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# NUTRITIONAL AND FRAILTY STATE TRANSITIONS IN THE SINGAPORE LONGITUDINAL AGING STUDY

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**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 ≥55y 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/m$^2$ 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 ± standard deviation. Differences in the distribution of categorical variables and continuous variables among different groups were evaluated using Chi-Square test and Kruskall-Wallis test respectively. Statistical

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

| Characteristics | Total | Frailty Status | | | | Nutritional Status | | |
|---|---|---|---|---|---|---|---|---|
| | | Robust | Pre-frailty | Frailty | P | Normal nutrition | At risk/Malnourished * | P |
| N | 1162 | 570 (52.1) | 487 (44.6) | 36 (3.29) | | 897 (79.8) | 227 (20.2) | |
| *Socio-demographic* | | | | | | | | |
| 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 |
| *Life style and behavior* | | | | | | | | |
| 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 |
| *Morbidities and physical health* | | | | | | | | |
| 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 |
| *Mental health status* | | | | | | | | |
| 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 |
| *Adverse outcomes* | | | | | | | | |
| 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".

**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 |
| *MNA-SF Nutritional Status* | | | | | | |
| 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 |
| *MNA-SF Nutritional Status* | | | | |
| 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** |
| *Frailty Status* | | | | |
| 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

| | MNA-SF Nutritional Status | | Baseline Robust Conversion to Pre-frailty/Frailty | | |
|---|---|---|---|---|---|
| **At baseline** | **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 |
| | **MNA-SF Nutritional Status** | | **Baseline Pre-frailty/Frailty Reversion to Robust** | | |
| **At baseline** | **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 transited 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

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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