

## Original Article

# Dietary education with customised dishware and food supplements can reduce frailty and improve mental well-being in elderly people: A single-blind randomized controlled study

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**Background and Objectives:** The elderly population is increasing rapidly worldwide, and frailty is a common geriatric syndrome. Comprehensive dietary management strategies may have beneficial effects on frailty prevention and reversal. This 3-month single-blind, paralleled, randomized controlled trial compared the effects of micronutrients and/or protein supplements, and a personalised diet on frailty status in elderly individuals. **Methods and Study Design:** Between 2014 and 2015, 40 prefrail or frail subjects aged  $\geq 65$  years were recruited at Miaoli General Hospital, Taiwan. Of these, 37 completed the study, and 36 were included in the analysis. Participants were randomly assigned to one of four treatment groups: (1) the control (2) multiple micronutrient supplements, (3) multiple micronutrients plus isolated soy protein supplement, and (4) individualised nutrition education with customised dishware and food supplements (mixed nuts and skimmed milk powder). Dietary intake, protein biomarkers, frailty score, and geriatric depression score were assessed. **Results:** Individualised nutrition education with customised dishware and food supplements significantly increased the participants' intake of vegetables, dairy, and nuts, in addition to increasing the concentration of urinary urea nitrogen. It yielded a significant reduction in frailty score ( $p < 0.05$ ) and a borderline reduction ( $p = 0.063$ ) in geriatric depression score. No significant beneficial changes were observed for the other two intervention groups. **Conclusions:** Our study indicated that a dietary approach with easy-to-comprehend dishware and food supplements to optimize the distribution of the consumption of six food groups improved frailty status and, potentially, psychological well-being in elderly people.

**Key Words:** frailty, nutrition education, customised dishware, Daily Food Guide, multiple dietary components

## INTRODUCTION

The proportion of the elderly population ( $\geq 65$  y) in Taiwan is rapidly increasing and is predicted to reach 20% of the population by 2025, creating a 'super-aged society'.<sup>1</sup> Frailty is a common geriatric syndrome. Compared with people without frailty, those with frailty have an increased risk of adverse health outcomes such as falls, disability, institutionalization, and mortality, which considerably increase cost of caring for this population.<sup>2,3</sup> To control age-related medical and social expenditure, identifying strategies to prevent or delay the onset of age-related disabilities, such as frailty and sarcopenia, is critical to public health.

Impaired nutritional status is associated with sarcopenia, poor muscle strength, diminished physical function

and frailty.<sup>4</sup> Many observational studies have examined the association between diet and frailty; however, such studies have focused on only single nutrients or food groups,<sup>5-8</sup> thereby failing to consider the synergy of various nutrients and food groups in a balanced diet.<sup>6</sup> To overcome this limitation, research has applied dietary

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Manuscript received 25 April 2017. Initial review completed 12 June 2017. Revision accepted 18 September 2017.

doi: 10.6133/apjn.032018.02

pattern analysis,<sup>9</sup> suggesting that the Mediterranean diet, a well-known prudent dietary pattern, has the potential to promote healthy aging and prevent frailty,<sup>9-17</sup> whereas the Western diet is associated with increased frailty.<sup>12</sup> Our previous study also indicated that a Taiwanese diet rich in fish, shell fish, vegetables, fruits, whole grains, and tea or coffee was associated with the absence of frailty.<sup>18</sup>

Dietary management, particularly in combination with physical therapy, is one of the most promising strategies for preventing or reversing frailty.<sup>19</sup> Studies on frailty management have assessed a wide range of dietary supplements, and most of such studies have focused on the supplementation of protein, energy, and vitamin D, either separately or in combination.<sup>5,20-25</sup> The reported effects of nutritional supplements on frailty prevention have been inconsistent.<sup>4,26-30</sup> The aforementioned observational studies have suggested that providing comprehensive dietary components may provide greater benefits for overall well-being, including prefrailty prevention and reversal, compared with single nutrients or food groups. Thus, we conducted a single-blind, parallel, randomised controlled trial to compare the effects of supplementation with multiple micronutrients and/or protein powders, and those of a diet followed the recommendations in Taiwan's Daily Food Guide on frailty and mental health in prefrail and frail elderly people.

## METHODS

### Participants

From November 2014 to April 2015, participants aged  $\geq 65$  years were recruited at Miaoli General Hospital, Miaoli City, Taiwan, through poster advertisements or physician referral. Candidates without severe disease (e.g. cancers under treatment, immobilization, or severe arthritis), diagnosed dementia, mental illness, or an inability to communicate were subjected to a simplified geriatric assessment conducted using a modified version of the L.

Fried criteria for identifying individuals at the prefrail to frail stage (Table 1).<sup>2,31,32</sup> All participants gave written informed consent before participating in the study. The study protocol was reviewed and approved by the Institutional Review Board on Biomedical Science Research, Academia Sinica (project AS-IRB-BM-14044). This trial has been registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) as ISRCTN02975089.

### Trial design and interventions

This study was a 3-month, single-blind, parallel group, randomised controlled trial that comprised four treatment groups (n=10 per group; Figure 1). Enrolment was conducted by the onsite patient manager. Because physical function (grip strength and gait speed) and physical activity are phenotypes that account for frailty levels, the influence of physical therapy should be balanced. Therefore, participants were randomly assigned to one of the four treatment groups by using a stratified randomisation method to ensure a balanced distribution of "receiving or not receiving physical therapy" in each of the four groups. One staff member conducted the assignment using a random allocation sequence provided by the principle investigator.<sup>33</sup>

Participants came to the hospital at fasted state in the morning at the baseline (V1), 1-month follow-up (V2), and 3-month follow-up (V3). At V1, participants provided basic information on sociodemographics, medical history, and medication. A typical dietary intake (the primary outcome measure) and a comprehensive geriatric assessment (secondary outcome measures), including a nutritional status assessment, modified L. Fried's frailty assessment, and depressive symptoms assessment, were conducted at all three visits. An overnight urine specimen was collected at V1 and V3. The supplements were provided at V1 for the first intervention month and at V2 for the rest of the intervention period. The study was

**Table 1.** Modified L. Fried criteria for frailty in Taiwan<sup>†</sup>

Frailty phenotype	Criteria
Weight loss	Unintentional weight loss of >3 kg or 5% of body weight over the previous year
Self-described exhaustion	Whether they had felt fatigue or exhaustion for >3 d in the previous week
Weak grip strength	1. Using a hand-held dynamometer 2. Dominant hand and then non-dominant hand in triplicate (mean of 3 measurements) 3. Lowest 20% group
	Men
	Women
	Men
	Women
	Men
	Women
Slow gait speed	Test of walking 10 m and the slowest 20% group
	Men
	Women
	Men
	Women
Low physical activity	1. Taiwan International Physical Activity Questionnaire- Short Form 2. Lowest 20% of caloric consumption
	Men
	Women
	Men
	Women

<sup>†</sup>Scoring system was based on the American L. Fried's study and amended for elderly people in Taiwan.<sup>2,31,32</sup> Participants with a 1-2 frailty score(s) were classified as prefrail, and those with a score  $\geq 3$  were classified as frail.

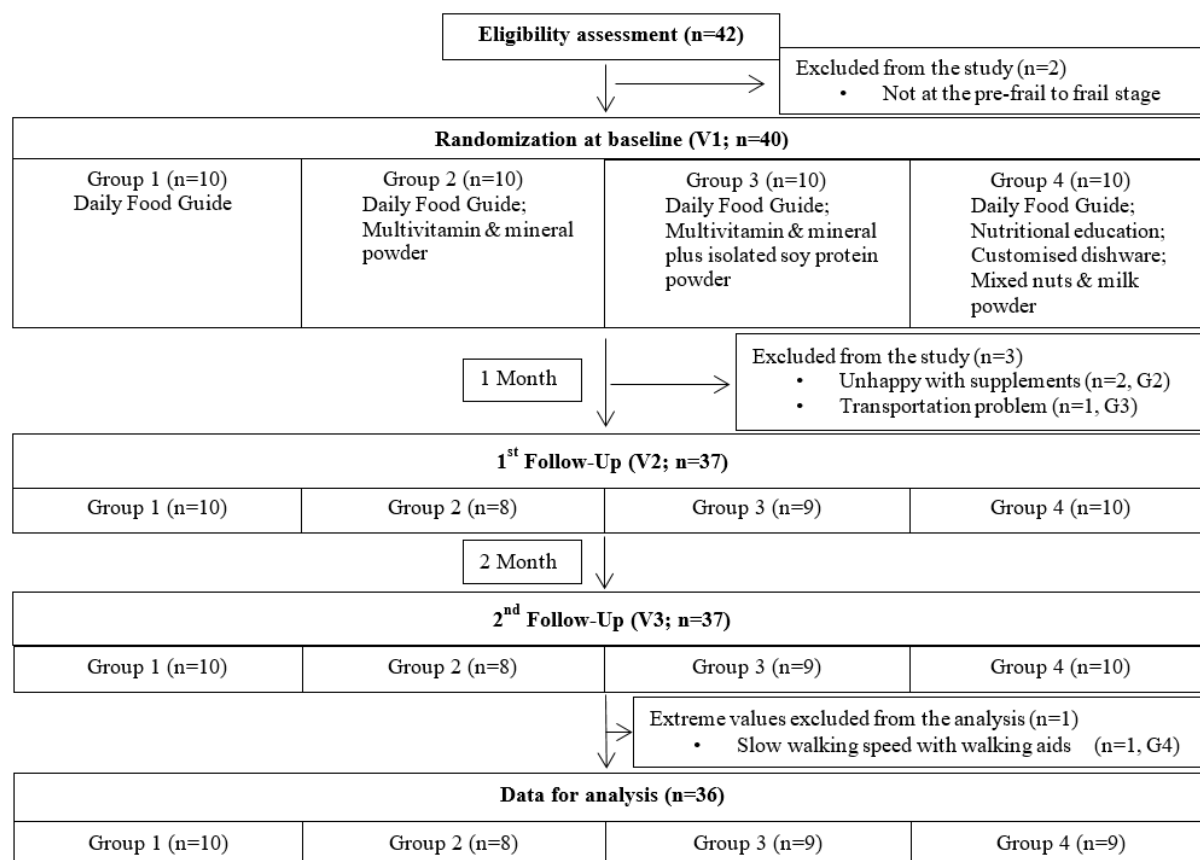


Figure 1. Trial design and flow of participants through the different stages of the frailty study.

terminated when V3 was completed, as originally designed.

The Daily Food Guide was published in 2011 by Taiwan's government to promote the idea of a nutritious and varied diet.<sup>34</sup> Depending on an individual's physical activity level and sex, the recommended number of servings of the six major food groups (whole grains and roots; beans, fish, meats and eggs; vegetables; fruits; dairy; and nuts and oils) are listed by energy level. Participants in the control group (Group 1), the multinutrient group (Group 2), and multinutrient and soy protein group (Group 3) received a leaflet about the Daily Food Guide (simplified in Supplementary Table 1) without advice from the dietitian. Those in Group 2 were also given 1.3 g/d of multivitamin and mineral powder (Supplementary Table 2), which provided the RDA level of nutrients. Those in Group 3 were given 1.3 g/d of multivitamin and mineral powder plus 16 g/d of isolated soy protein powder that provided 14.4 g/d of protein (60.8 kcal of energy) (Archer Daniels Midland Company, USA; Supplementary Table 3).<sup>35,36</sup> Those in the nutrition education, customised dishware, and food supplement group (Group 4) received two sessions of individualised nutrition education from a licensed dietitian (at V1 and V2); the objective of the provided education was to help the participants consume a nutritious diet with the appropriate distribution of the six food groups and achieve the RDA level of nutrients. Participants were provided with a set of customised dishware, in addition to being provided with 10 g/d of mixed nuts (cashews, pumpkin seeds, walnuts, macadamia, pine nuts, and almonds) and 25 g/d of milk powder (skimmed with calcium added), which provided 71.7 kcal/d of ener-

gy for 3 months (Supplementary Table 4). The measuring dishware set comprised a four-compartment divided plate, a bowl, a mug, and a spoon (designed by the Taiwanese Association of Diabetes Educators; Supplementary Figure 1). The objective was for the participant to fill the designated space on the plate with protein-rich foods and vegetables to consume the appropriate amounts of each. The bowl, mug, and spoon similarly assisted the participants with gauging the correct amounts of rice and fruits, dairy, and nuts and seeds. We provided food supplements because the Daily Food Guide recommends consuming one to two serving(s) of low-fat dairy products (one serving is 240 cc. of milk or 25 g of milk powder) and one serving (approximately 10 g) of nut and seeds per day, the intake of which was low among elderly people in Taiwan.<sup>36</sup>

#### Dietary and nutritional status assessment

Nutritional status was assessed using the Mini Nutritional Assessment-Short Form (MNA-SF) tool.<sup>37</sup> An MNA-SF score  $\geq 12$  indicates normal nutritional status; between 8 and 11 indicates a risk of malnutrition; and  $\leq 7$  indicates a state of malnutrition. Licensed dietitians, with the assistance of food models and measuring dishware, assessed dietary intake within the past month by inquiring about the participants' typical dietary pattern, most frequently consumed items, and the amount of food eaten at breakfast, lunch, dinner, and snack times. The dietary intake data were transformed into nutrient data by using a computerised worksheet based on the Taiwan Food Nutrient Database and associated software (FNDB971205, FNDB1010903). If any specific food was unavailable in the Taiwan Food Nutrient Database, the USDA National

Nutrient Database and the Food Composition Database of Japan were used. For anthropometric measures, participants emptied their pockets and removed all footwear and heavy clothing. Height and weight were measured to the nearest 0.1 cm or 0.1 kg by using a TANITA medical height and weight scale.

#### **Frailty assessment**

All participants were evaluated for frailty based on the modified L. Fried criteria (Taiwanese criteria are documented in Table 1). Five frail phenotypes were assigned: (1) unintentional weight loss, (2) self-reported exhaustion, (3) weak grip strength, (4) slow gait speed, and (5) low level of physical activity. To estimate frailty, participants scored 1 point from each phenotype if any of these were satisfied; a maximum score of five was possible. Participants were classified by their point scores as follows: 'robust' for 0 point; 'pre-frail' for 1 or 2 points; and 'frail' for  $\geq 3$ .

#### **Depression assessment**

The Geriatric Depression Scale-Short Form (GDS-SF), Chinese version, is a 15-item assessment tool that identifies depression in people aged  $\geq 65$  years.<sup>38,39</sup> Participants were classified by their point scores as follows: 'at risk of depression' for 5 to 9 points; and 'in a state of depression' for  $\geq 10$  points.

#### **Biospecimen collection and assays**

The first morning urine sample was collected by participants and brought into the hospital for urinary urea nitrogen and creatinine analysis. The analysis was performed by Roche/Hitachi Cobas c systems using enzyme-based colorimetric kits (COBAS, Roche Diagnostics GmbH, Mannheim, Germany). The mean intra-assays coefficients of variation were  $<4\%$ .

#### **Statistical methods**

Statistical analysis was performed using SAS version 9.4 (SAS Institute, North Carolina, USA). Before statistical analysis, data distribution and normality were examined using the Shapiro-Wilk test. For continuous variables, differences between groups at V1 were assessed by using ANOVA or the Kruskal-Wallis test (if nonnormally distributed). For categorical variables, the Fisher's exact test was used.

To determine the between-group differences in the effects of the nutritional interventions, mean changes (between V1 and V2, and between V1 and V3) were compared using ANOVA or the Kruskal-Wallis test (if nonnormally distributed). The overall effect of the intervention was determined through post hoc analysis by using Duncan and Dunn's correction (if nonparametric) if significant. The paired t-test or Wilcoxon signed-rank test (if nonnormally distributed) was applied to test the effects of the interventions within the treatment groups.

## **RESULTS**

### **Compliance**

Participants who received supplements were asked to complete a self-reported daily log. The compliance rate of Group 2, Group 3, and Group 4 was 97.7%, 86.3% and

92.5%, respectively; these rates were calculated based on the log sheet.

### **Baseline data**

A flowchart of the participant recruitment, treatment, and analysis processes is shown in Figure 1. Of the 40 participants who were randomly assigned to the various treatment groups initially, 37 (17 men and 20 women) completed the 3-month intervention and all three visits. One participant was ultimately excluded due to outlying data (a slow walking speed caused by the need for and use of walking aids). The study participants had an average age of 74 years, were slightly overweight (BMI: 26 kg/m<sup>2</sup>), and had an average GDS-SF score of 2.8. The participants' baseline characteristics are detailed in Table 2. At V1, no significant differences were observed between the four treatment groups in terms of frailty score, caloric intake, or most dietary consumption amounts of the six food groups, except for the number of servings of whole grains and roots and the concentration of urinary urea nitrogen (Table 3).

### **Effects of various nutritional interventions on nutritional status, dietary intake**

The effects of various nutritional interventions on dietary intake and nutritional status among the groups are detailed in Table 3. The results revealed significant overall treatment effects in terms of the mean changes in energy (including supplements) ( $p=0.003$ ) and serving numbers of vegetables ( $p=0.040$ ), dairy (including supplements) ( $p<0.001$ ), and nuts and oils (including supplements) ( $p=0.003$ ) among the four groups. The post hoc analysis showed that Group 4 had a significantly greater increase in the intake of vegetables and dairy and nuts, compared with Group 1. No statistically significant treatment effects were evident for the other food groups and MNA-SF.

### **Effects of various nutritional interventions on protein biomarkers**

We observed an overall treatment effect in terms of the mean change in urinary urea nitrogen for all groups ( $p=0.009$ ) after 3 months. The change in urinary urea nitrogen in Group 4 was significantly greater than in the other three groups, including Group 1 (Table 3).

### **Effects of various nutritional interventions on frailty assessment**

The effects of the various nutritional interventions on frailty assessment are detailed in Table 4. Although the change was not significantly different among the four groups, Group 4 showed significant reduction in the total frailty score after 3 months ( $p=0.031$ , Figure 2). Furthermore, no significant overall treatment effects were evident in the components of frailty score (such as weight, grip strength, 10-m gait speed, and physical activity) at both follow-up time points.

### **Effects of various nutritional interventions on depression assessment**

The results indicated a significant difference in the overall mean change in the GDS-SF score across all four

**Table 2.** Baseline characteristics of study participants, n=36†

	Control	Multinutrient	Multinutrient and soy protein	Nutrition education, customised dishware, and food supplement	<i>p</i> value‡
Number	10	8	9	9	
Age, years	75.9±1.7	73.5±2.4	75.0±2.4	72.8±1.6	0.672 (A)
BMI, kg/m <sup>2</sup>	24.6±1.1	25.5±0.9	25.5±1.1	28.4±1.2	0.086 (A)
Gender, men	6 (60)	2 (25)	4 (44.4)	4 (44.4)	0.560 (F)
Married status	8 (80)	5 (62.5)	5 (55.6)	8 (88.9)	0.395 (F)
Education level at junior school and above	3 (30)	3 (37.5)	4 (44.4)	2 (22.2)	0.815 (F)
Current smoker	1 (10)	1 (12.5)	1 (11.1)	0 (0)	0.887 (F)
Regular drinker	1 (10)	0 (0)	0 (0)	0 (0)	1.000 (F)
MNA-SF ≥12§	10 (100)	8 (100)	8 (88.9)	9 (100)	0.722 (F)
GDS-SF ≥10¶	1 (10)	0 (0)	1 (11.1)	0 (0)	0.442 (F)
Frailty score	1.80±0.25	1.50±0.27	1.78±0.36	1.44±0.24	0.705(K)
Frailty status					1.000 (F)
Pre-frail (frailty score 1-2)	8 (80)	7 (87.5)	7 (77.8)	8 (88.9)	
Frail (frailty score 3-5)	2 (20)	1 (12.5)	2 (22.2)	1 (11.1)	
Frailty component					
Unintentional weight loss	0 (0)	0 (0)	1 (11.1)	1 (11.1)	0.714 (F)
Exhaustion	7 (70)	4 (50)	3 (33.3)	6 (66.7)	0.381 (F)
Low handgrip strength	8 (80)	7 (87.5)	8 (88.9)	4 (44.4)	0.150 (F)
Low gait speed	3 (30)	1 (12.5)	2 (22.2)	1 (11.1)	0.803 (F)
Low physical activity	1 (10)	0 (0)	2 (22.2)	2 (22.2)	0.648 (F)
Clinical profile					
Hypertension	6 (60)	6 (75)	5 (55.6)	6 (66.7)	0.903 (F)
Diabetes	2 (20)	3 (37.5)	2 (22.2)	3 (33.3)	0.851 (F)
White blood cell, 10 <sup>3</sup> /μL	6.02±0.57	6.41±0.66	6.72±0.45	5.71±0.51	0.328 (K)
Red blood cell, 10 <sup>6</sup> /μL	4.56±0.19	4.61±0.15	4.19±0.18	4.43±0.22	0.406 (A)
Hemoglobin, g/dL	13.8±0.5	13.9±0.4	12.1±0.4	13.4±0.56	0.061 (K)
Platelet, 10 <sup>3</sup> /μL	227±18.8	196±27.2	227±11.9	210±13	0.599 (A)

MNA-SF: Mini Nutritional Assessment-Short Form; GDS-SF: Geriatric Depression Scale- Short Form; (A), ANOVA; (K), Kruskal-Wallis; (F), Fish's exact test

†Values are mean ± SEMs for continuous variables; number of participant (%) for categorical variables.

‡*p* values were based on ANOVA or Kruskal-Wallis test for continuous variables, and Fish's exact test for categorical variables.

§MNA-SF score of ≥12 was considered to indicate normal nutritional status.

¶GDS-SF score of ≥10 points was considered to indicate depression.

**Table 3.** Dietary assessment, nutritional biomarkers, and MNA of participants at the prefrail and frail stage at the baseline and 3 months post-intervention<sup>†</sup>

	Control			Multinutrient			Multinutrient and soy protein			Nutrition education, customised dishware, and food supplement			p value <sup>‡</sup>
	Baseline	Post	Δ	Baseline	Post	Δ	Baseline	Post	Δ	Baseline	Post	Δ	
Dietary assessment (serving)													
Energy, Kcal/day	1660±108	1706±125	45.6±110	1701±175	1590±163	-111±85.7	1684±175	1424±126**r	-261±89.6	1321±162	1566±98.9*t	245±97.3	<b>0.007 (A)</b>
			<b>AB</b>			<b>BC</b>			<b>C</b>			<b>A</b>	
Energy + supp., Kcal/day	-	1706±125	45.6±110	-	1590±163	-111±85.7	-	1483±125*r	-201±89.3	-	1643±112*t	322±101	<b>0.003 (K)</b>
			<b>AB</b>			<b>B</b>			<b>B</b>			<b>A</b>	
Whole grains and roots, bowl	2.95±0.36	2.49±0.39	-0.46±0.25	3.38±0.42	2.89±0.35	-0.48±0.3	2.74±0.3	2.36±0.24	-0.39±0.11	1.83±0.2	2.01±0.19	0.17±0.11	0.103 (A)
	<b>A</b>			<b>A</b>			<b>AB</b>			<b>B</b>			
Beans, fish, meats and eggs	3.28±0.36	4.66±0.84	1.38±0.73	3.44±0.58	3.88±0.44	0.44±0.41	4.91±1.00	4.02±0.45	-0.89±0.81	3.44±0.73	4.20±0.36	0.76±0.57	0.116 (A)
Beans, fish, meats and eggs + supp.	-	4.66±0.84	1.38±0.73	-	3.88±0.44	0.44±0.41	-	5.98±0.47	1.07±0.81	-	4.20±0.36	0.76±0.57	0.777 (A)
Vegetables	2.38±0.36	2.28±0.39	-0.1±0.24	3.00±0.38	2.98±0.41	-0.03±0.34	2.82±0.59	2.82±0.49	0.01±0.39	3.62±0.68	4.78±0.76*r	1.16±0.39	<b>0.040 (A)</b>
			<b>B</b>			<b>B</b>			<b>B</b>			<b>A</b>	
Fruits	1.08±0.32	1.75±0.25	0.68±0.41	2.13±0.31	2.38±0.51	0.25±0.38	1.96±0.39	2.23±0.16	0.27±0.4	1.78±0.29	2.44±0.57	0.67±0.49	0.818 (A)
Dairy + supp.	0.96±0.39	1.00±0.37	0.04±0.13	0.69±0.16	0.52±0.17	-0.17±0.13	0.52±0.18	0.46±0.2	-0.05±0.14	0.84±0.18	1.69±0.25***t	0.85±0.16	<b>&lt;0.001 (K)</b>
			<b>B</b>			<b>B</b>			<b>B</b>			<b>A</b>	
Nuts & oils + supp.	4.96±0.5	6.56±0.66*t	1.6±0.63	5.27±0.65	4.9±0.9	-0.37±1.03	5.98±0.75	4.80±0.85	-1.18±0.98C	4.50±0.76	7.79±0.61***t	3.29±0.65	<b>0.003 (A)</b>
			<b>AB</b>			<b>BC</b>						<b>A</b>	
Oils	4.76±0.45	6.21±0.63	1.45±0.66	5.15±0.65	4.47±0.6	-0.68±0.85	5.73±0.74	4.19±0.69	-1.54±0.83	4.28±0.66	6.17±0.59*t	1.89±0.63	<b>0.014 (K)</b>
Nuts + supp.	0.2±0.13	0.35±0.18	0.15±0.21	0.13±0.13	0.44±0.44	0.31±0.31	0.26±0.17	0.61±0.37	0.36±0.27	0.22±0.22	1.62±0.16*r	1.40±0.33	<b>0.025 (K)</b>
			<b>B</b>			<b>B</b>			<b>B</b>			<b>A</b>	
Daily protein, g/day	57.2±4.58	64.6±7.24	7.38±5.54	59.6±7.19	57.4±5.85	-2.17±2.8	63.3±8.73	53.5±4.12	-9.79±6.55	49.2±3.98	59.6±3.81	10.4±4.69	<b>0.039 (A)</b>
			<b>A</b>			<b>AB</b>			<b>C</b>			<b>A</b>	
Daily protein + supp., g/day	-	64.6±7.24	7.38±5.54	-	57.4±5.85	-2.17±2.8	-	67.2±4.14	3.92±6.52	-	64.5±4.86*t	15.0±4.88	0.174 (A)
Daily protein per BW, g/ kg	0.94±0.06	1.07±0.13	0.13±0.1	1.02±0.11	1±0.99	-0.02±0.05	0.98±0.13	0.84±0.07	-0.15±0.10	0.73±0.12	0.88±0.07	0.15±0.07	0.062 (A)
Daily protein+ supp. per BW, g/ kg	-	1.07±0.13	0.13±0.1	-	1±0.99	-0.02±0.05	-	1.05±0.07	0.07±0.1	-	0.96±0.09*t	0.22±0.07	0.289 (A)
Biomarkers													
UUN, mmol/L	280±23.2	277±25.5	-2.33±15.4	219±13	237±24.6	13.5±22.4	274±35.9	233±33	-41.5±36	189±16.3	295±45.1*t	106±38.3	<b>0.009 (A)</b>
	<b>A</b>		<b>A</b>	<b>AB</b>		<b>A</b>	<b>A</b>		<b>A</b>	<b>B</b>		<b>B</b>	
Urine creatinine, mmol/L	11±1.25	12.4±1.51	1.15±1.56	9.75±1.56	13.2±1.75*t	2.92±0.99	9±1.3	10±1.74	1.02±1.06	7.46±0.8	11.2±2.34	3.78±2.09	0.307 (K)
UUN / Urine creatinine	26±1.69	23.8±1.78	-2.25±2.48	26.1±3.6	18.7±1.79	-6.49±3.62	30.9±1.41	25.3±2.82	-5.65±2.53	26.8±2.6	28.6±2.42	1.81±3.59	0.197 (K)
MNA	13.4±0.27	13.5±0.22	0.10±0.23	13.8±0.16	13.4±0.26	-0.38±0.18	12.9±0.65	13.2±0.36	0.33±0.37	13.6±0.24	13.2±0.22	-0.33±0.24	0.231 (A)

BW: body weight; MNA: Mini Nutritional Assessment; (A): ANOVA; (K): Kruskal-Wallis; Δ: change from baseline; t: paired t-test; r: Wilcoxon signed-rank test; UUN: urinary urea nitrogen.

<sup>†</sup>Values are means±SEMs. N=8-10 per group. The results revealed significant between-group differences in whole grains and roots ( $p=0.020$ ) and urinary urea nitrogen ( $p=0.03$ ) at the baseline. No other significant between-group differences were identified at the baseline (ANOVA or Kruskal-Wallis test for nonnormally distributed data). Different capital letters in boldface within a row identify intervention groups significantly different from one another,  $p\leq 0.05$ . Within-group treatment effects was analysed based on the paired t-test or Wilcoxon signed-rank test (for nonnormally distributed data). Significance is shown by \* $p\leq 0.05$ , \*\* $p\leq 0.01$ , \*\*\* $p\leq 0.001$ .

<sup>‡</sup>Analysis of overall between-group treatment effects for each Δ derived from ANOVA or Kruskal-Wallis test for nonnormally distributed data (significant results in boldface). Different capital letters in boldface within a row identify intervention groups significantly different from one another,  $p\leq 0.05$ .

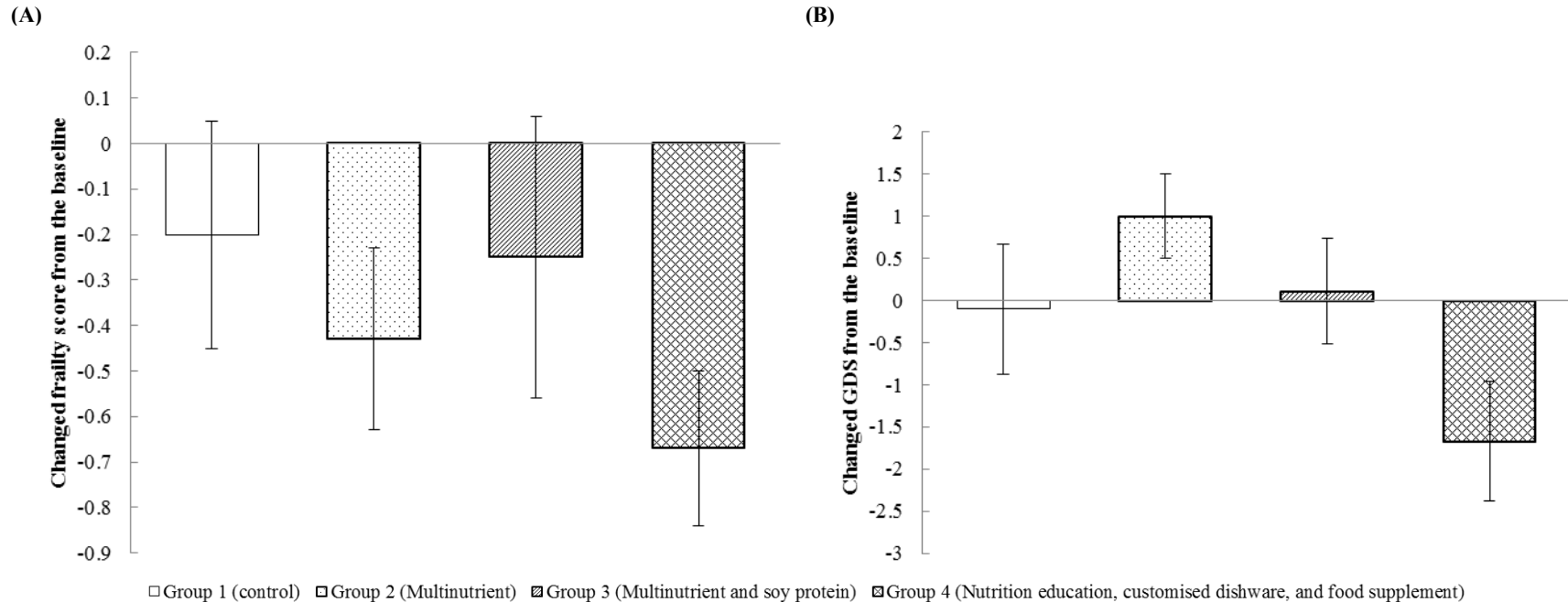
**Table 4.** Frailty and depression assessment in participants at the prefrail and frail stage at the baseline and 3 months post-intervention<sup>†</sup>

	Control			Multinutrient			Multinutrient and soy protein			Nutrition education, customised dishware and food supplement			<i>p</i> value <sup>‡</sup>
	Baseline	Post	Δ	Baseline	Post	Δ	Baseline	Post	Δ	Baseline	Post	Δ	
Weight, kg	60.9±2.97	61.8±2.78	0.88±0.88	58.2±2.79	57.5±2.79	-0.7±0.35	64.7±3.01	64.6±2.86	-0.11±0.57	69.9±4.10	69.2±3.92	-0.66±0.58	0.371 (K)
BMI, kg/m <sup>2</sup>	24.6±1.1	25.2±1.18	0.59±0.48	25.5±0.86	25.3±0.9	-0.27±0.16	25.5±1.14	25.5±1.05	0.01±0.24	28.4±1.19	28.4±1.22	-0.04±0.27	0.408 (K)
Right grip strength, kg	18.3±3.29	19.2±2.42	-0.96±1.11	17.3±2.2	20±3.16	2.67±1.80	19±2.03	20.1±2.10	1.07±0.86	22.2±2.12	23.5±2.38	1.13±1.29	0.271 (A)
Left grip strength, kg	19.6±2.57	19.2±2.31	-0.34±0.91	15.6±2.41	18.3±2.73* <sup>t</sup>	2.7±0.91	16.5±1.94	17.7±1.77	1.15±1.42	21.1±2.18	23.2±2.53	2.01±1.32	0.275 (A)
Gait speed, sec/10m	12.8±2.41	13.3±3.11	0.54±1	10.3±1.32	11.2±2.13	0.88±1.24	13.6±2.74	14.7±2.79	1.12±1.02	11±0.98	10.8±1.05	-0.25±0.65	0.828 (K)
IPAQ-SF, Kcal/week	1423±381	1572±327	149±170	2122±608	1810±365	-312±372	1206±331	1853±524* <sup>r</sup>	647±214	1817±448	1942±491	125±242	0.091 (A)

IPAQ-SF: International Physical Activity Questionnaire - Short Form; (A): ANOVA; (K): Kruskal-Wallis; t: paired t-test; r: Wilcoxon signed-rank test; Δ: change from baseline.

<sup>†</sup>Values are means±SEMs. N=8-10 per group. No significant between-group differences were identified at the baseline (ANOVA or Kruskal-Wallis test for nonnormally distributed data). Within-group treatment effects was analysed based on the paired t-test or Wilcoxon signed-rank test (for nonnormally distributed data). Significance is shown by \**p*≤0.05.

<sup>‡</sup>Analysis of overall between-group treatment effects for each Δ derived from ANOVA or Kruskal-Wallis test for nonnormally distributed data.



**Figure 2.** Effect of dietary treatment on frailty score and GDS. Data are mean (±SEMs) changes in total frailty score and GDS between the baseline and 3 months after nutritional interventions in Group 1 (control), Group 2 (multinutrient group), Group 3 (multinutrient and soy protein), and Group 4 (the nutrition education, customised dishware, and food supplements group). (A) The Wilcoxon signed-rank test (*p*=0.031) showed a significant reduction in total frailty score within Group 4 after 3 months. (B) The Kruskal-Wallis test (*p*=0.045) detected a significant difference in the overall mean change in GDS-SF score across all four groups after 3 months. The post hoc test, the Dunn's test, showed the existence of a between Group 2 and Group 4, but not between the other groups. Group 4 had the greatest decrease in GDS-SF score compared with other three groups, and this downward trend, tested by the Wilcoxon signed-rank test (*p*=0.063), was of borderline significance.

groups after 3 months ( $p=0.045$ ; Figure 2). The post hoc test, the Dunn's test, showed a difference between Group 2 and Group 4, but not between the other groups. Group 4 had the greatest decrease in GDS-SF score compared with the other three groups, and this downward trend ( $p=0.063$ ) was of borderline significance.

## DISCUSSION

The world population is rapidly aging. Dietary management by optimising the distribution of the six major food groups and providing sufficient nutrients may have beneficial effects on not only frailty prevention and reversal but also on total well-being. According to our review of the literature, the current study reveals for the first time that two sessions of individualised nutrition consultation (at V1 and at V2) assisted by customised dishware (comprising a four-compartment divided food plate for protein foods and vegetables, a bowl for rice and fruit, a mug for milk, and a spoon for nuts) and food supplements (mixed nuts and milk powder) could significantly increase the intake of vegetables, dairy, and nuts, in addition to increasing the concentration of urinary urea nitrogen at V3 in elderly people at prefrail or frail stages. This dietary approach reduced the participants' total frailty score and reduced the overall GDS-SF score. Our results revealed that our interventions, combining consultation sessions, customised dishware, and food supplements, acted collectively to improve the outcomes under consideration.

The success of our nutrition education may be attributed to the well-designed dishware that provides clear guidelines for the amount of food to be consumed. As long as the designated space on the plate is filled with the appropriate food types, the elderly user can consume sufficient protein-rich foods and vegetables. The bowl for whole grains and fruits, the mug for milk, and the spoon for nuts were also easy to comprehend and use among the study participants. The significant increase in the concentration of urinary urea nitrogen reflects an increased consumption of total protein from protein-rich foods such as beans, fish, meats, eggs, and milk.<sup>40,41</sup> Overall, the improvement of multiple dietary components included the increased consumption of vegetables, dairy, and nuts and an adequate amount of fruit intake, along with an increased concentration of urinary urea nitrogen.

The treatment group that only received the multinutrients with or without isolated soy protein (Group 2 and Group 3) did not have comparable results with respect to urinary urea nitrogen when compared with Group 4. In Group 2, some of the participants indicated that the vitamin powder was not palatable, although the self-reported daily log showed the compliance measure was satisfied. Mean protein intake and urinary nitrogen did not increase in Group 3. With the acceptable compliance of 86.3% and dietary recall data on protein-rich foods with and without the protein supplement, it is likely that the participants consumed the soy protein powder, but ate less-than-usual protein-rich foods.

Few nutritional intervention studies have examined the effects of nutritional education on frailty in elderly people. Rydwick, Frandin, and Akner reported that, in a 3-month intervention program, 22 community-dwelling, frail elderly participants under the personal supervision of a die-

titian improved their gait speed and increased their habitual physical activity levels, whereas group sessions covering topics such as nutritional needs for elderly people, meal frequency, and cooking methods did not.<sup>42</sup> However, nutritional status before and/or after the intervention was not described in the study, in contrast to our study and another by Nykänen and her colleagues.<sup>43</sup> Nykänen and her colleagues reported that after 1 year of individual dietary counselling, 77 community-dwelling elderly people tended to have a better frailty status and MNA, compared with the control group ( $n=82$ ). Their individual dietary counselling involved two face-to-face meetings with a dietitian and telephone calls every two months during the intervention period. They aimed to improve the diet, in line with the Finnish recommendations, by increasing the frequency of meals and/or adding energy and protein to those meals. This study and ours suggest that frailty reversal may be achieved through dietary pattern modification and because of the synergistic effects of multiple dietary components.

Additional intervention studies have been conducted to examine the effects of dietary supplementation on frailty in older adults.<sup>5,20,22,23,28,29</sup> These studies have tested a variety of dietary proteins or amino acids (e.g. whole protein, essential amino acids, leucine, and  $\beta$ -hydroxyl  $\beta$ -methyl butyrate), a higher caloric intake, and vitamin D supplements. Some studies have shown the benefits of protein supplements;<sup>20,22,23,27,30</sup> however, these beneficial effects tended to be found in individuals who were malnourished, severely frail, and had participated in interventions lasting longer than 3 months.<sup>4</sup> Our participants were mostly at the prefrail stage. In line with our result for Group 3, several studies with only protein supplementation have failed to result in a positive outcome.<sup>6,26,30,44-46</sup> This may suggest that the synergy of various nutrients and food groups in a balanced fashion may improve overall nutrition status and outperform individual nutrients.

Group 4 (the nutrition education group) exhibited a significant decrease in GDS-SF score, a validated measure for detecting depression.<sup>47</sup> Depression and frailty are mutually associated,<sup>48</sup> and may share underlying mechanisms such as chronic inflammation.<sup>49</sup> The increased intake of vegetables in the dietary consultation group may be beneficial because of their anti-oxidative and anti-inflammatory properties.<sup>4,50</sup> In addition, a nutritious diet that meets RDA levels could eliminate marginal deficiencies of multiple nutrients that have been associated with depression.<sup>51</sup> In one-carbon metabolism, deficiencies in multiple B-vitamins and iron decrease S-adenosylmethionine production and lead to homocysteine accumulation,<sup>52</sup> which may contribute to the development of depression symptoms.<sup>51</sup> Therefore, the potential for improved depressive levels may be derived from the increased consumption of vegetables (the main source of folate) as well as dairy and other protein-rich foods, which are rich in vitamin B-6.

This study has several limitations. Firstly, the small sample size may have made the experimental groups incomparable for a few traits and thus reduced our ability to demonstrate more significant findings. Secondly, the trial was conducted in individuals who were not at risk of malnutrition, as determined by MNA-SF tool at the base-



line; thus, the chance to observe improvement after intervention was less likely.<sup>4,5</sup> Thirdly, compliance was dependent on the self-reported daily log, which may or may not have been reliable. Finally, although enquiring on usual dietary patterns is a common practice in clinical setting, it tends to omit certain aspects of the typical diet. However, many of our participants were elderly residents living in rural areas who were not highly educated and, as such, unable to complete the dietary records or appropriately respond to a FFQ. Therefore, we found that dietary recall was the most appropriate approach for these elderly rural residents.

### Conclusion

Our results suggest that elderly participants at the frail stage (11%) or prefrail stage (89%) could change their dietary intake towards their nutritional needs with the help of two sessions of individualised nutrition consultation (at V1 and at V2) aided by customised dishware and supplements of mixed nuts and skimmed milk powder. We observed an increased intake of vegetables, dairy, and nuts and an adequate amount of fruits, along with an increased concentration of urinary urea nitrogen at the 3-month follow-up. The synergic effects of these multiple dietary components showed their potential to improve frailty status and, potentially, psychological well-being in elderly people.

### ACKNOWLEDGEMENTS

We would like to thank all volunteers who took part in the study and all of those who assisted with the study in Miao-Li Hospital. We thank the Institute of Biomedical Sciences, Academia Sinica for administrative assistance.

### AUTHOR DISCLOSURES

The authors have declared that no competing interests exist. This study has been funded by Sustainability Project Grant, Academia Sinica (AS-103-SS-A04), Taipei, Taiwan.

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**Supplementary table 1.** Taiwan's Daily Food Guide<sup>†</sup>

Level of physical activity	Low		Moderate low		Moderate	
Description	Static activity. Sleep, lying down, and sitting. Ex: reading or watching TV while sitting, etc.		Standing activity. Ex: Talking or cooking while standing.		Normal activity. Ex: Standing in the bus or MRT, doing housekeeping, shopping, etc.	
Gender	Men	Women	Men	Women	Men	Women
Energy (Kcal)	1700	1400	1950	1600	2250	1800
Whole grains and roots (bowl) <sup>‡</sup>	3	2	3	2.5	3.5	3
Beans, fish, meats, and eggs (serving) <sup>§</sup>	4	4	6	4	6	5
Vegetables (serving) <sup>¶</sup>	3	3	3	3	4	3
Fruits (serving) <sup>††</sup>	2	2	3	2	3.5	2
Dairy (serving) <sup>**</sup>	1.5	1.5	1.5	1.5	1.5	1.5
Oils and nuts (serving) <sup>§§</sup>	5	4	5	5	6	5
Cooking oils (serving)	4	3	4	4	5	4
Nuts and seeds (serving)	1	1	1	1	1	1

<sup>†</sup>The daily food guide was published in 2011 by Health Promotion Administration, Ministry of Health and Welfare, Taiwan (<https://goo.gl/pbImy4>).

<sup>‡</sup>A bowl of whole grains and roots is about one general household bowl of cooked brown rice (200g), toast (100g), or potatoes (360g), which provides 60 g of carbohydrate, 8 g of protein, 280 Kcal of energy.

<sup>§</sup>A serving of beans, fish, meats, and eggs is about 80 g of raw hard tofu, 35 g of raw fish, 30 g of raw skinless chicken breast, or an egg, which provides 7 g of protein, 5 g of fat, 75 Kcal of energy.

<sup>¶</sup>A serving of vegetables is about 100 g of edible raw vegetables, which provides 1 g of protein, 5 g of carbohydrate, 25 Kcal of energy.

<sup>††</sup>A serving of fruit is about 110 g of edible apple, 100 g of edible grapes, or 55 g of edible banana, which provides 15 g of carbohydrate, 60 Kcal of energy.

<sup>\*\*</sup>A serving of dairy is 240 cc. of milk, 25 g of milk powder, or 35 g of cheese, which provides 8 g of protein, 4 g of fat, 12 g of carbohydrate, 120 Kcal of energy.

<sup>§§</sup>A serving of oils and nuts provides 5 g of fat, 45 Kcal of energy. A serving of cooking oil is 5 cc. A serving of nuts and seeds is 7~8 g of cashews, pumpkin seeds, walnuts, macadamia, pine nuts, or almonds.

**Supplementary table 2.** Ingredients of multivitamins & mineral powder provided for Group 2 (multinutrient group) and Group 3 (multinutrient and soy protein group)

Ingredients	Quantity (mg/day)
Vitamin A	0.60
Vitamin B-1	1.20
Vitamin B-2	1.30
Vitamin B-6	1.60
Vitamin B-12	0.03
Vitamin C	100.00
Vitamin D	0.01
Vitamin E	12.06
Vitamin K	0.12
Biotin	0.03
Folic acid	0.60
Niacin	16.00
Pantothenic acid	10.00
Calcium	202.00
Phosphorus	125.05
Chloride	79.97
Chromium	0.45
Copper	2.00
Iodine	0.07
Iron	10.00
Magnesium	49.98
Manganese	5.01
Selenium	0.03
Zinc	15.00
Molybdenum	0.03
Total	1266.28

**Supplementary table 3.** Components of isolated soy bean powder provided for participants in Group 3 (multinutrient and soy protein group)

	Per 100g isolated soy protein powder	Per daily portion (16 g/day)
Energy (Kcal)	380	60.8
% Protein (N×6.25 mfb), min.	90	14.4
% Moisture, max.	6	0.86
% Fat (acid hydrolysis), max.	4	0.64
% Ash, max.	5	0.80
Typical amino acid	g/100 g protein	g/14.4 g protein
Aspartic Acid	11.5	1.66
Threonine	3.7	0.53
Serine	5.5	0.79
Glutamic Acid	19.2	2.76
Proline	5.2	0.75
Glycine	4.1	0.59
Alanine	4.3	0.62
Cystine	1.2	0.17
Valine	4.7	0.68
Methionine	1.4	0.20
Isoleucine	4.7	0.68
Leucine	8.0	1.15
Tyrosine	3.8	0.55
Phenylalanine	5.2	0.75
Histidine	2.5	0.36
Lysine	6.3	0.91
Arginine	7.5	1.08
Tryptophan	1.1	0.16
Typical minerals	mg/100 g protein	mg/14.4 g protein
Sodium	900-1300	129.6-187.2
Potassium	75-300	10.8-43.2
Calcium	50-150	7.2-21.6
Phosphorus	700-1000	100.8-144
Iron	8-13	1.2-1.9
Magnesium	25-100	3.6-14.4

**Supplementary table 4.** Nutrition facts of food supplements (mixed nuts and milk powder) provided for participants in Group 4 (nutrition education, customised dishware, and food supplement group)

	Per 100 g milk powder <sup>†</sup>	Per 100 g mixed nuts <sup>‡</sup>	Per day (25 g milk powder and 10g mixed nuts)
Energy (Kcal)	44	607	71.7
Protein (g)	4.5	21.9	3.3
Fat (g)	0	55.8	5.6
Carbohydrate (g)	4.2	16.5	3.2
Sodium (mg)	47	9.6	12.7

<sup>†</sup> Milk powder was skimmed with calcium added.

<sup>‡</sup> Mixed nuts included cashews, pumpkin seeds, walnuts, macadamia, pine nuts, and almonds.



**Supplementary figure 1.** Examples of customised dishware provided for participants in Group 4 (nutrition education, customised dishware, and food supplement group). In order to help the participants consume a nutritious diet with the appropriate distribution of the six food groups and achieve the RDA level of nutrients, participants were provided with a set of customised dishware to follow the recommendations in Taiwan's Daily Food Guide. The measuring dishware designed by the Taiwanese Association of Diabetes Educators was provided to help participants to quantify their food intakes. Examples of measuring dishware are showing in A-D:

- A. A four-compartment divided plate for protein-rich foods (upper three spaces) and vegetables (lower space). Each one of the upper three spaces (50 cc) equals one serving of beans, fish, meats, and eggs, and half lower space (115 cc) equals one serving of vegetables.
- B. A bowl for whole grains and roots and fruits. One serving of whole grains and roots (70 Kcal) equals a quarter bowls (60 cc) of cooked rice, or half bowl (120 cc) of noodle; one serving of fruit (60 Kcal) equals one bowl of chopped pineapple or cherry tomatoes.
- C. A spoon for nuts and oils. One spoon (15 cc) equals three servings of cooking oil or one serving of nuts and seeds.
- D. A mug for dairy. One mug (240 cc) equals one serving of dairy.

More details of one serving of each food group can be found in Supplemental material 1 or <https://goo.gl/pblmy4>.