Original Article

# The benefits of a novel chicken-based oral nutritional supplement for older adults: A double-blind randomized controlled trial

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**Background and Objectives:** A considerable proportion of older adults are lactose intolerant. The aim of this study was to investigate the clinical safety, efficacy, and tolerability of a chicken-based oral nutritional supplement (ONS). **Methods and Study Design:** Double-blind randomized controlled trial. Subjects in the intervention group received chicken-based ONS, and those in the control group received a similarly flavored oral fluid placebo. All subjects were followed-up every two months for a total of 6 months. **Results:** Thirty-eight older adults aged ≥70 years were recruited. The mean age and BMI were 81.5±5.6 years and 19.6±2.5 kg/m2. At the end of this trial, there was no statistically significant change in sarcopenia-related variables in the intervention group. However, the higher-level physical activity (PA) group within the intervention group had a significantly improved usual gait speed (UGS) compared to the lower-level PA group (p=0.04). The adjusted mean differences in UGS between the high and low level PA groups in the intervention and placebo groups were 0.149 m/sec and 0.083 m/sec, respectively. Significant difference was observed for changes in two bone markers between the intervention and placebo groups. **Conclusions:** The chicken-based ONS evaluated in this study was well-tolerated. No improvement of sarcopenia-related components was shown by the study ONS. Up to nearly an 80% increase in adjusted mean difference in UGS between the high and low level PA groups was observed in the nutritional intervention group compared to the zero-protein calorie placebo group. Significant improvement in age-related bone resorption was the earliest advantage of taking our ONS.

**Key Words: chicken-based, oral nutritional supplement, older adults, gait speed, bone marker**

## INTRODUCTION

Undernutrition is one of the most common and most neglected chronic conditions among older people, especially among those who are institutionalized.[1-2] Undernutrition poses serious threats to older people, including immunocompromised status leading to infection,[3] and poor musculoskeletal function leading to fall and fracture.[4] Alternatively, many chronic diseases cause undernutrition. Among those with chronic obstructive pulmonary disease, the prevalence of malnutrition and sarcopenia was 19.8% and 24.0% respectively, and the prevalence was found to increase with disease severity.[5] Nearly half of mild Alzheimer's dementia had appetite change, and 81.4% of Alzheimer's patients showed some eating and/or swallowing disturbances.[6] Incident sarcopenia during hospital stay is associated with nutritional status and the number of days of bed rest. Body mass index was found to predict incident sarcopenia with an adjusted odds ratio of 0.92 (95% confidence interval: 0.86-0.98).[7]

In routine clinical practice, oral nutritional supplements (ONS) are widely used to replenish nutritional deficiency, particularly among acutely ill and older patients.[8] The use of standard ONS in community also demonstrated cost effectiveness relative to clinically relevant outcomes.[9] However, the majority of ONS are milk-based, and approximately 75% of the world's population loses the ability to digest lactose, which is the main carbohydrate in milk, during their lifetime.[10] Thus, there is a need to develop new food alternatives that have functional health benefits that are specifically produced to meet the food-related demands of older adults.[11] In 2007, researchers at our center developed the first ever chicken-based formula for infants who are allergic to cow's milk. Study showed

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Manuscript received 11 August 2020. Initial review completed 16 August 2020. Revision accepted 09 September 2020.
doi: 10.6133/apjcn.202012_29(4).0009

that a significantly greater number of infants could tolerate chicken-based formula than soy formula with an OR of 8.0 (95% CI: 1.5-46.0).[12] Later study demonstrated that the growth parameters of infants fed with chicken-based formula were not different from those of normal infants.[13] This evidence demonstrates the safety and efficacy of our chicken-based formula, which is worth further investigation in older adults. Accordingly, the aim of this study was to investigate the efficacy, clinical safety, and tolerability of a chicken-based ONS designed to meet the needs of undernourished older adults who may have lactose intolerance.

## METHODS

### *Design and participants*

After receiving approval from the Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University to conduct this double-blind randomized controlled trial (COA no.Si747/2016), we registered the protocol with Thai Clinical Trials Registry (reg. no. TCTR 20170513001). The inclusion criteria were age 70 years or more, no severe cognitive impairment, body mass index (BMI) less than 23 kg/m$^2$, estimated glomerular filtration rate (eGFR) 60 mL/min or higher, ability to stand upright, and not having a cardiac pacemaker since bioelectrical impedance analysis (BIA) was used in all subjects to assess body composition. The exclusion criteria were hyperuricemia, gout, already on ONS or nasogastric tube feeding, taking antiresorptive drugs, and/or taking any drug, hormone, or herb that interferes with muscle mass, muscle strength, and/or bone metabolism.

Thirty-eight participants were sequentially recruited from the geriatric clinic of the Department of Preventive and Social Medicine, Siriraj Hospital, Bangkok, Thailand during April 2017 to December 2018. After obtaining written informed consent, study patients were randomized into either the intervention group or the placebo group in a double-blind method by drawing lots. All subjects and investigators were blind to the type of intervention throughout the study since the supplied drinks were all encoded from the production laboratory. Twenty-two and sixteen subjects were allocated to the intervention and placebo group, respectively. The intervention group received chicken-based ONS, and the placebo group received a similarly flavored drinking water for 6 months. All participants were scheduled for a follow-up visit every 2 months, with the last visit at the 6-month time point. Study subjects were instructed to maintain their normal level of physical activity, their normal diet, and that any other type of supplementation was strictly forbidden. At each follow-up visit, patients were checked for compliance, tolerability and adverse events, and their supply of study nutrition or placebo was replenished. During the trial, two participants in the intervention group withdrew from the study - one due to gastrointestinal complaint, and the other had to take care of a sick spouse. One case in the placebo group withdrew due to accidental fall with resulting hip fracture. Overall, 20 subjects in the intervention group and 15 subjects in the placebo group completed the trial (Figure 1).

### *Material*

Siriraj formula chicken-based ONS was originally developed by the Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University as an alternative food for infants who could not breast feed and who were allergic to cow's milk.[12] The Siriraj formula chicken-based ONS is produced, as follows: chicken breast meat is cleaned and homogenized to reduce the size of the particles to at least 10 μm. Vegetable oil and maltodextrins

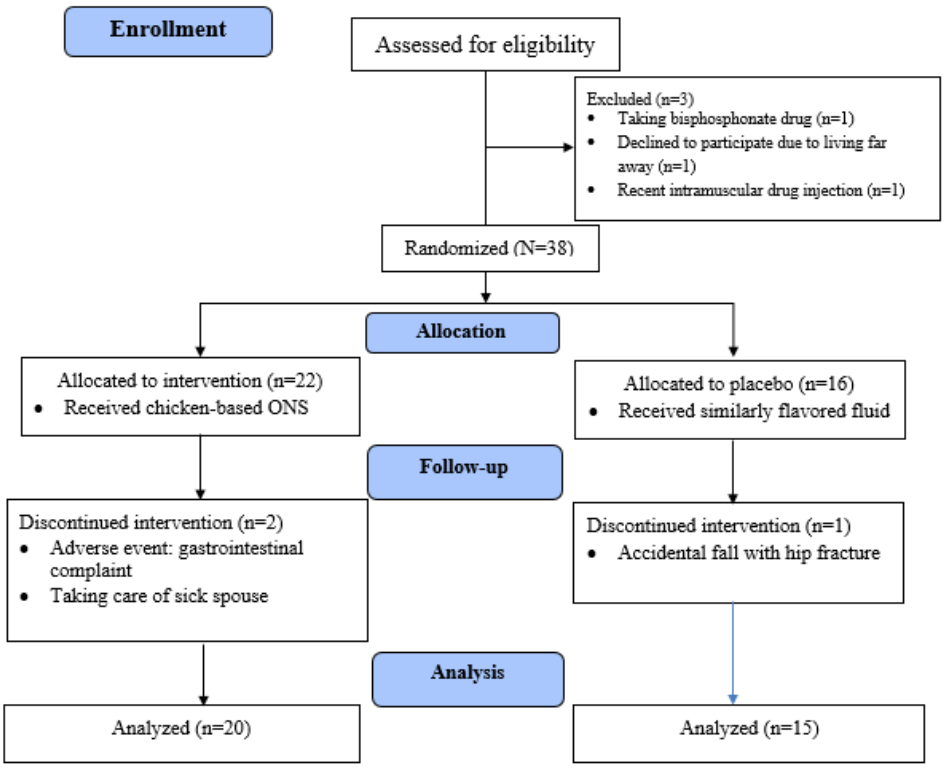


**Figure 1.** Subject recruitment.

are then added and mixed with the chicken particles. After the macronutrients are well mixed, all essential vitamins and minerals are added into the mixture with final blending of the ingredients. The final composition of the formula designed for older adults that was evaluated in this study are shown in Table 1. The ONS is packaged in a 150 mL retort pouch, and the recommended frequency is one time per day.

***Procedures***

After history taking, clinical examination, mental state examination, and chart review, current physical activity (PA) was assessed using the Physical Activity Questionnaire for Elderly Japanese (PAQ-EJ).[14] The 50th percentile of the population was 22.2 metabolic equivalent (MET)-h/week. This cut-off point was used to classify level of PA as either low level or high level of PA. All participants underwent handgrip strength testing while standing with full elbow extension. A Smedley handgrip dynamometer (Takei 5401; Takei Company Ltd, Tokyo Japan) was used throughout the study. Only the maximum reading out of 2 trials performed by the dominant hand in a maximum-effort isometric contraction was recorded. Quadriceps strength (QS), which indicates maximum isometric knee extension force, was measured by hand-held dynamometer (HHD) (Lafayette Manual Muscle Test System (MMT)® Model 01163; Lafayette Instruments, Indiana, USA). QS was tested two times in each leg (alternating between legs) with a 120s relaxation period between each of the 4 tests. Only the highest peak force (kilogram) was selected for the result. Muscle mass measurement was performed by BIA using a Tanita® model MC780MA (Tanita Corporation, Tokyo, Japan). Complete blood count, biochemical blood tests, including bone markers [namely, isomerized C-terminal telopeptides of type I collagen (beta-CrossLaps) and procollagen type I N propeptide (PINP)], were performed in the morning between 8:00 am and 9:00 am. Usual gait speed (UGS) was measured by walking in a usual way a distance of 6 meters. The recommended diagnostic algorithm from the Asian Working Group for Sarcopenia was employed to diagnose sarcopenia.[15]

***Outcomes***

Efficacy: New sarcopenia diagnosis and changes in the components of sarcopenia (i.e., muscle strength, height-adjusted muscle mass, and UGS), as well as changes in bone markers.

Safety/Tolerability: A reminder telephone call was made a few days before each follow-up appointment date. A thorough safety evaluation was performed at each follow-up visit, including (a) physician or physician assistant evaluation of adverse events via open-ended interview and comprehensive geriatric assessment; (b) vital signs measurement; and, (c) body weight measurement.

Adherence: Evaluation of the research protocol compliance, the amount of supplied drink remaining from the previous 2 months, and attending all scheduled follow-up appointments.

***Statistical analyses***

A sample size of 17 in each group would yield 80% power to detect a difference in means of beta-CrossLaps of 0.25 ng/mL assuming that the standard deviations of both

**Table 1.** Formula composition of the chicken-based formula for older adults evaluated in this study

| Per 100 mL | | Chicken-based formula† | Placebo‡ |
|---|---|---|---|
| Energy | kcal | 100 | 0 |
| Protein | g | 3 | 0 |
| Fat | g | 6 | 0 |
| Carbohydrate | g | 10 | 0 |
| Sodium | mg | 20 | 0 |
| Potassium | mg | 30 | 0 |
| Chloride | mg | 30 | 0 |
| Calcium | mg | 90 | 0 |
| Phosphorus | mg | 46 | 0 |
| Magnesium | mg | 7 | 0 |
| Iron | mg | 1 | 0 |
| Zinc | mg | 1 | 0 |
| Iodine | µg | 20 | 0 |
| Copper | µg | 30 | 0 |
| Vitamin A | µg | 40 | 0 |
| Vitamin B1 | µg | 90 | 0 |
| Vitamin B2 | µg | 90 | 0 |
| Vitamin B6 | µg | 50 | 0 |
| Vitamin B12 | µg | 10 | 0 |
| Vitamin C | mg | 10 | 0 |
| Vitamin D | µg | 0.9 | 0 |
| Vitamin E | mg | 0.4 | 0 |
| Niacin | mg | 1.0 | 0 |
| Folic acid | µg | 10 | 0 |
| Pantothenic acid | µg | 0.4 | 0 |
| Biotin | µg | 1.8 | 0 |

†Additional nutrients added to the chicken-based formula include fish oil 0.5 g, Inulin 0.5g, and fructooligosaccharide 1 g.
‡Placebo was made of drinking water with flavoring agents (chocolate or vanilla).

the intervention group and the placebo group are 0.25 ng/mL with a 0.05 two-sided significance level.[16] Thus, the target overall sample size was 34 cases.

Paired t-tests and unpaired t tests for normal distribution data and Mann-Whitney U tests for non-normal distribution data were used to compare quantitative variables, while chi-square tests were used to compare qualitative variables. Quantitative data are expressed as either mean ± standard deviation (SD) or median (interquartile range), and qualitative data are shown as number and percentage. Analysis of covariance (ANCOVA) was used to compare UGS at the 6-month endpoint between the high and low level PA groups adjusted for UGS at baseline. Statistical significance was set at a *p*-value <0.05. PASW Statistics (SPSS) for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyse.

## RESULTS

### *Enrollment and baseline characteristics*

The mean age and body mass index of participants were 81.5±5.6 years and 19.6±2.5 kg/m$^2$, respectively. Twenty-two cases (57.9%) were female. The prevalence of sarcopenia was 62.9%. There were no significant differences in baseline characteristics between the intervention and placebo groups, including age, gender, mental state examination, BMI, underlying diseases (hypertension, dyslipidemia, cerebrovascular disease), health behavior (smoking, alcohol drinking, level of PA, exercise regularity), sarcopenia, determinants of sarcopenia diagnosis, or bone markers (Table 2).

Since the results of cognitive assessment by Thai Mental State Examination in our subjects were below normal level (<24 points) as shown in Table 1, the nutritional history taken from our subjects would be inaccurate. It is also unknown whether nutritional information provided by family caregivers are reliable.[17] Therefore, all subjects were instructed to simply maintain their normal diet, and that any other type of supplementation was strictly forbidden. Correspondingly, there was no significant difference of nutritional biochemical markers between baseline and at 6-month measurement of both groups (Table 3). These findings would practically reveal that there was no dietary confounding factor during the trial.

### *Efficacy*

Among the various outcomes observed from this 6-month trial, change in bone markers was the earliest observed change. There were improvements in the beta-CrossLaps

**Table 2.** Baseline demographic and clinical characteristics

| Characteristics | Chicken-based ONS (n=20) | Placebo (n=15) | *p* |
|---|---|---|---|
| Age (years), mean±SD | 81.5±5.30 | 81.5±6.11 | 0.99 |
| Body weight (kg), mean±SD | 47.2±7.43 | 46.4±8.59 | 0.77 |
| TMSE, mean±SD | 22.9±4.97 | 21.6±4.52 | 0.51 |
| Female gender, n (%) | 12 (60.0%) | 10 (66.7%) | 0.69 |
| Hypertension, n (%) | 12 (60.0%) | 8 (53.3%) | 0.69 |
| Dyslipidemia, n (%) | 11 (55.0%) | 9 (60.0%) | 0.77 |
| Cerebrovascular disease, n (%) | 2 (10.0%) | 1 (6.7%) | 0.73 |
| Current smoker, n (%) | 0 (0.0%) | 1 (6.7%) | 0.45 |
| Alcohol drinker, n (%) | 5 (25.0%) | 3 (20.0%) | 0.73 |
| High level of physical activity, n (%) | 10 (50.0%) | 8 (53.3%) | 0.85 |
| Regular exercise, n (%) | 14 (70.0%) | 10 (66.7%) | 0.86 |
| Sarcopenia, n (%) | 7 (35.0%) | 8 (53.3%) | 0.28 |
| Physical activity (METs-h/week), median (IQR) | 22.0 (14.3,40.5) | 27.0 (5.70,33.2) | 0.55 |
| Body mass index (kg/ht$^2$), mean±SD | 19.7±2.51 | 19.5±2.59 | 0.83 |
| Handgrip strength (kg), mean±SD | 23.1±6.92 | 18.5±6.92 | 0.06 |
| Quadriceps strength (kg), mean±SD | 15.7±3.78 | 14.2±3.05 | 0.21 |
| Usual gait speed (m/sec), mean±SD | 0.82±0.32 | 0.71±0.29 | 0.30 |
| Height-adjusted muscle mass (kg/ht$^2$), mean±SD | 5.87±0.87 | 5.61±0.77 | 0.35 |
| Body fat mass (kg), mean±SD | 10.4±4.98 | 12.1±4.28 | 0.30 |
| P1NP (ng/mL), mean±SD | 55.1±27.0 | 46.5±14.9 | 0.28 |
| Beta-CrossLaps (ng/mL), mean±SD | 0.61±0.28 | 0.52±0.26 | 0.30 |

SD: standard deviation; TMSE: Thai Mental State Examination; METS: metabolic equivalents; P1NP: procollagen type I N-terminal propeptide; IQR: interquartile range.

**Table 3.** Comparisons of nutritional biochemical markers between baseline and at 6-month measurement within each group by paired t-test

| | Chicken-based ONS | | | Placebo | | |
|---|---|---|---|---|---|---|
| | Baseline mean±SD | 6 months mean±SD | *p* | Baseline mean±SD | 6 months mean±SD | *p* |
| Albumin (g/dL) | 4.27±0.27 | 4.39±0.18 | 0.527 | 4.03±0.25 | 4.00±0.36 | 0.861 |
| Total cholesterol (mg/dL) | 186±15.2 | 185±23.0 | 0.859 | 166±32.1 | 169±28.5 | 0.667 |
| Triglyceride (mg/dL) | 108±46.1 | 104±33.0 | 0.660 | 103±23.7 | 132±40.5 | 0.059 |
| Hemoglobin (g/dL) | 12.4±1.33 | 12.4 ±0.97 | 0.828 | 12.6±1.21 | 12.4±1.58 | 0.427 |
| Total lymphocyte count (x10$^6$/L) | 1732±966 | 1927±942 | 0.111 | 2087±555 | 1823±527 | 0.134 |

and PINP bone markers between the intervention and placebo groups with p-values of 0.036 and 0.024, respectively. Moreover, significant improvement in both bone markers was observed between baseline and 6 months only in the intervention group, with *p*-values of 0.001 and 0.006 for beta-CrossLaps and P1NP, respectively (Table 4). There were no statistically significant changes in handgrip strength, quadriceps strength, height-adjusted appendicular muscle mass, UGS, or sarcopenia between groups.

However, when we categorized all participants into high or low level of baseline PA using the 50th percentile of overall PA, there was significant difference in adjusted UGS at 6 months between the high and low level PA groups within the intervention group ($p$=0.04). The adjusted UGS in the high and low level PA groups was 0.93 and 0.78 m/sec, respectively. This effect was not observed in the placebo group ($p$=0.50). Since the adjusted mean difference ± standard error (SE) in the UGS between the high and low level PA groups in the intervention and placebo groups was 0.149±0.067 and 0.083±0.118 m/s, respectively, up to nearly an 80% increase in the adjusted mean difference in UGS between the high and low level PA groups was shown in the nutritional intervention group compared to the placebo group (Table 5).

***Safety/Tolerability***

All participants included in the analysis attended all scheduled follow-up appointments. Twenty out of twenty-one participants (95.2%) in the intervention group tolerated our ONS satisfactorily. Only one case discontinued ONS due to gastrointestinal complaint (described as 'feeling unwell in my tummy'). This symptom spontaneously resolved after drink discontinuation (described as 'it stopped within few days after I didn't take the supplied drink').

## DISCUSSION

Undernutrition is fairly common among older adults due to physiology of aging and the higher prevalence of age-related chronic diseases.[5-7] Adherence to nutrient-dense foods and a high-quality diet is, therefore, central to physical, mental, and social well-being among the very old.[18] Consistent with that requirement, the objective of this study was to evaluate the clinical safety, efficacy, and tolerability of a novel chicken-based ONS designed to meet the needs of undernourished older adults who may have lactose intolerance. The subjects recruited for this study were in very old age group with a mean age of 81.5 years. The mean BMI (19.6 kg/m$^2$) was near the lower limit of normal nutritional status. Moreover, the prevalence of sarcopenia was quite high (62.9%) compared to

**Table 4.** Comparisons of the clinical effects of chicken-based ONS and placebo within each group (paired t-test) and between chicken-based ONS and placebo groups (unpaired t-test)

| Markers | Chicken-based ONS (n=20) | Placebo (n=15) | $p^{**}$ |
|---|---|---|---|
| Beta-CrossLaps (ng/mL) | | | |
| Baseline | 0.62±0.28 | 0.52±0.26 | 0.30 |
| 6 months | 0.45±0.21 | 0.48±0.24 | 0.69 |
| Difference | 0.16±0.18 | 0.03±0.17 | 0.036 |
| $p^{*}$ | 0.001 | 0.46 | |
| P1NP (ng/mL) | | | |
| Baseline | 55.1±27.0 | 46.5±14.9 | 0.28 |
| 6 months | 44.9±19.3 | 47.5±15.7 | 0.67 |
| Difference | 10.1±14.6 | -1.05±12.7 | 0.024 |
| $p^{*}$ | 0.006 | 0.75 | |
| Height-adjusted muscle mass (kg/ht$^2$) | | | |
| Baseline | 5.87±0.87 | 5.61±0.77 | 0.354 |
| 6 months | 5.95±1.00 | 5.67±1.07 | 0.436 |
| Difference | -0.077±0.28 | -0.06±0.45 | 0.921 |
| $p^{*}$ | 0.241 | 0.587 | |
| Handgrip strength (kg) | | | |
| Baseline | 23.1±6.92 | 18.5±6.92 | 0.060 |
| 6 months | 22.1±7.22 | 18.7±7.30 | 0.173 |
| Difference | 0.96±2.02 | -0.20±2.21 | 0.116 |
| $p^{*}$ | 0.047 | 0.731 | |
| Quadriceps strength (kg) | | | |
| Baseline | 15.7±3.8 | 14.2±3.05 | 0.206 |
| 6 months | 16.0±2.6 | 15.8±3.47 | 0.899 |
| Difference | -0.27±3.39 | -1.67±3.00 | 0.211 |
| $p^{*}$ | 0.730 | 0.049 | |
| Usual gait speed (m/sec) | | | |
| Baseline | 0.82±0.32 | 0.71±0.29 | 0.297 |
| 6 months | 0.85±0.31 | 0.80±0.34 | 0.655 |
| Difference | -0.03±0.16 | -0.09±0.20 | 0.301 |
| $p^{*}$ | 0.379 | 0.084 | |

P1NP: procollagen type I N-terminal propeptide.
*Paired t-test, **Unpaired t-test

**Table 5.** Comparisons of usual gait speed between patients with low level and high level of physical activity.

| Activity level | Mean±SD | | Adj. mean±SE at 6 months | Adj. mean difference±SE | *p* | 95% CI of mean difference |
|---|---|---|---|---|---|---|
| | Baseline | 6 months | | | | |
| Chicken soup | | | | | | |
| Low level of physical activity | 0.70±0.34 | 0.69±0.30 | 0.78±0.05 | 0.149±0.067 | 0.04 | 0.008 to 0.291 |
| High level of physical activity | 0.95±0.27 | 1.02±0.23 | 0.93±0.05 | | | |
| Placebo | | | | | | |
| Low level of physical activity | 0.58±0.26 | 0.65±0.35 | 0.76±0.08 | 0.083±0.118 | 0.50 | -0.174 to 0.340 |
| High level of physical activity | 0.82±0.28 | 0.94±0.28 | 0.84±0.08 | | | |

SD: standard deviation; SE: standard error; CI: confidence interval; Adj.: Adjusted by Analysis of Covariance (ANCOVA).

general data in older adults aged 60-70 years, which ranged from 5% to 13%, and then increasing to 11-50% in people aged 80 or older.[19]

At the end of this 6-month trial, our chicken-based ONS was found to be clinically safe for consumption by older people with only one case of mild, self-improved gastrointestinal complaint. Lactose intolerance is one of the most common forms of food intolerance.[20] Therefore based on the results of this study, chicken-based ONS would be expected to have a higher rate of tolerability than milk-based ONS among older adults.

The original chicken-based ONS for infants from which our formula for older people was modified has been widely and successfully used in Thailand for the last 14 years. To satisfy some specific requirements for older adults, we increased the amount of some essential nutrients that are relevant to the health of older adults, including energy, protein, carbohydrate, and fat (sunflower oil and soybean oil). Decreased appetite, lowered energy intake, and reduced energy expenditure contribute to a 1% to 2% per decade decrease in resting metabolic rate between the ages of 20 and 70.[21] In response, energy per 100 mL of the infant formula was increased from 67 to 100 kcal in the formula for older adults (Table 1). Similarly, the recommended protein intake for older adults is higher than that for adults (i.e., from 0.8 g/kg body weight per day to 1.2 g/kg per day), and this can be achieved by either improving diet or by adding protein supplement. This level of protein intake can help older adults maintain and regain lean body mass and function.[22] Hence, the protein content per 100 mL of the infant formula was increased from 2 to 3 g in the formula for older adults.

The energy and protein in the ONS taken by the intervention group explains the nearly 80% increase in adjusted mean difference in UGS between participants who already had a high level of PA and those who had a low level of PA in the intervention group compared to the placebo group. This finding also supports the critical relationship between engaging in sufficient levels of PA and consuming adequate nutrition to promote optimal musculoskeletal health in older adults.[23-24] Any PA recommendation must take into account the important role that nutrition plays in ensuring that older people can maximize the benefits from the PA in which they engage. A nutritional guideline graphic (Modified MyPyramid for Older Adults) emphasizes the significant role of PA at the base of the pyramid as a basic requirement apart from consuming an adequate and appropriate diet.[25] Although an increase in UGS was observed in both the high and low level PA subgroups in the placebo group during the trial (as shown on Table 5), these increases can be explained by the placebo effect, which is exerted and observed when participants are recruited into any intervention trial. However, there was no significant difference between the two subgroups by ANCOVA ($p$=0.50).

Interestingly, bone marker changes could be observed within the 6-month study period, and change in bone markers was the earliest observed change among all of the measured outcomes, regardless of PA level. As highlighted in the Modified MyPyramid for Older Adults nutritional guideline graphic, vitamin D and calcium are two essential nutrients at the top of the pyramid that need to be supplemented in older adults via fortified foods and/or dietary supplements.[25] Although we did not measure the baseline level of vitamin D or calcium intake, we could see the benefits of these two supplemented nutrients in the increased bone health of study subjects. The effect of vitamin D supplementation reducing age-related bone resorption in older women was also observed in another 6-month trial.[26] Calcium and vitamin D supplementation was also shown to reduce bone resorption in older women in just 6 weeks.[27] This evidence demonstrating the success of supplementation with these vitamins suggests that those who take our ONS formula regularly will probably not have to take more vitamin supplements to meet the daily requirement of each micronutrient.

However, our ONS formula did not demonstrate muscle mass or muscle strength increase. This negative finding well agreed with two 24-week randomized controlled trials in frail older men that showed positive effects of a milk-based protein supplement on physical performance when taken alone, and on lean body mass when taken along with a strength training regimen.[28-29] Since our study did not include an exercise program, our result only showed benefit related to UGS increase, but not for muscle mass. Two additional reasons that may explain our negative outcomes include a possible need to add high-quality protein (i.e., approximately 10 g of essential amino acids) to maximally stimulate skeletal muscle protein synthesis, and the need for a longer-term trial to observe significant change in muscle mass.[30]

***Strengths and limitations***

This is the first study to investigate the clinical safety, tolerability, and efficacy of the first of its kind chicken-

based ONS using a double-blind randomized controlled design. The baseline characteristics of both groups were indifferent. Since this is a pioneer work, the small number of participants and the rather short 6-month trial period are the limitations that need to be addressed in future study. A special version of chicken-based ONS for sarcopenia prevention and treatment could be another novel ONS that would require the addition of branched-chain essential amino acids. Additionally, since the placebo is a zero-protein calorie drink, our ONS has not been proved to be superior to other kinds of ONS.

In summary, our chicken-based ONS for older adults was well-tolerated with only one case of minor gastrointestinal complaints. Its preliminary main benefit on musculoskeletal function was an 80% increase in the adjusted mean difference in usual gait speed among those who were already engaged in a high level of PA in daily life compared to placebo. In addition, significantly decreased bone resorption was identified as the earliest advantage of taking our chicken-based ONS for older adults.

**ACKNOWLEDGEMENTS**

The authors gratefully acknowledge the patients that agreed to participate in this study.

**AUTHOR DISCLOSURES**

All authors declare no personal or professional conflicts of interest relating to any aspect of this study. This study was partially funded by a grant from Prof. Emeritus Pairoj Oonsombat, MD, who set up the research funding in Department of Preventive and Social Medicine.

**REFERENCES**

1. Volkert D. Malnutrition in older adults - urgent need for action: a plea for improving the nutritional situation of older adults. Gerontology. 2013;59:328-33. doi: 10.1159/000346142.
2. Kerstetter JE, Holthausen BA, Fitz PA. Malnutrition in the institutionalized older adult. J Am Diet Assoc. 1992;92:1109-16.
3. Maggini S, Pierre A, Calder PC. Immune function and micronutrient requirements change over the life course. Nutrients. 2018;10. doi: 10.3390/nu10101531.
4. Esquivel MK. Nutritional assessment and intervention to prevent and treat malnutrition for fall risk reduction in elderly populations. Am J Lifestyle Med. 2018;12:107-12. doi: 10.1177/1559827617742847.
5. de Blasio F, Di Gregorio A, de Blasio F, Bianco A, Bellofiore B, Scalfi L. Malnutrition and sarcopenia assessment in patients with chronic obstructive pulmonary disease according to international diagnostic criteria, and evaluation of raw BIA variables. Respir Med. 2018;134:1-5. doi: 10.1016/j.rmed.2017.11.006.
6. Kai K, Hashimoto M, Amano K, Tanaka H, Fukuhara R, Ikeda M. Relationship between eating disturbance and dementia severity in patients with Alzheimer's disease. PLoS One. 2015;10:e0133666. doi: 10.1371/journal.pone.0133666.
7. Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A et al. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. J Cachexia Sarcopenia Muscle. 2017;8:907-14. doi: 10.1002/jcsm.12224.
8. Stratton RJ, Elia M. A review of reviews: A new look at the evidence for oral nutritional supplements in clinical practice. Clinical Nutrition Supplements. 2007;2:5-23. doi:10.1016/j.clnu.2007.04.004.
9. Elia M, Normand C, Laviano A, Norman K. A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in community and care home settings. Clin Nutr. 2016;35:125-37. doi: 10.1016/j.clnu.2015.07.012.
10. Deng Y, Misselwitz B, Dai N, Fox M. Lactose intolerance in adults: biological mechanism and dietary management. Nutrients. 2015;7:8020-35. doi: 10.3390/nu7095380.
11. Baugreet S, Hamill RM, Kerry JP, McCarthy SN. Mitigating nutrition and health deficiencies in older adults: A role for food innovation? J Food Sci. 2017;82:848-55. doi: 10.1111/1750-3841.13674.
12. Jirapinyo P, Densupsoontorn N, Wongarn R, Thamonsiri N. Comparisons of a chicken-based formula with soy-based formula in infants with cow milk allergy. Asia Pac J Clin Nutr. 2007;16:711-5. doi: 10.6133/apjcn.2007.16.4.18
13. Kangwanpornsiri C, Jirapinyo P, Densupsoontorn N, Poungkaew J, Wongarn R, Thammonsiri N, Jatutipsompol C. Growth of infants with cow's milk allergy fed chicken-based formula. J Med Assoc Thai. 2013;96:20-5.
14. Yasunaga A, Park H, Watanabe E, Togo F, Park S, Shephard RJ, Aoyagi Y. Development and evaluation of the physical activity questionnaire for elderly Japanese: the Nakanojo study. J Aging Phys Act. 2007;15:398-411. doi: 10.1123/japa.15.4.398.
15. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014;15:95-101. doi: 10.1016/j.jamda.2013.11.025.
16. Bunyaratavej N, Kitimanon N, Boonthitikul S. Study of the level of biochemical bone markers: NMID osteocalcin and bone resorptive marker (beta CTx) in Thai women. J Med Assoc Thai. 2001;84 Suppl 2:S560-5.
17. Keller U. Nutritional laboratory markers in malnutrition. J Clin Med. 2019;8. doi:10.3390/jcm8060775.
18. Granic A, Mendonça N, Hill TR, Jagger C, Stevenson EJ, Mathers JC, Sayer AA. Nutrition in the very old. Nutrients. 2018;10. doi: 10.3390/nu10030269.
19. von Haehling S, Anker SD. Cachexia as a major underestimated and unmet medical need: facts and numbers. J Cachexia Sarcopenia Muscle. 2010;1:1-5. doi: 10.1007/s13539-010-0002-6.
20. Di Costanzo M, Berni Canani R. Lactose intolerance: common misunderstandings. Ann Nutr Metab. 2018;73(Suppl 4):30-7. doi: 10.1159/000493669.
21. Bernstein M, Munoz N. Position of the Academy of Nutrition and Dietetics: food and nutrition for older adults: promoting health and wellness. J Acad Nutr Diet. 2012;112:1255-77. doi: 10.1016/j.jand.2012.06.015.
22. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. 2013;14:542-59. doi: 10.1016/j.jamda.2013.05.021.
23. Shad BJ, Wallis G, van Loon LJ, Thompson JL. Exercise prescription for the older population: The interactions between physical activity, sedentary time, and adequate nutrition in maintaining musculoskeletal health. Maturitas. 2016;93:78-82. doi: 10.1016/j.maturitas.2016.05.016.
24. Sjöblom S, Sirola J, Rikkonen T, Erkkilä AT, Kröger H, Qazi SL, Isanejad M. Interaction of recommended levels of physical activity and protein intake is associated with greater physical function and lower fat mass in older women: Kuopio Osteoporosis Risk Factor- (OSTPRE) and Fracture-

Prevention Study. Br J Nutr. 2020;123:826-39. doi: 10.1017/s0007114520000045.
25. Lichtenstein AH, Rasmussen H, Yu WW, Epstein SR, Russell RM. Modified MyPyramid for older adults. J Nutr. 2008;138:5-11. doi: 10.1093/jn/138.1.5.
26. von Hurst PR, Stonehouse W, Kruger MC, Coad J. Vitamin D supplementation suppresses age-induced bone turnover in older women who are vitamin D deficient. J Steroid Biochem Mol Biol. 2010;121:293-6. doi: 10.1016/j.jsbmb.2010.03.054.
27. Prestwood KM, Pannullo AM, Kenny AM, Pilbeam CC, Raisz LG. The effect of a short course of calcium and vitamin D on bone turnover in older women. Osteoporos Int. 1996;6:314-9. doi: 10.1007/bf01623391.
28. Tieland M, van de Rest O, Dirks ML, van der Zwaluw N, Mensink M, van Loon LJ, de Groot LC. Protein supplementation improves physical performance in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc. 2012;13:720-6. doi: 10.1016/j.jamda.2012.07.005.
29. Tieland M, Dirks ML, van der Zwaluw N, Verdijk LB, van de Rest O, de Groot LC, van Loon LJ. Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc. 2012;13:713-9. doi: 10.1016/j.jamda.2012.05.020.
30. Paddon-Jones D, Rasmussen BB. Dietary protein recommendations and the prevention of sarcopenia. Curr Opin Clin Nutr Metab Care. 2009;12:86-90. doi: 10.1097/MCO.0b013e32831cef8b.