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Effectiveness of *Cosmos caudatus* Extract in Improving Health-Related Parameters among Older Adults with Sarcopenia: A Study Protocol

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ABSTRACT

This is a randomized, two-arm, double-blind, placebo-controlled study that will be performed among older adults in Kelantan, Malaysia, for 12 weeks. This study aims to determine the effectiveness of a 12-week *Cosmos caudatus* (*C. caudatus*) extract supplementation on dietary intake, cognition, mental health, sleep quality, disability, gut microbiota, physical activity, frailty, metabolites, and protein synthesis pathways among older adults with sarcopenia. This study will involve 64 older adults diagnosed with sarcopenia that will be enrolled and randomly allocated with 1:1 ratio, where 32 subjects required in both intervention and placebo group. The intervention group will receive 500 mg/day of *C. caudatus* supplementation, while the placebo group will be given 500 mg/day of maltodextrin. Study outcomes including sarcopenia status, dementia, motoric cognitive risk, dietary pattern, anthropometric data, physical fitness, mental health, disability and sleep quality will be measured. Blood will be taken for analysis of protein synthesis pathways (using blood plasma) and untargeted metabolomics at baseline and the 12th week. Fecal sample will be collected from a subsample of 24 subjects for gut microbiota analysis. This study is one of the pioneers randomized controlled trials to evaluate *C. caudatus* efficacy on various health related outcomes among sarcopenic community-dwelling elderly. This study findings are hoped to have the potential to improve health awareness of *ulam* or fresh salad consumption, specifically *C. caudatus* and prove its effectiveness as a nutraceutical product for older adults with sarcopenia. The Australian New Zealand Clinical Trials Registry (ANZCTR) has this trial listed as registered with code (ACTRN12623000046606p).

Keywords: *Cosmos caudatus*, older adults, randomized controlled trial, sarcopenia

INTRODUCTION

In Southeast Asia, the aging population has been expanding, with the proportion of individuals 65 years of age and older increasing from 6% to 11% between the years 1990 and 2019 (You *et al.* 2021). This phenomenon has caused a rise in the number of elderly with disabilities and dependency that is related to sarcopenia. Sarcopenia is an age-related condition characterized by a gradual loss of muscle mass and muscle function in the skeletal system (Papadopoulou 2020). Over 50 million older adults currently suffer from sarcopenia, and over the next 40 years, the figure is projected to rise to 200 million (Ramoo *et al.* 2022). Sarcopenia might cause other geriatric syndromes, including poor mental health, frailty, and, to some extent, significant disabilities (Gao *et al.* 2021; Aurelia *et al.* 2015; Ramoo *et al.* 2022).

To date, some of the most effective treatments for sarcopenia are nutritional therapies, physical activity, and androgen therapy, apart from other behavioral and pharmacological strategies (Aurelia *et al.* 2015). *Ulam* which is mostly made up of fresh leaves of medicinal plants that have numerous therapeutic properties, has been widely used, but studies

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on the development of *ulam* as a nutraceutical product are still limited (You *et al.* 2018). One of the notable *ulams* used as nutraceutical products is *Cosmos caudatus* (*C. caudatus*), referred to as *ulam raja* in the local tongue (You *et al.* 2021). *C. caudatus* possesses a variety of pharmacological properties, such as antidiabetic, antibacterial, antioxidant, antihypertensive, antihyperlipidemic, and antiosteoporosis (Moshawih *et al.* 2017). *C. caudatus* ethanolic extract is able to inhibit α-glucosidase (Ahda *et al.* 2023). *C. caudatus* methanolic extract is effective in inhibiting the growth of certain microorganisms, including E. coli and S. aureus, in oyster mushrooms (Yusoff *et al.* 2015). An aqueous extract of *C. caudatus* is effective in decreasing the heartbeat and amplitude of stroke volume induced by adrenaline (Cheng *et al.* 2015).

Most studies regarding the use of *C. caudatus* are pre-clinical animal studies, but the clinical effect of *C. caudatus* in humans is still obscure. Human clinical studies using *C. caudatus* demonstrated that supplementation with *C. caudatus* improves insulin sensitivity, C-Reactive Protein (CRP), and serum metabolite levels of branched-chain amino acids (Cheng *et al.* 2016). You *et al.* (2021) discovered the efficacy of *C. caudatus* in improving global cognition, overall mood disturbance, tension, and oxidative stress among the elderly with mild cognitive impairment. To date, no studies have been done on *C. caudatus* being used as an intervention for sarcopenic older adults. Thus, the purpose of this study is to determine the effectiveness of a 12-week *C. caudatus* extract supplementation on dietary intake, cognition, mental health, sleep quality, disability, gut microbiota, physical activity, frailty, metabolites, and protein synthesis pathways among older adults with sarcopenia.

METHODS

Design, location, and time

This study is a double-blind placebo-controlled randomized trial for a period of 12 weeks. Table 1 shows the subjects' schedule for their enrollment, interventions, assessments, and time of visits. This research will involve sarcopenic older adults who live in five districts in Kelantan, Malaysia, including Machang, Kota Bharu, Pasir Mas, Tumpat, and Bachok. Subjects were recruited in February 2024.

The Human Research Ethics Committee (JEPeM) at Universiti Sains Malaysia has approved this study protocol (USM/JEPeM/22080543). This research will be performed according to the Declaration of Helsinki. Subjects will be required to sign an informed consent form before participating in this study. Once they were enrolled, they will be briefed on the participant information sheet.

Sampling

The sample size was calculated using the formula by Chan (2003). Thirty-two subjects will be recruited for each treatment and control group with a post-intervention standard deviation of 0.37 meters per second, 80% power, and a 95% confidence interval with an additional drop-out rate of 20%. The mean and standard deviation calculations were based on the research by Kim *et al.* (2012) that evaluated the effect of nutrition and exercise intervention in improving walking speed among community-dwelling sarcopenic in older adults over a three-month period.

The sampling method used for screening is called convenient sampling. After the researcher obtained the number of subjects with sarcopenia, the scouting procedure will be done for a randomized controlled trial. A 1:1 allocation ratio will be used to randomly assign subjects to the intervention or control groups. The randomization sequence of the subjects will be generated using a randomization website (https://www.randomization.com) by simple randomization.

Inclusion criteria. Subjects aged 60 years and older diagnosed with sarcopenia in accordance with the 2019 guidelines of the Asian Working Group for Sarcopenia (AWGS) (only meeting two criteria: low muscle mass and poor muscle strength or poor physical performance), non-smoking, not taking any other vitamins or herbal or traditional medications, and not consuming fruits or vegetables or not meeting the recommended intake of two servings of fruits and at least three servings of vegetables will be recruited.

Exclusion criteria. Older adults who are undergoing regular hemodialysis, bedridden, hospitalized, or living in a long-term care facility, have severe sarcopenia (meeting all the three criteria of AWGS 2019 namely poor muscle strength, low muscle quantity, and poor physical performance), gastrointestinal

surgery or gastrointestinal radiation therapy or chemotherapy, chronic kidney diseases, diarrhoea, chronic constipation or gastrointestinal diseases (inflammatory bowel disease, irritable bowel syndrome, haemorrhoid, diverticulitis), dementia, and also those who are on tube feeding or antibiotics for the past 30 days, corticosteroid, immunosuppressants, warfarin therapy or on medications affecting intestinal motility such as laxatives, antidepressants, opioid, anticholinergic, prebiotic and probiotic during the study period will be excluded.

Intervention. The treatment group will receive 500 mg/day of *C. caudatus* extract (two capsules per day of size 0), while the control group will receive a similar dose of maltodextrin daily for 12 weeks. The dosage of 500 mg/day is based on prior research by You *et al.* (2021). Subjects with mild cognitive impairment were given 500 mg of *C. caudatus* supplement for 12 weeks, and no adverse effects were reported.

Patient safety. Subjects will be asked if they experienced any side effects such as diarrhea, flatulence, headache, or rashes following the consumption of *C. caudatus*. These side effects are rarely observed, but if suspected, treatment needs to be stopped and reported as an adverse outcome. Proper medical treatment will be given to the subjects who claimed to experience side effects after consuming *C. caudatus* supplementation. Subjects who are non-compliant with the study procedure, such as not consuming the given amount of *C. caudatus* for more than 20% of the study duration or experiencing side effects, were excluded from the study.

Adherence. Weekly telephone calls will be made to monitor adherence and address subjects' concerns, such as the presence of any side effects after consuming *C. caudatus* supplementation. Compliance will be monitored by the researcher by asking the subjects to return the supplement bottle every month. Moreover, the subjects will be given a small diary with a medication chart and will be required to mark the chart daily after consuming the supplements.

Study outcome. Table 2 shows the study outcomes including primary outcome and secondary outcome.

Data collection

Subjects from both groups will be required to present for data collection at three different points: baseline, 6th week, and 12th week. Data that will be collected include sociodemographic profile, blood pressure, anthropometry, physical fitness, dietary intake, assessment of sarcopenia, motoric cognitive risk syndrome, mental health, sleep quality, disability, frailty (physical, cognitive, and social), fecal collection, and blood withdrawal. Only blood withdrawal and fecal collection which will be done twice, at baseline and the 12th week.

The subjects will be asked regarding their socio-demographic profiles, which include questions regarding their age, sex, household income, employment status (current and past), marital status, education level, living arrangement, and smoking status. Medical history includes the current and past comorbidities experienced by individuals or any surgical procedure done in the past year. Medication or dietary supplement intake will be recorded. An Omron digital blood pressure monitor will be used to measure blood pressure. Anthropometry will include measurements of height, weight, and calf circumference. The Karada Scan Omron Body Composition Monitor HBF-214 by Omron Healthcare, Kyoto, Japan, will be used to measure weight. A Seca North America, Chino, USA, stadiometer will be used to measure height. For older adults with scoliosis, height is measured using arm span, which is the separation between the middle tips of two fingers. For height estimation using arm span, the formula by Shahar and Pooy (2003) will be used for height calculation. Calf circumference is the measurement of the broadest part of the calf. It is taken when the subject is sitting with his feet touching the ground. Two readings will be taken for the anthropometric measurements, and the analysis will utilize the mean of the two readings.

Assessment of sarcopenia. Sarcopenia will be diagnosed using the AWGS (2019) guideline. In this study, only subjects with sarcopenia will be selected, and those with severe sarcopenia is excluded. Those with sarcopenia will have the following criteria:

Low skeletal muscle mass (Skeletal muscle index=M<7 kg/m^2, W:<5.7 kg/m^2)
AND Poor muscle strength (handgrip strength=M:<28 kg, W:<18 kg)
OR Poor physical performance (SPPB score ≤9)

Chen *et al.* (2020)

Meanwhile, severe sarcopenia is indicated by meeting all criteria, including low skeletal muscle mass, poor muscle strength, and poor

physical performance (Chen *et al.* 2020). Hand grip strength will determine muscle strength, which will be assessed using a hand dynamometer by Fabrication Enterprises Inc., New York, USA. Poor handgrip strength is determined by a value of less than 28 kg for men and less than 18 kg for women (Chen *et al.* 2020). The Short Physical Performance Battery (SPPB) will be used to assess muscle performance, which includes three major assessments: gait speed, balance tests, and a chair stand test. Poor physical performance is indicated by a total score of nine or below (Chen *et al.* 2020). Low muscle mass will be assessed using the Karada Scan Omron Body Composition Monitor HBF-214 by Omron Healthcare, Kyoto, Japan. It is indicated by appendicular Skeletal Muscle Index (SMI) values of less than 7 kg/m² for men and less than 5.7 kg/m² for women (Chen *et al.* 2020).

Assessment of dementia. Dementia will be assessed using the Montreal Cognitive Assessment-Bahasa Malaysia (MoCA-BM) with a Cronbach's α coefficient of 0.691 (Razali *et al.* 2014). A higher score denotes better cognitive ability. The score runs from 0 to 30. Subjects with scores of 22 and below will be at risk of having dementia (Mohamed Fuad *et al.* 2020).

Assessment of dietary intake. Subjects' habitual dietary consumption will be evaluated using a validated Diet History Questionnaire (DHQ). To assess dietary patterns, food items will be divided into 14 groups according to their commonalities, or references to the study by Fakhruddin *et al.* (2019). For diet quality, it will be categorized according to the Standardized Malaysian Healthy Eating Index (S-MHEI). A maximum score of 100 can be achieved by combining the elements of the new S-MHEI, which uses a density standard that is less restrictive as it focuses on an individual's nutrient intake (Jailani *et al.* 2021). Table 3 shows the components of S-MHEI.

Assessment of Motoric Cognitive Risk (MCR) syndrome. Verghese (2013) first introduced the concept of MCR syndrome, a high-risk clinical syndrome that has excellent predictive value for dementia. If any subject fulfills all criteria listed in Table 4, they will be identified as having MCR syndrome.

Assessment of mental health. The General Health Questionnaire (GHQ-12), which has been validated in Malay and has a Cronbach's α coefficient of 0.85, will be used to evaluate mental health (Ibrahim *et al.* 2014). The overall score is between 0 and 12, with 12 items. Impaired mental health is indicated by a higher score. The optimum cut-off point for GHQ-12 is 75% of the total score, which is 9.

Assessment of sleep quality. The Pittsburgh Sleep Quality Index (PSQI-M), which has been validated in Malay and has a Cronbach's α coefficient of 0.74 (Farah *et al.* 2019), will be used to evaluate the quality of sleep. The overall score is between 0 and 21. Those who receive a total score higher than five are deemed to have poor quality sleep.

Assessment of disability. Disability will be evaluated using the World Health Organization Disability Assessment Schedule (WHODAS-12). Total score ranging from 0 to 48. A cut-off score of 16 is considered an indicator of disability as it represents the 95th percentile of impairment based on WHO normative data (Mayrink *et al.* 2018).

Assessment of frailty. Frailty can be divided into a few aspects, which are physical frailty, cognitive frailty, and social frailty: a). Physical frailty: Will be determined using the Fried physical phenotype. These are the cut-off points. The phenotypes are shown in Table 5;

Positive for ≥3 frailty phenotypes=Physically frail

Positive with 1 or 2 phenotypes=Pre-fail

None=Robust

(Liu *et al.* 2020)

b). Cognitive frailty: Will be assessed based on the three criteria below: 1). Physical frailty: The subject met at least 3 criteria from the Fried physical phenotype indicating physical frailty; 2). Cognitive impairment: Assessed using MoCA as mentioned in the dementia assessment, but with a cut-off point for cognitive impairment of < 26 (Razali *et al.* 2014); 3). Functional limitation: Assessed using Instrumental Activities of Daily Living (IADL) in the Malay version. The scoring and details were explained in the MCR syndrome assessment; c). Social frailty: Will be assessed using a social frailty questionnaire developed by Makizako *et al.* (2015). There are five items in this questionnaire. Subjects will be robust if the score is 0, pre-social frailty if 1, and social frailty if 2–5 (Makizako *et al.* 2015).

Physical fitness test. Physical fitness comprises a back scratch test, a 2-minute step

test, a chair sit and reach test, and a Borg scale: a). Back scratch test will be used to assess the flexibility of the upper body in the shoulder joint and shoulder arch on both the left and right sides (Seiler *et al.* 2016); b). 2-minute step test will be done to evaluate aerobic capacity, thus evaluating the subjects' level of functional fitness (Bohannon & Crouch 2019); c). Chair sit-and-reach test will be done to evaluate the flexibility of the lower body (Mayorga-Vega *et al.* 2014); d). Borg Rating of Perceived Exertion (RPE) scale is an instrument used to measure a person's effort and exertion, dyspnea, and exhaustion during physical labor (Williams 2017).

Gut microbiota analysis. Fecal samples will be collected to determine the quantity of gut microbiota. Gut microbiota analysis will be conducted on a subsample of 24 subjects (12 from the treatment group and 12 from the control group).

Blood withdrawal. A total of 6 mL of fasting blood will be obtained by venepuncture of the median cubital vein into serum separator tubes by a trained phlebotomist from Pathlab. The blood samples collected will be centrifuged in the Pathlab laboratory to separate the serum and plasma. Blood plasma will be used for Western blot analysis to detect changes in the IGF-Akt-mTOR pathway. This analysis will be conducted in the Molecular Biology Laboratory of the School of Health Sciences, Universiti Sains Malaysia. The Western Blot analysis will be done according to the adapted protocol by Singh *et al.* (2021) and Jaleel *et al.* (2005). The blood serum collected will be used for the untargeted metabolomics analysis using Nuclear Magnetic Resonance (H-NMR) spectroscopy. This will be done based on the papers by Mostafa *et al.* (2017).

Data analysis

Statistical Package for the Social Sciences (SPSS) (SPSS Inc., Chicago, USA) version 26 will be used to analyze the data. Categorical data will be shown in percentage, whereas continuous data will be shown in Mean±SD. The normality test will be done using the Shapiro-Wilk test prior to univariate analysis. An independent t-test will be used for baseline analysis to compare the

Table 1. Time schedule for subjects' enrolment, interventions, assessments, and time visits

Timepoint	Study period				
	Enrolment	Allocation	Post-allocation (Intervention)		
			Baseline	6th week	12th week
	Jan 2024	Feb 2024	Mar 2024	Apr 2024	May 2024
Enrolment					
Eligibility screen	X	-	-	-	-
Informed consent	X	-	-	-	-
Allocation	-	X	-	-	-
Interventions					
500 mg/day of Cosmos caudatus extract	-	-			
Assessments					
Dietary intake	-	-	X	X	X
MCR syndrome	-	-	X	X	X
Mental health	-	-	X	X	X
Sleep quality	-	-	X	X	X
Disability	-	-	X	X	X
Frailty	-	-	X	X	X
Physical fitness test	-	-	X	X	X
Blood withdrawal	-	-	X	-	X
Fecal collection	-	-	X	-	X

MCR: Motoric Cognitive Risk

study outcomes of both the treatment group and the control group. The effectiveness of the *C. caudatus* supplementation will be assessed using a two-way repeated measure ANOVA adjusted for possible confounding factors. Intention-To-Treat (ITT) analysis will be used in this investigation, meaning that all subjects will be included in the analysis regardless of whether they follow the treatment plan or finish the study, which will help to minimize selection bias. The significance level (α) will be set at 0.05, while the confidence level is at 95% for the test, and the significant p-value will be considered at <0.05.

DISCUSSION

Sarcopenia is a disease associated with aging that is usually not diagnosed in clinical practice, even when there is substantial overlap of the sarcopenia phenotype degree with comorbidities that share the same associated risks and health effects as sarcopenia (Qaisar *et al.* 2021). Therefore, the purpose of this study is to examine the factors that are related to sarcopenia, including dietary intake, cognition, mental health, sleep quality, disability, gut microbiota, physical activity, frailty, metabolites, and protein synthesis

Table 2. Study outcomes

Category	Expectation
Primary outcome	
1. Changes in sarcopenia parameters	The consumption of *C. caudatus* supplementation for 12 weeks will improve older adults' muscle mass, muscle strength and physical performance.
Secondary outcome	
1. Changes in dietary intake	The consumption of *C. caudatus* supplementation for 12 weeks will improve older adults' overall nutrient intake, dietary pattern and S-MHEI score.
2. Changes in motoric cognitive risk syndrome	The consumption of *C. caudatus* supplementation for 12 weeks will reduce the criteria of MCR syndrome that they initially met.
3. Changes in mental health	The consumption of *C. caudatus* supplementation for 12 weeks will reduce the GHQ-12 score among older adults.
4. Changes in sleep quality	The consumption of *C. caudatus* supplementation for 12 weeks will reduce the PSQI score among older adults.
5. Changes in disability	The consumption of *C. caudatus*supplementation for 12 weeks will reduce the WHODAS score among older adults.
6. Changes in gut microbiota	The consumption of *C. caudatus* supplementation for 12 weeks will improve older adults' microbial composition (increased beneficial bacteria and decreased harmful bacteria) and improve microbial diversity.
7. Changes in physical fitness	The consumption of *C. caudatus* supplementation for 12 weeks will increase the back scratch test, 2-minute step test, chair sit and reach test, and Borg scale score among older adults.
8. Changes in frailty	The consumption of *C. caudatus* supplementation for 12 weeks will reduce the criteria of physical, cognitive and social frailty that they initially met.
9. Changes in metabolites pathways	The consumption of *C. caudatus* supplementation for 12 weeks will improve older adults' beneficial metabolic pathways such as glycolysis, oxidative phosphorylation, enhanced synthesis and utilization of amino acids, and better lipid processing.
10. Changes in IGF1-AKT-mTOR pathway	The consumption of *C. caudatus* supplementation for 12 weeks will give significant differences in protein expression (increase IGF-1, AKT Phosphorylation, mTOR Phosphorylation and their downstream targets) to indicate pathway activation.

AKT: Protein Kinase B; GHQ-12: General Health Questionnaire; IGF-1: Insulin-like Growth Factor 1; MCR: Motoric Cognitive Risk; mTOR: Mammalian Target of Rapamycin; PSQI: Pittsburgh Sleep Quality Index; S-MHEI: Standardized Malaysian Healthy Eating Index; WHODAS: World Health Organization Disability Assessment Schedule

Table 3. Standardized Malaysian Healthy Eating Index (S-MHEI) components and scoring

Dietary components	Type	Min. Score criteria	Max. Score criteria
Total grains	Adequacy	0 serving/ 1,000 kcal	1.4 servings/ 1,000 kcal
Whole grains			0.7 servings/ 1,000 kcal
Fruits			0.9 servings/ 1,000 kcal
Vegetables			1.2 servings/ 1,000 kcal
Fish			0.4 servings/ 1,000 kcal
Meat, Poultry, and Eggs			0.4 servings/ 1,000 kcal
Legumes and Nuts			0.4 servings/ 1,000 kcal
Milk and Milk Products			0.9 servings/ 1,000 kcal
Total Fat	Optimal	0–≥55% TEI	25–30% of TEI
Added Sugar	Moderation	≥25% TEI	≤5 % of TEI
Sodium		≥2,300 mg	<1,925.0 mg

TEI: Total Energy Intake; Adapted from Jailani *et al.* (2021)

Table 4. Motoric Cognitive Risk (MCR) syndrome criteria

Criteria	Explanation
Absence of dementia	Assessed using MoCA as mentioned in dementia assessment
SCD	Assessed using item 10 on GDS-15. If the answer is 'Yes', this indicates that the subject has subjective cognitive decline
Slow gait	Measured by having the subjects walk back and forth at their normal rate across a 6-meter course. A slow gait will be 1 standard deviation slower than the population's mean gait.
Preserved activities of daily living	Determined using IADL in Malay version questionnaire with Cronbach's α coefficient of 0.838 (Kadar *et al.* 2018). Higher score indicates higher functionality and lower dependency

GDS-15: Geriatric Depression Scale; IADL: Instrumental Activities of Daily Living; SCD: Subjective Cognitive Decline

pathways. This study is the first to look at the effects of *C. caudatus* on various health-related parameters among sarcopenic older adults. Even though there is limited evidence regarding the effectiveness of *C. caudatus* as a therapy for sarcopenia, *C. caudatus* is chosen due to its phytochemical contents and benefits for muscle health. A prior study found that *C. caudatus* contained many flavonoids, including quercetin and catechin (Ahda *et al.* 2023). A previous study found that quercetin inhibits inflammatory receptors and their signaling pathway to decrease skeletal muscle atrophy, which might be important to prevent sarcopenia (Le *et al.* 2014). Non-flavonoid chemicals found in *C. caudatus* consist of phenolic acids, which have been shown to benefit muscles by stimulating muscle growth and/or decreasing muscular atrophy, as well as improving mitochondrial quality and lowering oxidative stress and inflammation (Nikawa *et al.* 2021).

In conclusion, the findings from this study will be able to prove the effect of *C. caudatus* on acting as a nutraceutical product for older adults with sarcopenia. The scientific data from this research could raise public health awareness of *ulam* intake, specifically *C. caudatus*, which could contribute to a further decrease in the risk of sarcopenia, a more active lifestyle, a better quality of life, and subsequently reduce the cost of healthcare, especially among older adults.

CONSENT FOR PUBLICATION

The subjects will be explained regarding the publication of their details and needed to sign

Table 5. Physical frailty phenotype

Phenotype	Explanation
Unintentional weight loss	Greater than or equal to 4.5 kg or 5% of body weight in the last one year will be asked to subject
Exhaustion	Assessed by asking 2 questions from the CES-D scale which are 'I felt that everything I did was an effort' and 'I could not get going'. Then, the frequency of how the subject felt as such would also be asked. Subjects will be considered exhausted if they answered "2 = occasionally or a moderate amount of time (3–4 days)" or "3 = most or all the time (5–7 days)"
Weakness	Evaluated using handgrip strength with same procedure and cutoff points as sarcopenia assessment.
Slowness	Assessing the usual walking speed of subject along a distance of 4.6 m. Those with >7 seconds (for male with height <173cm or female with height < 159 cm) and >6 seconds (for male with height >173 cm or female with height >159 cm), will be categorized as positive for frailty in this category
Low physical activity	Based on RAPA questionnaire. Subjects who are classified as sedentary or underactive will be considered as positive for frailty in this category (Mohd Hamidin *et al.* 2018).

CES-D: Center for Epidemiologic Studies Depression; RAPA: Rapid Assessment of Physical Activity

the informed consent form before participating in this research. Every form is anonymous and will be input into SPSS software. The data obtained will remains confidential. Only members of the research team will have access. The data will not be used to personally identify the participants; instead, they will be displayed in groups. The specific subjects' identities won't be disclosed following the publication. All study-related data will be kept safe and accessible to a limited number of people. Study records denoted by respondent codes will be kept apart from all other records that include names or other personally identifiable information, such as registration forms and informed consent forms.

The corresponding author can provide the datasets used and/or analyzed for this study upon reasonable request.

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DECLARATION OF CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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