, the observation that worsening nutritional status and its association with worsening frailty status among other participants suggests that monitoring changes in nutritional status and appropriate interventions to improve nutritional health should be recommended in early interventions to prevent and reduce the severity of frailty among older people in the population.

In this regard, early interventions should consider screening, assessment and interventional measures for both malnutrition and frailty together, given the intimate relations between the two. Indeed both constructs share phenotypic similarities (25, 26) and overlapping pathophysiological pathways, though still not fully understood. However, they are not interchangeable constructs, and represent distinct geriatric syndromes (27, 28). The presence of either one or both syndromes in the same individual increases dramatically the risk of future adverse health outcomes that are preventable. More interventional studies should be conducted to identify the interventional modalities for different modifiable risk factors and their individual and combined efficacy (such as protein supplementation and exercise) in improving functional and mortality outcomes.

The design of a large representative population-based cohort of older persons makes the study results generalizable to multi-ethnic Asian populations of community-dwelling older persons. However, some limitations still exist in our study. First, the changes of health behaviors/status from baseline to the 5-year follow-up is not considered in our study, which may also be associated with transitions of nutritional or frailty status. The second is the younger age of cohort (≥ 55 years) and limited

number of participants classified as frail and malnourished. Third, although the MNA is currently most widely accepted for measuring global malnutrition, given the known phenotypic similarities of malnutrition and physical frailty, it is difficult to determine the extent to which the observed close association between nutritional and frailty state transitions is due to the conflation of measurement items in the two constructs. Indeed there are non-physical measurement items in the MNA that do not overlap with physical frailty, but future studies should consider using other more specific and biological measures of nutritional status.

Conclusion

Changes in nutritional states are associated with frailty state transitions, and monitoring changes in nutritional status is recommended for the prevention and severity reduction of frailty among older people in the community.

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