Cognitive frailty among Malaysian older adults: baseline findings from the LRGS TUA cohort study

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Purpose: This study was aimed at determining the presence of cognitive frailty and its associated factors among community-dwelling older adults from the “LRGS-Towards Useful Aging (TUA)” longitudinal study.

Patients and methods: The available data related to cognitive frailty among a sub-sample of older adults aged 60 years and above (n=815) from two states in Malaysia were analysed. In the LRGS-TUA study, a comprehensive interview-based questionnaire was administered to obtain the socio-demographic information of the participants, followed by assessments to examine the cognitive function, functional status, dietary intake, lifestyle, psychosocial status and biomarkers associated with cognitive frailty. The factors associated with cognitive frailty were assessed using a bivariate logistic regression (BLR).

Results: The majority of the older adults were categorized as robust (68.4%), followed by cognitively pre-frail (37.4%) and cognitively frail (2.2%). The data on the cognitively frail and pre-frail groups were combined for comparison with the robust group. A hierarchical BLR indicated that advancing age (OR=1.04, 95% CI:1.01–1.08, p<0.05) and depression (OR=1.49, 95% CI:1.34–1.65, p<0.001) scored lower on the Activity of Daily Living (ADL) scale (OR=0.98, 95% CI:0.96–0.99, p<0.05), while low social support (OR=0.98, 95% CI:0.97–0.99, p<0.05) and low niacin intake (OR=0.94, 95% CI:0.89–0.99, p<0.05) were found to be significant factors for cognitive frailty. Higher oxidative stress (MDA) and lower telomerase activity were also associated with cognitive frailty (p<0.05).

Conclusion: Older age, a lower niacin intake, lack of social support, depression and lower functional status were identified as significant factors associated with cognitive frailty among older Malaysian adults. MDA and telomerase activity can be used as potential biomarkers for the identification of cognitive frailty.

Keywords: frailty, mild cognitive impairment, cognitive frailty, older adults

Introduction
Frailty and cognitive decline have been identified as potent risk factors for dementia, functional decline, disability, poor quality of life, and mortality.1 Even though it has been shown that both frailty and cognitive impairment are related,2 these constructs were studied separately in most researches.3,4 To address this gap, a new construct called cognitive frailty was introduced by the International Academy on Nutrition and Aging (I.A.N.A) and the International Association of Gerontology and Geriatrics (I.A.G.G).5

Cognitive frailty has been described as a heterogeneous clinical manifestation characterized by the simultaneous presence of both physical frailty and cognitive...
impaired cognitive functional status. This may be useful in identifying older adults without dementia. Specifically, this concept may be useful in identifying individuals with cognitive impairment caused by physical and non-neurodegenerative conditions and to promote interventions that can lead to an improved quality of life among older adults.

Several population-based studies estimated the prevalence rate of cognitive frailty to be in the range of 1.0% to 12.0%, whereas in clinical settings, the figure was much higher at 10.7% to 40%. Cognitive frailty can be influenced by a number of risk factors, including vascular, lifestyle, physical activity, smoking status, and psychosocial factors as well as potential effects of a poor nutritional status. Moreover, although some emerging biomarkers are able to properly capture both the risk of future physical and cognitive decline individually, they may not be particularly specific for cognitive frailty. It is necessary to identify possible biomarkers that can serve better in determining the risks of cognitive frailty and can potentially be used as a molecular signature for targeted interventions.

The aim of this study was to identify the presence of cognitive frailty and its comprehensive associated factors, including biomarkers, dietary intake, physical function and psychosocial status among multi-ethnic community-dwelling older adults in Malaysia.

Materials and methods

This was a cross-sectional study that used the previously reported methodology of the LRGS TUA study as its baseline. A sub-sample of 815 older adults from two states, namely Selangor and Perak, participated in this study, and the complete data on their physical and cognitive status was analysed. The data of 30 participants who matched the age and gender criteria were analysed for cognitive frailty biomarkers. The inclusion criteria were individuals aged 60 years and above with no documented major psychiatric illnesses or mental disorders. Participants with a Mini-Mental State Examination (MMSE) score of 14 and below (moderately severe or severe cognitive impairment) were excluded from this study. The study protocol was conducted in accordance with the Declaration of Helsinki and approved by the Medical Research and Ethics Committee of Universiti Kebangsaan Malaysia. The written informed consent of the participants and/or their relatives was obtained before enrolment.

The sampling for the study was done with the assistance of the Department of Statistics, Malaysia. Briefly, the participants were recruited using a multi-stage random sampling method from two states with the highest prevalence of older adults according to the zone, namely, Perak (North) and Selangor (Central). The sampling method for this study involved three stages; the primary sampling unit (PSU) was the selection of the state; the secondary sampling unit (SSU) was the random selection of 35 census circles (CCs) from each selected state; and the tertiary sampling unit (TSU) was the selection of 20 living quarters (LQs). The CCs were chosen with the older adults making up at least 10% of the total population in the selected CCs.

Operationalization of cognitive frailty

The classification of cognitive frailty was done based on the simultaneous presence of physical pre-frailty/frailty and subjective cognitive decline (SCC)/mild cognitive impairment (MCI), as summarized in Table 1.

The frailty assessment at the baseline was assessed based on the criteria used in the Cardiovascular Health Study. The presence of one or two criteria was defined as pre-frailty, and the presence of three or more criteria was defined as frailty. On the other hand, the classification of the cognitive status was carried out using pre-tested questionnaires and was based on a multi-dimensional domain that included physical functions, subjective and objective memory impairments, psycho-cognitive functioning, major diseases, health status, and quality of life. The participants were categorized as having MCI if they met the criteria by Petersen et al. (Table 1).

Study instrument and data collection technique

Face-to-face interviews were conducted with the participants using a standardized questionnaire, and measurements were made for a number of parameters. The questionnaire consisted of information on the socio-demography, neuropsychological and psychosocial functions, lifestyle and dietary intake of the participants. Other than that, the biophysical parameters, which included anthropometry, blood pressure, physical fitness, and functional status, were measured. The details of each protocol were previously published by Shahar et al. Since the measurements took quite some time to be completed, the participants were allowed to rest in between the data collection or tests, and refreshments and monetary incentives were provided.
Socio-demography and health condition
The socio-demography and health variables obtained included gender, age, education level, ethnicity, marital status, employment status, household income, smoking status, alcohol intake, and medical history.

Nutritional status and clinical profile
The nutritional status indicators included measurements of the weight, height, arm span, waist circumference, hip circumference, mid-upper arm circumference, and calf circumference as well as body composition [fat percentage (%), fat mass (kg), free fat mass (kg), and muscle mass (kg)]. Then, the Body Mass Index (BMI) was computed. The body circumference was measured using a non-extensible and flexible plastic measuring tape. The body composition was measured via the bio-impedance analysis (BIA) using the In Body S10 (Bio-space Co. Ltd, Korea). The systolic and diastolic blood pressures were also measured using a calibrated digital automatic blood pressure monitor (OMRON, Japan).

Fitness and functional status
A Senior Fitness Test (SFT) was used to measure physical fitness. A total of six fitness tests were administered, namely, the 2 min step, chair sit and reach, chair stand, time-up-and-go, back scratch and hand grip tests. The Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) were used to assess the functional status.

Cognitive function test
Among the cognitive function tests administered were the Digit Span Forward and Backward test for attention and working memory, the Rey Auditory Verbal Learning Test (RAVLT) for verbal memory, the Digit Symbol for information processing, the Visual Reproduction Test I & II (VR I & VR II) to assess visual memory, the Mini-Mental State Examination (MMSE), and the Montreal Cognitive Assessment (MoCA) for global functions.

Psychosocial
The Geriatric Depression Scale-15 (GDS) was used to assess potential depressive symptoms. Social support was assessed using the Medical Outcomes Study Social Support Survey (MOS-SS). Disability was measured using the 12-item version of WHODAS 2.0.

Dietary intake
The dietary intake was obtained using a validated Dietary History Questionnaire (DHQ) and the nutrient intake was analysed using the Nutritionist Pro software. The output from the Nutritionist Pro was then exported into an Excel database.

Table 1 Classification of robust, cognitive pre-frailty and cognitive frailty group

|                  | Robust | Cognitive Pre-Frailty | Cognitive Frailty |
|------------------|--------|-----------------------|-------------------|
| Frailty          | Normal physical status | Shrinkage (subjective report of unintentional weight loss of 5 kg and above over the last year); | Weakness (hand grip is less than the cut-off points mentioned on the original reference, adjusted for gender and body mass index); |
|                  |        | Exhaustion and poor endurance and energy (indicating by self-reporting of exhaustion, identified by two questions from the CES-D scale); | Slowness (gait speed more than the cut-off points mentioned on the original reference, adjusted for gender and height); |
|                  |        | Low physical activity, identified by low scores (in the lowest tertile) of the physical activity scale for elderly (PASE) | |
| Pre-frailty      | =1–2 criteria | MMSE score (≥19) | MMSE score (≥19) |
| Mild Cognitive Impairment | No cognitive impairment | Self-report measure based on item 10 of the 15-item GDS | Self-report measure based on item 10 of the 15-item GDS |
|                  |        | Exclusion of concurrent AD dementia or other dementias | Exclusion of concurrent AD dementia or other dementias |
|                  |        | Objective memory impairment [poor performance in one or more cognitive tests (Digit span and RAVLT) with a score of at least 1.5 SD below the mean average] | Objective memory impairment [poor performance in one or more cognitive tests (Digit span and RAVLT) with a score of at least 1.5 SD below the mean average] |

Abbreviation: RAVLT, Rey Auditory Verbal Learning Test.
Laboratory analysis
A total of 20 mL of fasting peripheral venous blood was drawn by a phlebotomist using a butterfly syringe for the analysis of cognitive frailty biomarkers [superoxide dismutase (SOD), malonaldehyde (MDA), DNA damage (% tail moment (TM) and tail density (TD)), vitamin D, brain-derived neurotrophic factor (BDNF) and telomerase] and biochemical indices [fasting blood sugar, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides].

Statistical analysis
All the analyses were conducted using the IBM Statistical Package for Social Sciences (IBM SPSS), version 23.0 (SPSS Inc., Chicago, IL, USA). The statistical significance level was fixed at alpha <0.05 for all the tests. Descriptive and frequency analyses were executed for the prevalence of cognitive frailty. Comparisons of the sociodemographic factors, blood pressure, anthropometry, body composition, biochemical analysis, physical fitness tests, cognitive assessments, depression scale, psychosocial assessments, and dietary intake between the cognitively frail and robust groups were analysed using chi-squared (χ²) tests for the categorical variables, and independent t-tests for the continuous variables. However, any independent variable that was used to define or score the cognitively frail group was excluded from the set of independent variables. The results were presented as n (%) and the mean ± standard deviation for normally distributed data.

A hierarchical binary logistic regression (BLR) was performed to determine the factors associated with cognitive frailty in a multivariate model. First, all the significant variables in the univariate analysis were categorized into 4 different groups according to (1) sociodemographic and medical status; (2) fitness, nutritional status, clinical profile, social support, functional and depression status; (3) dietary intake and; (4) biomarkers associated with cognitive frailty. Then, a hierarchical binary logistic regression was conducted for the four categories. Variables which appeared significant (p<0.05) in each model were selected to be entered into the final binary logistic model. The significant variables in the final model were those factors that were associated with cognitive frailty among the study population.

Results
The majority of the participants were categorized as robust (68.4%), followed by cognitively pre-frail (37.4%), and cognitively frail (2.2%). The data of the cognitively frail group were combined with those of the cognitively pre-frail group (39.6%) due to the lower prevalence of cognitive frailty as compared with the robust group (68.4%). As shown in Table 2, the mean age of the participants was 68.86±6.12 years old, with the majority of them being Chinese (50.9%), followed by Malays (39.5%), and Indians (9.1%). The cognitively frail group had a significantly lower mean year of education and household income compared to the robust group (p<0.05).

Table 3 shows that the blood pressure of the cognitively frail group was lower than that of the robust group, but only the diastolic blood pressure was significant (p<0.05). With respect to the anthropometric measurements, the cognitively frail group had a lower mean value for the calf circumference. The fat-free mass and skeletal muscle mass were lower compared to those of the robust group (p<0.05). The performance of the cognitively frail group, which was measured by means of physical fitness tests (2 min step, hand grip, chair stand, time up & go and back scratch) was lower than that of the robust group (p<0.05). All the cognitive assessments (digit span, RAVLT, digit symbol, MoCA, VR I and VR II) in the cognitively frail group had significantly lower scores compared to the robust group (p<0.05). Furthermore, the cognitively frail group had a significantly lower mean value for the psychosocial and physical function assessments (IADL and ADL) (p<0.05). The mean value for WHODAS indicating disability and the Geriatric Scale for Depression (GDS-15) were significantly higher among the cognitively frail group compared to the robust group (p<0.05). The cognitively frail group also had a significantly lower mean value for social support, as indicated by the MOSS scores (p<0.05).

With respect to the dietary intake (Table 4), the energy and macronutrient (protein, carbohydrate, fat, and fibre) intakes appeared to be lower than those of the robust group, but were not significantly different. However, the nutrients, including riboflavin and niacin, had a significantly lower mean value among the cognitively frail group than the robust group (p<0.05). An analysis of the randomly chosen age- and gender-matched subsamples for the biomarkers showed no significant difference in the SOD, Vitamin D and BDNF values among the older adults with cognitive frailty. In addition, the participants with cognitive frailty had a higher tendency of experiencing DNA damage with a higher percentage of TD as compared...
to the robust participants, but there was no significant difference. However, the MDA level was significantly higher in the cognitively frail group while the telomerase level was lower compared to the robust group for the biomarker parameters ($p<0.05$) (Table 5).

The final model was indicated by the results of the hierarchical logistic regression, where advancing age (OR=1.04, 95% CI:1.01–1.08, $p<0.05$), depression (OR1.49, 95% CI:1.34–1.65, $p<0.001$), low functional status as indicated by the ADL (OR=0.98, 95% CI:0.96–0.99, $p<0.05$), low social support (OR=0.98, 95% CI:0.97–0.99, $p<0.05$), and low niacin intake (OR=0.94, 95% CI:0.89–0.99, p<0.05) were found to be significant factors associated with the cognitively frail group (Table 6).

**Discussion**

In the present study, the prevalence rate of cognitive frailty among the multi-ethnic older population in Malaysia was 2.2%, and this was comparable with the findings from among the Japanese (2.7%) and Italian (2.5%) population. A higher prevalence rate (39.6%) was shown when both the cognitively pre-frail and cognitively frail were combined into a single group. The Singapore Longitudinal Ageing Studies (SLAS) also combined the cognitively frail and cognitively pre-frail categories and obtained a prevalence rate of 10.7% among Chinese population, which was lower than the figure reported in the present study. The discrepancy in the prevalence rates may be due to the number of older participants in the present study and the difference in the study population.

Pre-frailty is clearly different from normal aging, based on the clinical, functional and behavioural factors and biomarkers involved in the pathological aging process, hence, suggesting that it can be grouped together with frailty to be considered as a target group for possible interventions.

This study found that every increase of one year in age is associated with increasing odds of the incidence of

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**Table 2 Sociodemographic data associated with cognitive frailty [presented as n (%) or mean ± SD]**

| Parameter | Robust (N=490) | Cognitive Frailty (N=325) | Total (N=815) | p-value |
|-----------|----------------|--------------------------|--------------|---------|
| Age | 67.63±5.54 | 69.44±6.23 | 68.86±6.12 | <0.001* |
| Gender | | | | |
| Men | 234 (36.3) | 138 (42.5) | 372 (45.6) | 0.151 |
| Women | 256 (63.7) | 187 (57.5) | 443 (54.4) | |
| Ethnic | | | | |
| Malay & Indian | 265 (54.1) | 135 (41.5) | 400 (49.1) | <0.001* |
| Chinese | 225 (45.9) | 190 (58.5) | 415 (50.9) | |
| Years of education | | | | |
| ≤6 years | 293 (59.8) | 234 (72.0) | 527 (64.7) | <0.001* |
| >6 years | 197 (40.2) | 91 (28.0) | 288 (35.3) | |
| Occupation | | | | |
| Not working | 395 (80.2) | 265 (86.9) | 660 (87.6) | 0.652 |
| Working | 53 (11.8) | 40 (13.1) | 93 (12.4) | |
| Household income | | | | |
| Low income (<RM1500) | 317 (65.8) | 239 (74.2) | 556 (69.2) | 0.013* |
| High income (>RM1500) | 165 (34.2) | 83 (25.8) | 248 (30.8) | |
| Marriage status | | | | |
| Single/widow/widower/divorced | 136 (27.8) | 89 (27.4) | 225 (27.6) | 0.936 |
| Married | 354 (72.2) | 236 (72.6) | 590 (72.4) | |
| Smoking status | | | | |
| Past or non-smokers | 58 (11.8) | 42 (12.9) | 100 (12.3) | 0.664 |
| Smoking | 432 (88.2) | 283 (87.1) | 715 (87.7) | |
| Medical profile | | | | |
| Hypertension | 435 (53.4) | 260 (53.1) | 175 (53.8) | 0.830 |
| No | 380 (46.6) | 230 (46.9) | 150 (46.2) | |
| Dyslipidaemia | | | | |
| Yes | 283 (34.7) | 160 (32.7) | 123 (37.8) | 0.133 |
| No | 532 (65.3) | 330 (67.3) | 202 (62.2) | |
| Diabetes Mellitus | | | | |
| Yes | 242 (29.7) | 142 (29) | 100 (30.8) | 0.585 |
| No | 573 (70.3) | 348 (71) | 225 (69.2) | |
| Heart disease | | | | |
| Yes | 79 (9.7) | 42 (8.6) | 37 (11.4) | 0.186 |
| No | 736 (90.3) | 448 (91.4) | 288 (88.6) | |

Note: *Significant at $p<0.05$ using Chi-square test.
cognitive frailty among older Malaysian adults. Advancing age has consistently been reported as a major risk factor for both physical frailty and cognitive impairment.\(^1\)\(^,\)\(^27\) In addition, the presence of multiple subclinical and age-related comorbidities in older adults may exacerbate the decline in several physiological systems, resulting in homeostatic imbalance or frailty,\(^28\) brain aging and consequently, cognitive decline.\(^1\) Besides, aging is associated

### Table 3
Fitness, cognitive assessments, nutritional status, clinical profile, functional status and depression status of the subjects [presented as n (%) or mean ± SD]

| Parameters                                | Robust (N=490) | Cognitive Frailty (N=325) | Total (N=815) | p-value |
|-------------------------------------------|----------------|--------------------------|---------------|---------|
| **Anthropometry**                         |                |                          |               |         |
| Body mass index (kg/m\(^2\))              |                |                          |               |         |
| Underweight                               | 12 (2.5)       | 13 (4.0)                 | 25 (3.1)      | 0.357   |
| Normal                                    | 229 (46.8)     | 149 (45.8)               | 378 (46.4)    |         |
| Overweight                                | 182 (37.2)     | 110 (33.8)               | 292 (35.9)    |         |
| Obese                                     | 66 (13.5)      | 53 (16.3)                | 119 (14.6)    |         |
| Waist circumference (cm)                  | 89.6±10.91     | 88.9±11.19               | 89.50±11.31   | 0.222   |
| Hip circumference (cm)                    | 98.48±10.91    | 97.78±9.44               | 98.17±9.29    | 0.337   |
| Mid-upper arm circumference (cm)          | 28.98±3.18     | 28.62±3.42               | 28.87±3.44    | 0.126   |
| Calf circumference (cm)                   | 34.37±3.63     | 33.81±3.64               | 34.01±3.65    | 0.034   |
| **Body composition**                      |                |                          |               |         |
| Fat (%)                                   | 38.54±10.19    | 38.68±10.25              | 38.61±10.42   | 0.840   |
| Fat mass (kg)                             | 24.81±8.82     | 24.22±9.45               | 24.52±9.29    | 0.377   |
| Fat-free mass (kg)                        | 38.66±8.3      | 37.07±7.59               | 37.37±8.09    | 0.006   |
| Skeletal muscle mass (kg)                 | 20.66±5.00     | 19.70±4.53               | 19.88±4.83    | 0.006   |
| **Clinical profile**                      |                |                          |               |         |
| Systolic blood pressure (mmHg)            | 139.48±20.71   | 138.69±20.40             | 139.83±21.01  | 0.597   |
| Diastolic blood pressure (mmHg)           | 77.59±12.75    | 75.56±12.96              | 76.92±13.02   | 0.030   |
| **Fitness**                               |                |                          |               |         |
| 2-min step test                           | 68.17±25.85    | 63.68±26.00              | 65.21±26.13   | 0.016   |
| Chair stand test                          | 10.56±2.91     | 9.80±3.29                | 10.09±3.06    | 0.001   |
| Time-up and go                            | 10.11±2.85     | 10.72±3.29               | 10.69±3.09    | 0.005   |
| Chair sit and reach                       | 3.33±10.22     | 4.63±3.64                | 4.38±1.10     | 0.086   |
| Back scratch test                         | 13.83±12.52    | 17.36±14.58              | 16.43±13.83   | <0.001  |
| **Depression**                            |                |                          |               |         |
| No depressive symptoms                    | 434 (88.6)     | 240 (73.8)               | 674 (82.7)    | <0.001  |
| Depressive symptoms                       | 56 (11.4)      | 85 (26.2)                | 141 (17.3)    |         |
| **Cognitive assessments**                 |                |                          |               |         |
| Digit symbol                              | 6.18±3.12      | 5.53±2.77                | 5.59±2.84     | 0.003   |
| Digit span                                | 7.92±2.50      | 8.09±2.61                | 7.81±2.53     | 0.349   |
| RAVLT                                     | 39.10±10.88    | 38.97±10.11              | 38.32±10.59   | 0.871   |
| MoCA                                      | 20.45±5.46     | 19.53±5.42               | 19.59±5.57    | 0.018   |
| VR I                                      | 53.43±33.16    | 48.42±32.87              | 49.15±32.82   | 0.036   |
| VR II                                     | 45.63±36.85    | 39.50±36.05              | 40.00±35.94   | 0.020   |
| **Functional status**                     |                |                          |               |         |
| IADL                                      | 13.15±1.47     | 12.83±1.92               | 12.80±1.98    | 0.004   |
| ADL                                       | 41.50±9.58     | 37.88±10.24              | 38.81±10.41   | <0.001  |
| WHODAS                                    | 5.28±8.42      | 6.86±9.27                | 6.67±9.50     | 0.013   |
| **Social support**                        |                |                          |               |         |
|                             | 39.92±14.18    | 35.77±15.05              | 39.32±14.49   | <0.001  |

Note: *Significant at p<0.05 using Independent t-test.

Abbreviations: RAVLT, Rey Auditory Verbal Learning Test; MoCA, Montreal Cognitive Assessment; VR I, Visual Reproduction I; VR II, Visual Reproduction II; IADL, Instrumental Activity of Daily Living; ADL, Activity of Daily Living.
with inadequate social integration and social support that may lead to a decline in physical and mental functions.29

The lack of social support was apparent among the cognitively frail subjects, where a decrease of 1 unit in the MOSS scores increased the risk of cognitive frailty by 2%. Social support, in terms of providing assistance and encouragement to older adults, is a protective function against frailty and cognitive dysfunction.30,31 Social support among older adults has a proximal relationship with depression,32,33 which appeared to be higher among the

| Nutrients      | Robust (N=490)   | Cognitive Prefrailty/Frailty (N=325) | Total       | p-value |
|----------------|------------------|--------------------------------------|-------------|---------|
| Energy (kcal)  | 1655±445         | 1612±436                             | 1659±453    | 0.184   |
| Protein (g/kg) | 1.15±0.38        | 1.13±0.42                            | 1.14±0.41   | 0.771   |
| Carbohydrate (%) | 53.37±7.96  | 53.05±7.66                           | 53.70±7.96  | 0.564   |
| Fat (%)        | 29.62±7.96       | 29.79±6.40                           | 29.42±7.20  | 0.749   |
| Vit A (µg RE)  | 400.5±296.24     | 420.40±308.48                        | 393.01±286.40 | 0.374 |
| Vit C (mg)     | 127.87±83.27     | 126.54±80.21                         | 122.12±84.30 | 0.826 |
| Vit D (µg)     | 0.36±0.84        | 0.39±1.32                            | 0.33±1.00   | 0.725   |
| Vit E (mg)     | 7.30±4.066       | 6.54±1.801                           | 9.15±4.81   | 0.725   |
| Riboflavin (mg)| 1.29±0.52        | 1.19±0.47                            | 1.23±0.50   | 0.005*  |
| Niacin (mg)    | 10.34±3.95       | 9.45±3.21                            | 9.91±3.76   | 0.001*  |
| Calcium (mg)   | 510.39±227.71    | 522.19±260.76                        | 508.99±241.54 | 0.508 |
| Iron (mg)      | 13.72±5.34       | 13.35±5.06                           | 13.49±5.27  | 0.323   |
| Zinc (mg)      | 3.66±1.87        | 3.57±1.74                            | 3.56±1.86   | 0.502   |

Note: *Significant at p<0.05 using Independent t-test.

| Analysis        | Status (M ± SD) | F     | t       | p-value |
|-----------------|-----------------|-------|---------|---------|
| SOD (u.e/min/mg protein) | 9.36±7.30 | 9.39±9.11 | 0.546 | −0.009 | 0.993 |
| MDA (nmol/L)    | 1.97±0.75       | 2.71±0.66 | 0.184 | −2.469 | 0.020* |
| DNA in tail (%) | 12.37±4.68      | 14.02±4.97 | 0.274 | −0.783 | 0.441 |
| Tail Moment (%) | 1.61±0.67       | 1.59±0.55 | 0.752 | 0.086  | 0.933 |
| Vitamin D (nmol/L) | 49.73±18.33 | 52.27±7.65 | 2.167 | −0.369 | 0.721 |
| BDNF (nmol/L)   | 13.80±1.75      | 12.85±2.17 | 0.590 | 0.956  | 0.354 |
| Telomerase (nmol/L) | 7.16±1.25 | 5.76±0.90 | 2.315 | 2.577  | 0.027* |

Note: *Significant at p<0.05 using Independent t-test.
Abbreviation: MDA, malonaldehyde.

| Parameters     | B      | Standard error | OR (95% CI) | p-value |
|----------------|--------|----------------|-------------|---------|
| Age            | 0.038  | 0.18           | 1.04 (1.01–1.08) | 0.030*  |
| GDS category   |        |                |             |         |
| No depressive symptoms | 0.397  | 0.05           | 1.49 (1.34–1.65) | <0.001* |
| Depressive symptoms |       |                |             |         |
| ADL            | −0.024 | 0.01           | 0.98 (0.96–0.99) | 0.028*  |
| Social support | −0.021 | 0.01           | 0.98 (0.97–0.99) | 0.001*  |
| Niacin (mg)    | −0.066 | 0.03           | 0.94 (0.89–0.99) | 0.030*  |

Note: *Significant at p<0.05 using Binary Logistic Regression.
Abbreviations: GDS, Geriatric Depression Scale-15; ADL, Activities of Daily Living.
cognitively frail participants. Depression is often accompanied by neurocognitive deficits and physical frailty, whereby it is associated with greater disability and an increased risk of dementia. A persistent depressive mood, anxiety, impatience, and behavioural suppression may also reduce an individual’s desire to participate in social activities, and impede access to a necessary social support system, thereby resulting in an increased risk of disabilities among older adults. Disability, as indicated by the lower ADL scores, was indicated among the cognitively frail subjects, where a reduction of 1 point increased the risk of cognitive frailty by 2%. In line with this finding, ADL impairment has been reported to be a predictive factor of future cognitive impairment and physical frailty.

With respect to dietary intake, this study found that lowering the intake of niacin by 1 mg would increase the risk of the incidence of cognitive frailty by 6%, and the niacin intake of the participants did not even meet the recommendation for older adults (16 mg/day). Niacin deficiency will lead to the occurrence of pellagra, whereby a patient can develop neurological deficits manifesting as dementia. Several studies have proposed that niacin has a therapeutic effect on depression, which often accompanies physical frailty and cognitive impairment. This suggests that niacin may be a potential biomarker and predictor for cognitive frailty among older adults.

In a subsample analysis, the age- and gender-matched cognitively frail participants showed a higher level of oxidative stress, as indicated by their MDA levels, compared to the robust participants. Ingles et al. reported that frail older adults displayed more oxidative damage than the non-frail participants. Moreover, several studies have reported the contribution of high plasma MDA levels in the neurodegenerative process of dementia. Oxidative stress may also increase the rate of telomere shortening by site-specific DNA damage to the telomere sequence. Besides, the telomerase level was found to be lower among the cognitively pre-frail/frail participants in the present study, and this may have reduced their ability to repair the damage done to the DNA, whereby the percentage of TM was higher among the cognitively frail participants. The presence of functional telomerase is a necessary condition for maintaining the telomere length, hence, preserving healthy cell and long-term immune functions. Even though no study has been done on the direct interaction between telomerase activity and cognitive frailty, telomere shortening is associated with both physical frailty and cognitive decline. In line with this, the contribution of telomere shortening to persistent DNA damage response during replicative senescence, and the irreversible loss of the division potential of somatic cells have been reported. Hence, the presence of oxidative stress and the absence of telomerase activity in preserving the telomere length may be one of the factors for determining the development of cognitive frailty among older adults, and further research involving a larger sample size is needed.

This study had several limitations. Although the participants were selected randomly, the sample did not represent all the ethnic groups in the Malaysian community. The majority of the participants who were recruited from two out of the 14 states in Malaysia were Chinese, whilst the Malays are the major ethnic group in the Malaysian community. The two selected states may also not be representative of the other 12 states, particularly those in East Malaysia. Furthermore, this study could not elucidate the predictive validity of the risk factors due to its cross-sectional design. Hence, a longitudinal study should be carried out to determine the ability of cognitive frailty to predict dementia. However, the findings of this study provided substantial insights into the prevalence of cognitive frailty among older Malaysian adults, and identified several factors associated with cognitive frailty.

Conclusion
In conclusion, the prevalence of robust, cognitive pre-frailty and cognitive frailty among older adults in Malaysia was 60.4%, 37.4%, and 2.2%, respectively. Being older, having a low niacin intake, depression, low functional status and lack of social support were associated with cognitive frailty among older Malaysian adults. The results of this study also suggest that MDA and telomerase can be used as potential biological markers for the identification of cognitive frailty. Future studies are warranted to further investigate the prevalence and risk factors of cognitive frailty among the entire Malaysian population, and to develop simple screening tools to identify cognitive frailty among older adults. This study can also be a stepping stone for future researchers to develop prevention and intervention strategies against cognitive frailty.

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Disclosure

The authors report no conflicts of interest in this work.

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