ORIGINAL ARTICLE

Journal of Cachexia, Sarcopenia and Muscle 2020; **11**: 26–37
Published online 29 January 2020 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.12504

Comprehensive geriatric intervention in community-dwelling older adults: a cluster-randomized controlled trial

Yuya Watanabe[1,2,3,4]*, Yosuke Yamada[2,4], Tsukasa Yoshida[2,4,5], Keiichi Yokoyama[6,7], Motoko Miyake[3], Emi Yamagata[8], Minoru Yamada[9], Yasuko Yoshinaka[6,7], Misaka Kimura[2,3]* & for Kyoto-Kameoka Study Group

[1]*Faculty of Health and Sports Science, Doshisha University, Kyoto, Japan,* [2]*Laboratory of Applied Health Sciences, Kyoto Prefectural University of Medicine, Kyoto, Japan,* [3]*Department of Health and Sports Sciences, Kyoto Gakuen University, Kameoka, Japan,* [4]*Section of Healthy Longevity Research, National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health and Nutrition, Tokyo, Japan,* [5]*Senior Citizen's Welfare Section, Kameoka City Government, Kameoka, Japan,* [6]*Non-profit Organization Genki-up AGE Project, Kameoka, Japan,* [7]*Department of Business Administration, Kyoto Gakuen University, Kameoka, Japan,* [8]*Faculty of Nursing, Doshisha Women's College of Liberal Arts, Kyotanabe, Japan,* [9]*Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tokyo, Japan*

Abstract

Background In longevity societies, one of the most serious social issues is sarcopenia and/or frailty. Preventing them is important for maintaining independence and quality of life in the older population. This study investigated the effect of a self-monitoring comprehensive geriatric intervention programme (CGIP) on physical function and muscle size in community-dwelling older adults. We compared the effects of a CGIP using weekly class-styled (CS) sessions and a home-based (HB) programme.

Methods The 526 participants were randomized into one of two groups (CS 251, HB 275) based on their residential districts. We conducted a 12 week CGIP, which consisted of low-load resistance exercise, physical activity increments, oral function improvements, and a nutritional guide. All participants were encouraged to attend two 90 min lectures that included instructions on the CGIP. They were provided with exercise materials (triaxial-accelerometers/pedometers, ankle weights, and elastic bands) and diary logs. The CS group attended 90 min weekly sessions and independently executed the programme on other days, whereas the HB group only received instructions on how to execute the programme. Physical functions, such as knee extension strength (KES), normal and maximum walking speed, the timed up-and-go test, and anterior thigh muscle thickness (MT), were measured and analysed using intention-to-treat analysis before and after the 12 week intervention.

Results Of the 526 participants identified, 517 (CS 243 age 74.0 ± 5.4 women 57.2%, HB 274 age 74.0 ± 5.6 women 58.8%) were enrolled. Nine (CS 8, HB 1) were excluded from the analysis because they did not participate in the pre-intervention measurements. Both interventions significantly improved KES (CS 18.5%, HB 10.6%), normal walking speed (CS 3.7%, HB 2.8%), and MT (CS 3.2%, HB 3.5%). Greater improvement of KES was observed in the CS group ($P = 0.003$). Maximum walking speed (CS 4.7%, HB 1.8%; $P = 0.001$) and timed up-and-go (CS −4.7%, HB −0.2%; $P < 0.001$) significantly improved in the CS group only.

Conclusions The intervention was effective in preventing sarcopenia and/or frailty. Most physical functions and MT improved after both interventions. The HB intervention is cost-effective and may help prevent sarcopenia and/or frailty in the large older population.

Keywords Self-monitoring intervention; Behavioural change programme; Low-load resistance exercise; Physical function

Received: 26 February 2019; Revised: 1 July 2019; Accepted: 9 September 2019
**Correspondence to: Yuya Watanabe, Faculty of Health and Sports Science, Doshisha University, 1-3 Tatara Miyakodani, Kyotanabe-shi, Kyoto 610-0394, Japan. Phone: +81-774-65-6720, Fax: +81-774-65-6720, Email: yuwatana@mail.doshisha.ac.jp. Misaka Kimura, Organization for Supporting Active Health, Kyoto University of Advanced Science, 1-1 Nanjo-Otani, Sogabe, Kameoka-shi, Kyoto 621-8555, Japan. Email:kimura.misaka@kuas.ac.jp*
Kyoto Gakuen University was renamed Kyoto University of Advanced Science w.e.f. 1 April 2019.

Introduction

Countries with longevity societies, such as Japan, face health problems associated with the increased proportion of their older population. In these countries, one of the most serious social issues is frailty, characterized by a decrease in physiological reserve and resistance to stressors, as well as increased vulnerability to adverse events.[1] Frailty is considered a major public health challenge of the 21st century. Recently, frailty has been recognized as a multidimensional phenotype that includes physical frailty, psychological decline, and sociological frailty.[2,3] Furthermore, it has been suggested that sarcopenia may be the primary or one of the major components of frailty, especially physical frailty. Recent meta-analyses have found that sarcopenia is associated with negative health outcomes, such as functional decline and mortality.[4,5] In addition, frailty increases the cost of medical and/or health care services. Therefore, preventing sarcopenia and/or frailty is important to maintain the independence and quality of life of the older population.

Resistance training has been considered the most effective intervention to increase muscle mass and strength in older people.[6–8] In particular, resistance training with a high load [~80% one-repetition maximum (1RM)] is well known as an effective prevention for sarcopenia.[9,10] However, resistance training with a high load requires exercise facilities (e.g. exercise machines) and supervised instructions in most cases. Therefore, it may be difficult for many community-dwelling older adults to perform high-load resistance training, as they may not have access to facilities or instruction. On the other hand, low-load exercise requires minimal equipment and does not require specialized facilities. Meanwhile, several studies have found hypertrophic effects of low-load resistance training in older adults. Watanabe *et al*. reported that low-load resistance training with a slow movement protocol (30–50% 1RM, 8–13 repetitions × 3 sets) led to significant increases in muscle size and strength in robust older participants.[11,12] Van Roie *et al*. also demonstrated that low-load resistance training with high volume (20% 1RM, 80–100 repetitions × 1 set) caused muscle hypertrophy in older adults.[13] In addition, other studies have found that muscle mass and physical function can be improved by increasing physical activity[14] and/or imposing an additional load during daily activities using a slightly weighted shoe in the older adults.[15] Therefore, an intervention programme based on these findings may be useful as a population-based approach for community-dwelling older adults to prevent sarcopenia.

Nutritional status has also been considered an essential factor to counteract sarcopenia. In particular, protein intake has been considered important for older individuals. Previous studies reported the connection between dietary protein intake and the maintenance of muscle mass,[16,17] muscle strength, and/or performance[18,19] in community-dwelling older adults. Clinical guidelines for sarcopenia, supported by the Japanese Association on Sarcopenia and Frailty, recommend proper nutritional intake in addition to exercise for prevention and/or improvement of sarcopenia.[20,21] Furthermore, oral function, such as feeding and swallowing, is an important factor for nutrition intake.[22] Oral dysfunction has been found to be strongly associated with dysphagia.[23] Kikutani *et al*. reported that oral functional training, such as training of the tongue, lips, and cheeks, improved oral function and nutritional condition.[24] Therefore, it is desirable that elements of oral function and nutrition, in addition to exercise, be incorporated into an intervention programme for sarcopenia prevention.

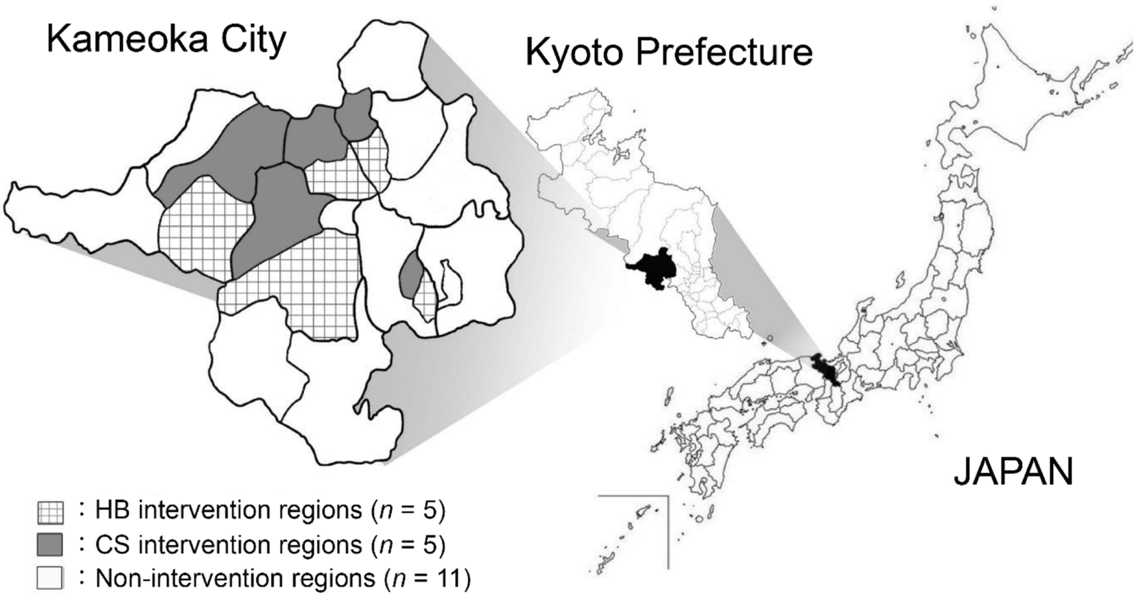
The Ministry of Health, Labour and Welfare of Japan presented the importance of comprehensive community-based approaches to reduce the number of older adults certified for long-term care and the associated costs.[25] In accordance with the Ministry of Health, Labour and Welfare report, our research group designed a comprehensive geriatric intervention programme (CGIP) consisting of resistance exercise, physical activity increments, oral functional care, and a nutritional guide. Using this CGIP, we conducted a cluster-randomized controlled trial (RCT) in Kameoka City, Kyoto Prefecture, Japan. The aim of this research paper was to evaluate the effects of a 12 week CGIP on daily physical activities, physical functions, and skeletal muscle size, in community-dwelling older people. We also compared the effects between a self-monitoring supervised and a self-monitoring unsupervised programme delivery approach. We hypothesized that a CGIP with supervision would be more effective than one without supervision, although both types would improve the aforementioned variables.

Materials and methods

Participants

We launched a population-based study (Kyoto-Kameoka Study) in July 2011. The target population was 16 474 of 19 424 community-dwelling older individuals, who did not have a long-term care certification, in Kameoka City.[26] The following is a brief account of the study protocol.[27] The Kameoka City office staff member who was not involved in the measurement or the intervention randomly selected 10 intervention regions from a total of 21 in Kameoka City (*Figure* 1). One investigator of our research group allocated the 10 intervention regions randomly (one-to-one allocation ratio) into a self-monitoring CGIP with either a weekly supervised class-styled (CS) group (five regions) or a home-based (HB) group (five regions).[27] The CGIP was intended to modify health behaviours and was susceptible to neighbourhood factors. Therefore, in order to ensure unbiased estimation of intervention effects, we adopted a cluster-RCT approach in order to minimize potential social interactions between participants and intervention arm contamination.[28]

Figure 1 Intervention and non-intervention regions in Kameoka City. CS, class-styled; HB, home-based.



On 14 February 2012, we sent postal invitations to the 4831 older people living in the intervention regions inviting them to attend a physical check-up. From those invited, a total of 1463 took part. The physical check-up was conducted at a community centre in each intervention region between March and April 2012. An additional examination was conducted in September 2012. After receiving their check-up results and an explanation of the intervention programme, 526 older adults expressed willingness to participate in the CGIP. Two hundred and fifty-one individuals were set to the CS group and 275 to the HB group according to their region of residence (*Figure* 2). The participants played no part in choosing the programme or their group. Because CS and HB interventions were explicitly different from each other and easily distinguished by investigators, the current study was set as unblinded trial. The CONSORT 2010 checklist is displayed in Supporting Information, *Table* S1.

All participants were fully informed of the purpose, procedures, and risks of the study and provided written informed consent before participation. The ethics committee of Kyoto Prefectural University of Medicine and the National Institute of Health and Nutrition approved the study protocol (RBMR-E-372 and NIHN187-3). This study has been registered in a clinical trial database (UMIN000008105).

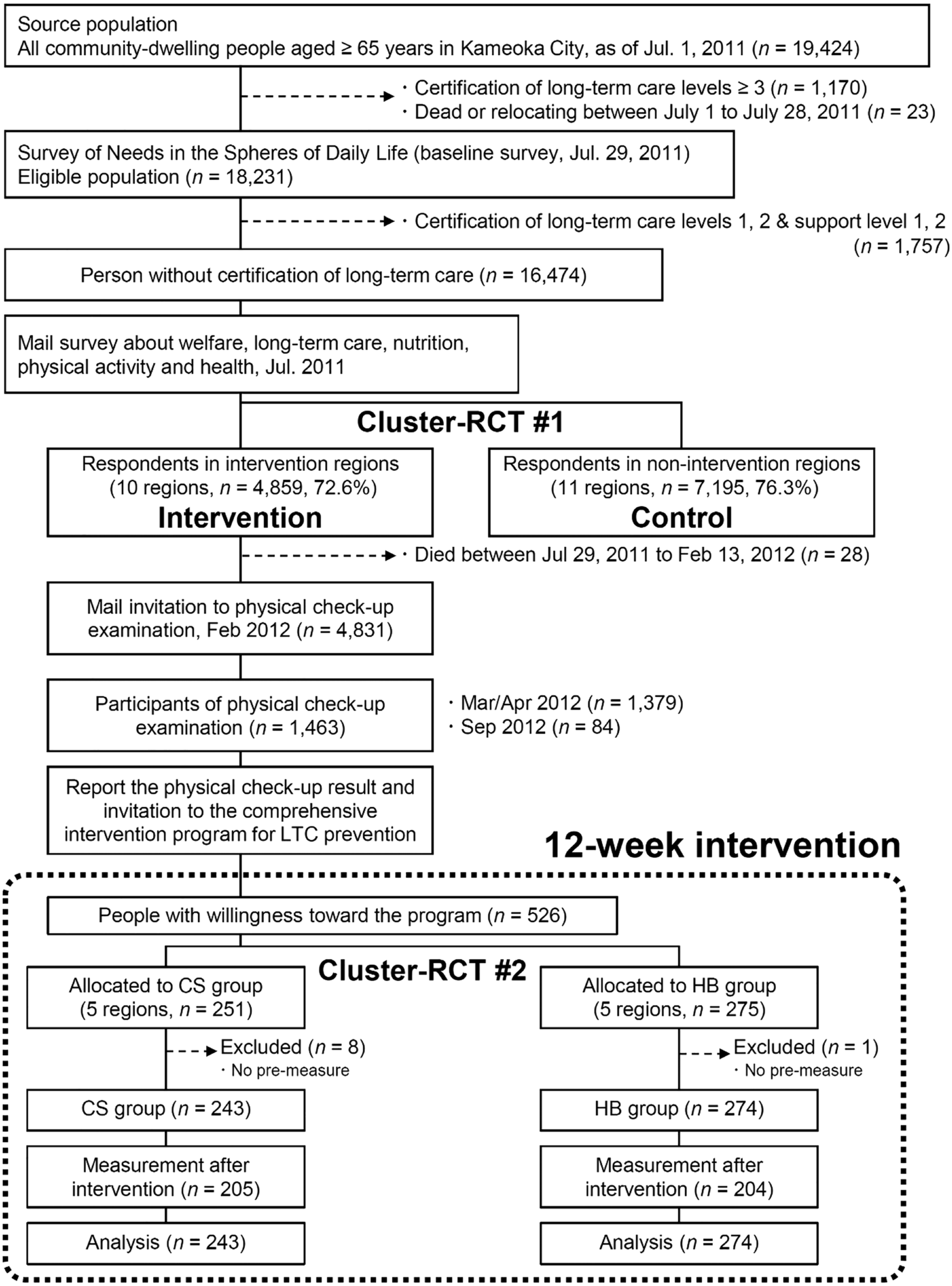
Comprehensive geriatric intervention programme

The detailed protocol of the CGIP was recently reported elsewhere.[27] The programme included the following four elements: low-load resistance exercises using body weight and/or elastic band, physical activity increments (up to 2500 steps/day from baseline), oral functional care, and a nutritional guide. In the first and second weeks of the intervention period, all participants were encouraged to take part in two 90 min lectures that included instructions on exercise, a professional dental hygienist lecture, and a professional dietitian lecture. Together, a certified strength and conditioning specialist (CSCS) from the National Strength and Conditioning Association and a physical therapist designed the resistance exercise programme. It was composed of eight exercises (e.g. squats, single leg raises, and side raises) with multiple sets (Supporting Information, *Figure* S1). A slow movement method[11,12,29,30] was applied to these resistance exercises. In addition, a single set that was to be performed quickly was added to the three lower-limb exercises after 5 weeks. The CSCS from our research group supervised all exercise instructions. During the lectures, three exercise materials (a triaxial-accelerometer, a single set of 500 g ankle weights, and an elastic band; Supporting Information, *Figure* S2) and daily self-monitoring logs (Supporting Information, *Figure* S3) were provided to all participants. All participants were instructed to record their daily step counts, the resistance exercise and oral motor exercise status (did or did not perform), and nutrition status as part of the log.[27]

After the third week of the intervention period, the CS group attended weekly 90 min supervised exercise sessions and was instructed to carry out the programme independently on the other days. The HB group was provided instructions on the programme but did not receive supervision. Between the fifth and sixth week of the intervention period, the HB group was offered an optional lecture. The

DOI: 10.1002/jcsm.12504

Figure 2 A flow chart of the cluster-RCT. CS, class-styled; HB, home-based; LTC, long-term care; RCT, randomized controlled trial. Cluster-RCT #1: Long-term comparison between 10 intervention regions and 11 non-intervention regions (LTC certification, medical cost, and mortality); cluster-RCT #2: short-term comparison between the CS (five regions) and HB (five regions) groups (daily physical activities, physical functions, and skeletal muscle size). This research paper reported the results of the cluster-RCT #2.



participants in the HB group carried out the programme independently at home. The only difference between the two types of intervention was weekly supervised sessions after the third week for the CS group. All lectures and sessions were held at the community centres of each region in Kameoka City. Six members of our laboratory including the CSCS, health fitness programmer, and physical therapist managed all lectures, weekly sessions for CS group, and optional lecture for HB group. They delivered the exercise programme instructions in the lectures and sessions. The community-dwelling volunteers supported the operation of the lectures and sessions. The number of participants in each lecture and session ranged between 6 and 30. We asked the participants not to perform the CGIP if they had a pain or unfavourable health condition. The educational leaflets for the CGIP are available for free download as supplemental documents of our paper,[27] and the exercise and oral care programmes are available online as movie files (http://www.kyoto-houkatucare.org/kaigo-yobou-manual/).

Outcome measures

Physical functions and lower-limb muscle size were the primary outcome measures. In this study, a battery of physical function tests composed of grip strength, knee extension strength (KES), normal and maximum walking speeds, timed up-and-go (TUG) test, five-time chair standing test, 30 s chair standing frequency, functional reach test, chair stepping test, and a vertical jump index (VJI) was conducted. Muscle thickness (MT) was also measured as a biomarker of muscle mass in the lower limbs as the anterior thigh muscles are considered representative muscles used in daily life activities. These measurements were carried out before and after the 12 week intervention, as described elsewhere.[31–38] Members of our laboratory and staff, who were trained by our researchers, conducted these measurements. There were no changes in trial outcomes after the trial commenced.

Grip strength was measured using the Smedley Hand Dynamometer (Grip-D, TKK5401; Takei Scientific Instruments, Niigata, Japan).[31–33] Two trials at maximum effort, separated by a brief rest period, were performed for each hand separately, and the mean value of the higher grip strength for each hand was used for analysis.

Knee extension strength of the right leg at an angle of 90° (0° representing full extension) was measured in a sitting position on a custom-made dynamometer chair (TKK5710e; Takei Scientific Instruments Co, Ltd, Niigata, Japan).[31,32,34] After the participants were familiarized with the test procedure, two trials at maximum effort were made with a 1 min recovery period. The greater value obtained was used for analysis.

The walking test was conducted, and the time (in seconds) was measured using a stopwatch.[31] The walking test of a 10 m distance at normal and maximum speeds was repeated twice. The walking speed (in m/s) was calculated as 6 m divided by the walking time, excluding the first and the last 2 m. The 6 m walking time was measured during the first trial for both speeds. In cases of measurement failure of the 6 m walking time, a repeat measurement was conducted during a second trial.

The time (in seconds) of TUG was measured using a stopwatch.[35] The participants were asked to stand up from a standard chair, walk a distance of 3 m at maximum pace, turn, walk back to the chair, and sit down as quickly as possible. They were also instructed not to run during the procedure.

The five-time chair standing test and the 30 s chair standing test were conducted.[31] The participants were instructed to stand up and sit down as quickly as possible on a firm, padded, armless chair. The five-time sit-to-stand time was measured using a stopwatch, and the number of repetitions for 30 s was counted.

The functional reach test[31] was performed using the functional reach device (TKK5802; Takei Scientific Instruments Co, Ltd, Niigata, Japan). The participants were asked to stand straight, put the left arm at the side of the body, and the right arm forward horizontally (basic posture). They were then instructed to reach out as far as possible in front of them. Two trials were performed with a brief rest period in between, and the longer distance obtained was used for analysis.

Chair stepping for 20 s was assessed.[31] The participants were instructed to sit on a chair, fully adducting their knees, and holding the sides of the chair with both hands, letting the feet work freely. Both feet were placed within two parallel lines 30 cm apart on the floor as the starting position. The participants then opened and closed their feet as quickly as possible without stepping on the lines.

Vertical jump height was measured using a jump gauge (Jump Meter-MD, TKK5106; Takei Scientific Instruments, Niigata, Japan).[31,33,36] After familiarization with the procedure, each participant performed two maximal jumps with lower-limb counter-movement. Arm swings were allowed in the first jump, while the second jump was performed with hands on the waist. The higher value was used for analysis. The VJI was calculated by multiplying jump height and body weight (m × kg).[37]

Muscle thickness of anterior portions of the right thigh (i.e. knee extensor muscles) was measured using B-mode ultrasound imaging.[34,38] Transverse images were obtained using a B-mode ultrasound imaging device (SonoSite 180 Plus; SonoSite Japan, Tokyo, Japan) and a multi-frequency linear transducer (5–10 MHz). The measurements were made with the participants standing completely relaxed. The measurement position was the midpoint between the lateral epicondyle of the femur and the anterior superior iliac spine. The scanning head was pre-treated with a water-soluble transmission gel that provided acoustic contact without compressing the skin surface. The measurements were repeated twice (a third trial was performed if there was a difference >2 mm between the two measurements), and the median of these values used for analysis. Two investigators, who were research experts trained in the technical aspects of using the ultrasound machine, performed the measurements. The intra-class correlation coefficient and mean coefficient of variation for the evaluations were 0.994 and 1.485%, respectively. In addition, the inter-class correlation coefficient was 0.991.

The secondary outcome was physical activity. The total number of steps per day and moderate-to-vigorous physical activity was evaluated using a triaxial-accelerometer.[39–41] Moderate-to-vigorous physical activity was obtained by multiplying metabolic equivalents with hours (METs × hour). In accordance with the Exercise and Physical Activity Guide,[42–45] we calculated the percentage of participants with >10 and >23 METs × hour/week.

Sample size calculation

This study was planned with an effect size of 0.35, a significance level of 0.05, and a power of 95%. Thus, at least 214 participants were needed for each group to detect a difference between conditions. In this study, the 526 older adults were randomized, by region, into one of two groups (251 in the CS group and 275 in the HB group). Therefore, the sample size of this study was sufficiently large to detect statistically significant differences.

Statistical analysis

Statistical analyses were performed using SPSS (version 22.0; SPSS Japan, Tokyo, Japan). Physical characteristics and physical function values are reported as mean ± standard deviation. Adherence to the sessions and daily log returns are reported as medians and interquartile ranges. In order to investigate the minimum effects of the CGIP, the intention-to-treat principle was used. Specifically, if the outcome value was missing for the participant, we inserted the baseline value for that outcome (i.e. the last observation carried forward approach).[46,47] All variables obtained were analysed with a repeated two-way analysis of variance (group × time) using a Bonferroni post hoc procedure. In addition, the effect size was calculated to evaluate the clinical significance of the CGIP using mean and standard deviation values, before and after the intervention. The differences in sex ratio, adherence, and daily log returns between the groups were analysed using χ^2 or Mann–Whitney *U* test. Baseline mail survey and the post-intervention questionnaire survey were analysed using χ^2, Fisher's exact, or Mann–Whitney *U* test. For all statistical tests, $P < 0.05$ was considered significant.

Results

Of 526 older adults identified, 517 (CS 243, HB 274) were enrolled (*Figure* 2). Demographic status based on baseline mail survey[26] in both groups is described in *Table* 1. There were significant more people who took medicine in the CS group than the HB group (P = 0.032). Some self-reported diseases such as diabetes (P = 0.004), osteoporosis and arthropathy (P = 0.012) were significantly higher in the CS group compared with the HB group. Nine (CS 8, HB 1) did not participate in the physical function measurements before the intervention and were excluded from the analysis. There were no changes in methods such as eligibility criteria after trial commencement. No significant harms, unintended side effects, or health-related problems reported by the participants in the intervention programme were observed throughout the whole intervention period, although a few participants had exercise-induced muscle pain in the early weeks of the programme.

Table 2 shows the physical characteristics and adherence to the intervention in both groups. No significant difference in sex ratio was observed between the groups (P = 0.720). The median attendance rate for both initial lectures was 100% for both the CS and HB groups. In the CS group, the median adherence to the weekly sessions, including the two lectures, was 90.9% (75–100%). In the HB group, 69.0% of the participants took part in the optional session held in the fifth or sixth week of the intervention period. A total of 409 out of 517 participants took part in the measurements after the intervention. There was a significantly higher attendance rate in the CS group than in the HB group (CS 84.4%, HB 74.5%; P = 0.004). The median rates of daily log return during the intervention period were 100% (67–100%) in the CS group and 100% (50–100%) in the HB group. No significant difference was observed between the groups in the daily log returns (P = 0.994).

The outcomes of both groups before and after the 12 week intervention are summarized in *Table* 3. Before the intervention, the normal walking speed and TUG test of the HB group were significantly better than those of the CS group ($P < 0.05$). In addition, the KES of the HB group was tended to be better than that of the CS group (P = 0.053). Significant interactions (group × time) were observed between KES, the maximum walking speed, and TUG test ($P < 0.05$). Although KES was significantly improved after interventions in both groups ($P < 0.001$), the change in the CS group was greater than in the HB group (P = 0.003). The maximum walking speed and TUG test significantly improved after intervention in the CS group ($P < 0.01$), whereas no such changes were seen in the HB group. Significant time effects were observed in all other variables, such as MT and VJI, in both groups, although no significant interactions were observed (*Table* 3).

There were no significant baseline differences in physical activity. Significant interactions (group × time) were

Table 1 Baseline characteristics of health-related variables

Variables	CS (n = 251) N		HB (n = 275) N		P-value
Education attainment (y)	227	12.3 ± 2.6	250	12.2 ± 2.6	0.754
Lives alone (%)	239	25 (10.5)	261	27 (10.3)	0.632
Poor subjective economy status (%)	238	153 (64.3)	267	167 (62.5)	0.712
Good self-reported health (%)	239	210 (87.9)	265	233 (87.9)	1.000
Current drinker (%)	245	103 (42.0)	269	100 (37.2)	0.279
Current smoker (%)	244	15 (6.1)	264	16 (6.1)	1.000
Arthralgia (%)	244	93 (38.1)	269	104 (38.7)	0.899
Good sleep quality (%)	248	189 (76.2)	270	196 (72.6)	0.346
Taking medication (%)	240	203 (84.6)	256	197 (77.0)	0.032
Self-reported diseases being treated or have sequelae (medical history)	251		275		
None (%)		16 (6.4)		38 (13.8)	0.006
Hypertension (%)		93 (37.1)		96 (34.9)	0.649
Stroke-related disease (%)		8 (3.2)		7 (2.5)	0.795
Cardiovascular diseases (%)		26 (10.4)		37 (13.5)	0.286
Diabetes (%)		33 (13.1)		16 (5.8)	0.004
Dyslipidaemia (%)		38 (15.1)		26 (9.5)	0.061
Pneumonia, bronchitis (%)		10 (4.0)		11 (4.0)	1.000
Gastrointestinal, liver, or gallbladder diseases (%)		25 (10.0)		26 (9.5)	0.883
Kidney or prostate diseases (%)		13 (5.2)		20 (7.3)	0.323
Osteoporosis, arthropathy (%)		51 (20.3)		33 (12.0)	0.012
Fall, fracture (%)		9 (3.6)		6 (2.2)	0.434
Cancer (%)		10 (4.0)		7 (2.5)	0.461
Blood or immune diseases (%)		4 (1.6)		3 (1.1)	0.615
Depression (%)		3 (1.2)		3 (1.1)	1.000
Dementia (%)		3 (1.2)		2 (0.7)	0.673
Parkinson's disease (%)		0 (0.0)		0 (0.0)	—
Eye-related diseases (%)		36 (14.3)		50 (18.2)	0.234
Ear-related diseases (%)		16 (6.4)		15 (5.5)	0.655
Other diseases (%)		25 (10.0)		35 (12.7)	0.319

Education attainment is expressed as means ± standard deviation and using t-test for statistics. Depression and dementia are expressed as number (rate) and using Fisher's exact test for statistics. Others are expressed as number (rate) and using χ^2 test for statistics. CS, class-styled; HB, home-based.

Table 2 Baseline characteristics and adherence in both intervention groups

Variables	CS (n = 243)	HB (n = 274)	P-value
Age (y)	74.0 ± 5.4	74.0 ± 5.6	0.876
Number of women, n (%)	139 (57.2%)	161 (58.8%)	0.720
Height (cm)	156.4 ± 8.7	156.6 ± 8.4	0.803
Weight (kg)	55.8 ± 10.0	56.1 ± 9.7	0.752
Body mass index (kg/m^2)	22.8 ± 3.3	22.8 ± 3.0	0.874
Participation in both initial lectures (%)	100 (100–100)	100 (100–100)	0.146
Participation in post-intervention physical measurement, n (%)	205 (84.4%)	204 (74.5%)	0.004
Daily log return (%)	100 (67–100)	100 (50–100)	0.994

Characteristics of the participants are expressed as means ± standard deviation. Participation in both initial lectures and daily log return are reported as median and interquartile ranges. CS, class-styled; HB, home-based.

observed regarding the daily number of steps (P = 0.006). Although the mean number of daily steps was significantly increased in both groups after the 12 week intervention, the increase in the CS group was significantly greater than in the HB group. Weekly METs hour also increased significantly in both groups (time effect: $P < 0.001$). There was a trend of a greater increase in the CS group compared with the HB group (P = 0.062). The percentage of those with $>$10 and $>$23 METs × hour/week increased after the 12 week intervention in both groups ($>$10: from 67.4% to 73.2% in the CS group, from 68.4% to 73.4% in the HB group; $>$23: from 27.2% to 44.2% in the CS group, from 23.6% to 31.6% in the HB group).

Discussion

We examined the effect of the CGIP, delivered with and without supervision, on community-dwelling older adults. Results showed that daily physical activities were significantly increased and most physical functions, such as KES, were

Table 3 Primary and secondary outcomes before and after the intervention in both groups

	CS (n = 243)				HB (n = 274)				Time effect	Interaction
	N	Before	After	Change	N	Before	After	Change	P-value	P-value
Primary outcomes										
Grip strength (kg)	243	26.4 ± 7.8	26.6 ± 7.7	1.5 (0.03)	273	26.9 ± 7.7	27.1 ± 7.9	1.1 (0.03)	0.017 (5.8)	0.768 (0.1)
Knee extension strength (kg)	239	27.8 ± 10.9	31.3 ± 10.9***	18.5†† (0.32)	264	29.7 ± 10.9	31.9 ± 11.2***	10.6 (0.20)	<0.001 (110.4)	0.017 (5.7)
Normal walking speed (m/s)	241	1.35 ± 0.25†	1.39 ± 0.26**	3.7 (0.15)	270	1.40 ± 0.25	1.43 ± 0.26**	2.8 (0.12)	<0.001 (16.9)	0.629 (0.02)
Maximum walking speed (m/s)	238	1.81 ± 0.32	1.89 ± 0.34***	4.7†† (0.24)	269	1.84 ± 0.34	1.86 ± 0.34	1.8 (0.06)	<0.001 (32.8)	0.001 (11.1)
Timed up-and-go test (s)	237	7.59 ± 2.17††	7.17 ± 2.16***	−4.7††† (0.19)	266	7.07 ± 1.78	7.00 ± 1.93	−0.2 (0.04)	<0.001 (23.0)	<0.001 (12.4)
Five-time chair standing (s)	235	8.36 ± 2.67	7.34 ± 2.55***	−9.7 (0.39)	263	8.29 ± 2.58	7.48 ± 2.14***	−7.3 (0.34)	<0.001 (85.0)	0.286 (1.1)
Chair standing for 30 s (numbers)	230	20.1 ± 5.6	22.6 ± 6.3***	15.5 (0.42)	256	20.2 ± 5.6	22.4 ± 6.4***	12.8 (0.36)	<0.001 (110.4)	0.479 (0.5)
Functional reach (cm)	241	35.5 ± 8.0	36.7 ± 7.4**	6.1 (0.16)	270	36.1 ± 7.6	37.2 ± 7.3**	5.3 (0.15)	<0.001 (15.5)	0.876 (0.02)
Chair stepping (numbers)	242	26.3 ± 6.1	29.0 ± 6.6***	11.8 (0.43)	269	26.3 ± 5.8	28.7 ± 5.7***	11.6 (0.41)	<0.001 (179.1)	0.412 (0.7)
Vertical jump index (m × kg)	218	12.1 ± 5.1	12.6 ± 5.2***	7.2 (0.10)	254	12.3 ± 5.3	12.8 ± 5.6***	5.0 (0.09)	<0.001 (25.1)	0.855 (0.03)
Anterior thigh MT (mm)	242	41.6 ± 6.5	42.7 ± 6.3***	3.2 (0.18)	271	42.7 ± 6.6	44.0 ± 6.5***	3.5 (0.20)	<0.001 (66.8)	0.526 (0.4)
Secondary outcomes										
Daily number of step (numbers)	233	5006 ± 2782	6324 ± 3496***	1318†† (0.42)	253	4903 ± 2890	5595 ± 3447***	692 (0.22)	<0.001 (80.0)	0.006 (7.8)
MVPA (METs × hour/week)	233	18.1 ± 14.9	23.8 ± 17.5***	5.8 (0.36)	253	17.7 ± 13.7	21.2 ± 18.0***	3.5 (0.22)	<0.001 (58.2)	0.062 (3.5)

Data are expressed as means ± standard deviation. The changes in primary outcomes are expressed as percentages, while the changes in secondary outcomes are expressed as increments. The *F* values are shown in parentheses in *P*-value column. The effect size was shown in parentheses in change column. CS, class-styled; HB, home-based; METs, metabolic equivalents; MT, muscle thickness; MVPA, moderate-to-vigorous physical activity.

*<0.05 vs. before intervention.

**<0.01 vs. before intervention.

***<0.001 vs. before intervention.

†<0.05 CS vs. HB.

††<0.01 CS vs. HB.

†††<0.001 CS vs. HB.

significantly improved in both groups. In addition, anterior thigh MT also increased in both groups. Furthermore, significantly greater improvements in KES, the maximum walking speed, and the TUG test were recorded in the CS intervention compared with the HB intervention. These results support our hypothesis. A particularly meaningful finding was that significant interactions were observed in only three parameters. Thus, there was no significant difference in most training effects between the CS and HB interventions. These results suggest that the CGIP was effective in improving not only physical function and but also muscle mass, which fundamentally supports physical function. This study found that both types of intervention (CS and HB) were effective in improving the physical fitness of older adults. Therefore, we expect that the CGIP will have positive effects on the participants' lifespan beyond the 12 week intervention, such as decreasing in the number of new long-term care certifications. Longer-term follow-up after this intervention (cluster-RCT #1 in *Figure* 2) is needed to confirm such effects.

Several recent guidelines for older adults show that increased physical activity and resistance training provide various health benefits.[20,21,48] Epidemiological studies have highlighted the positive effects of performing resistance training. Kamada *et al*. reported a quadratic relationship between time in resistance training and all-cause mortality, and that a moderate amount of resistance training (≥150 min/week) may be beneficial to longevity.[49] Stamatakis *et al*. showed that resistance training with body weight yielded comparable health results (e.g. reduction of all-cause mortality) to gym-based training.[50] In this study, resistance exercise with body weight or rubber band followed a slow movement protocol.[11,12,29,30] Some research groups have previously reported the effects of a resistance training programme using such as low movement protocol in a small sample of older participants.[30,51,52] This study found that the slow movement protocol was effective for preventing sarcopenia regardless of intervention type in a large sample size. The results from the questionnaire survey following the intervention showed that there was no significant difference in exercise frequency per week between the groups (CS 3–4 times, HB 4 times; $P > 0.05$). Therefore, it would be considered that many participants in both groups completed the programme habitually. We believe that the implementation of a habitual exercise programme induced improvement of physical functions and increased anterior thigh MT in the current study. Therefore, we believe that the CGIP will bring health benefits in the future.

The current study showed greater increase in KES after the CS intervention. Significant improvements in maximum walking speed and TUG were observed in the CS group only. Tanimoto *et al*. reported that the slow movement protocol had a detrimental effect on dynamic sports movements.[53] Therefore, several quickly performed exercises were included in this CGIP.[27] The post-intervention questionnaire also showed that the CS group conducted the quick leg raise and quick squats significantly more than the HB group ($P < 0.01$: unpresented data) when performing the programme in daily life. Greater implementation of the quick exercises may have been due to greater familiarity from the weekly sessions in the CS group, which may have contributed to the significant improvements in KES, maximum walking speed, and TUG found in the current study. Further investigation is needed to understand the effects of quick exercise for older adults.

Physical activity is one of the important factors in preventing sarcopenia and frailty in older adults. On the other hand, a review article suggests that exercise interventions for older adults may lead to decreases in non-programme-related physical activity and increases in sedentary time.[54] This unintended effect may have a negative impact on the health of older individuals. In our study, the mean number of daily steps significantly increased after both interventions (*Table* 3). Our approaches intended to maintain the participants' motivation, such as distribution of triaxial-accelerometer or recording of their own daily step count, may contribute to a significant increase in physical activity in the community-dwelling older adults.

Nutritional factors are similarly essential for health in older people. Previous studies have shown that nutritional status, particularly protein intake, has a beneficial effect on the prevention of sarcopenia[19–22] or frailty.[55,56] In addition, oral functions, such as feeding and swallowing, are important factors for nutrition intake. Therefore, we designed a multifactorial intervention programme that included several frailty-related elements for community-dwelling older adults.[27] We consider that approaches to oral function and nutrition in this study may have additionally contributed to improvements in physical function and lower-limb muscle size.

There were some limitations to this study. First, there was no control group. Owing to the absence of a non-intervention group, we cannot conclude that physical function did not improve simply as a result of being enrolled in this study. Second, it is noted that the individuals performing the assessments and measurements were not blind to group allocation. Because the participants were allocated according to their region of residence in this study, the participant groups could not be blinded. Although we adopted this approach to avoid social interactions between the participants and intervention arm contamination, we cannot completely exclude the possibility of measurement bias. Third, we think that the clinical significance of the findings should be qualified. This study observed significant improvements in most physical functions in both groups. However, several variables had small effect sizes, despite being statistically significant. For example, the change in grip strength may not be clinically meaningful. The intensity of exercise in the CGIP was low; therefore, it is possible that the effect size induced by the CGIP was not large (0.43 or less). However, it is valuable to know that a practical programme without special equipment improved physical functions in older adults, even though the clinical effect was small. Fourth, the participants of this study were older adults who attended a physical check-up and conducted the CGIP of their own volition. Thus, they may be more interested in their own health and physical function than other older adults. However, as this study demonstrated positive effects for the selected population, which included participants with diseases such as hypertension or diabetes (*Table* 1), we think that the CGIP is widely applicable. Last, we cannot conclude which specific factors in the CGIP contributed to the short-term effects of this intervention. The results should be understood as the overall effect of multiple elements. Future research should examine the specific components of this type of intervention to clarify their effects.

Conclusions

The CGIP in the current study, which included exercise, oral function care, and a nutritional guide, resulted in functional improvements and muscle hypertrophy. It is important to note that most physical functions and anterior thigh MT improved even after HB intervention. This result indicates that a programme delivered via a few motivational lectures may be sufficient to prevent sarcopenia and/or frailty if participants habitually follow a programme. Therefore, the HB intervention may be a cost-effective method to improve physical function and muscle mass.

In this study, the physical fitness of the participants in both groups had a significant improvement. Thus, the intervention may be effective in preventing sarcopenia and/or frailty in the older population, thereby leading to a decrease in the number of new long-term care certifications.

Acknowledgements

The authors thank all participants in this study, as well as Kameoka City, Kyoto Prefecture, Kyoto Dental Hygienists' Association, Kyoto Dietetic Association, and Kyoto Kameoka Study Group for helping with the experiments. All authors certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.[57]

Conflict of interest

The authors report no conflict of interest.

Funding

This work was supported by JSPS KAKENHI grant numbers 24240091 (M.K.), 25750360 (Y.W.), and 11J00333 (Y.Y.), Health Labour Sciences Research Grant (H30-Choju-Ippan-006) from the Ministry of Health, Labour and Welfare of Japan, research grants from Kyoto Prefecture, and the Descente and Ishimoto Memorial Foundation for the Promotion of Sports Science.

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 Eight resistance exercises in the intervention program
Figure S2 The exercise materials provided to all participants
Figure S3 The daily self-monitoring logs
Table S1 CONSORT 2010 checklist for reporting a cluster-randomized controlled trial

References

1. Fried LP, Tangem CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci* 2001;**56A**: M146–M156.
2. Mulasso A, Roppolo M, Giannotta F, Rabaglietti E. Associations of frailty and psychosocial factors with autonomy in daily activities: a cross-sectional study in Italian community-dwelling older adults. *Clin Interv Aging* 2016;https://doi.org/10.2147/CIA.S95162.
3. Xue Q-L, Bandeen-Roche K, Varadhan R, Zhou J, Fried LP. Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. *J Gerontol A Biol Sci Med Sci* 2008;**63**:984–990.
4. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. *PLoS ONE* 2017;**12**: e0169548, https://doi.org/10.1371/journal.pone.0169548.
5. Liu P, Hao Q, Hai S, Wang H, Cao L, Dong B. Sarcopenia as a predictor of all-cause mortality among community-dwelling older people: a systematic review and meta-analysis. *Maturitas* 2017;**103**:16–22.
6. Borst SE. Interventions for sarcopenia and muscle weakness in older people. *Age Ageing* 2004;**33**:548–555.
7. Peterson MD, Rhea MR, Sen A, Gordon PM. Resistance exercise for muscular strength in older adults: a meta-analysis. *Ageing Res Rev* 2010;**9**:226–237.

8. Peterson MD, Sen A, Gordon PM. Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. *Med Sci Sports Exerc* 2011;**43**:249–258.
9. Frontera WR, Meredith CN, O'Reilly KP, Knuttgen HG, Evans WJ. Strength conditioning in older men: skeletal muscle hypertrophy and improved function. *J Appl Physiol* 1988;**64**:1038–1044.
10. Fiatarone MA, Marks EC, Ryan ND, Meredith CN, Lipsitz LA, Evans WJ. High-intensity strength training in nonagenarians. Effects on skeletal muscle. *JAMA* 1990;**263**: 3029–3034.
11. Watanabe Y, Tanimoto M, Ohgane A, Sanada K, Miyachi M, Ishii N. Increased muscle size and strength from slow-movement, low-intensity resistance exercise and tonic force generation. *J Aging Phys Act* 2013;**21**:71–84.
12. Watanabe Y, Madarame H, Ogasawara R, Nakazato K, Ishii N. Effect of very low-intensity resistance training with slow movement on muscle size and strength in healthy older adults. *Clin Physiol Funct Imaging* 2014;**34**:463–470.
13. Van Roie E, Delecluse C, Coudyzer W, Boonen S, Bautmans I. Strength training at high versus low external resistance in older adults: effects on muscle volume, muscle strength, and force-velocity characteristics. *Exp Gerontol* 2013;**48**: 1351–1361.
14. Yamada M, Mori S, Nishiguchi S, Kajiwara Y, Yoshimura K, Sonoda T, et al. Pedometer-based behavioral change program can improve dependency in sedentary older adults: a randomized controlled trial. *J Frailty Aging* 2012;**1**:39–44.
15. Ikenaga M, Yamada Y, Mihara R, Yoshida T, Fujii K, Morimura K, et al. Effects of slightly-weighted shoe intervention on lower limb muscle mass and gait patterns in the elderly. *Jpn J Phys Fitness Sports Med* 2012;**61**:469–477.
16. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. *Am J Clin Nutr* 2008;**87**:150–155.
17. Meng X, Zhu K, Devine A, Kerr DA, Binns CW, Prince RL. A 5-year cohort study of the effects of high protein intake on lean mass and BMC in elderly postmenopausal women. *J Bone Miner Res* 2009;**24**: 1827–1834.
18. Gregorio L, Brindisi J, Kleppinger A, Sullivan R, Mangano KM, Bihuniak JD, et al. Adequate dietary protein is associated with better physical performance among postmenopausal women 60–90 years. *J Nutr Health Aging* 2014;**18**:155–160.
19. Isanejad M, Mursu J, Sirola J, Kröger H, Rikkonen T, Tuppurainen M, et al. Dietary protein intake is associated with better physical function and muscle strength among elderly women. *Br J Nutr* 2016;**115**:1281–1291.
20. Kuzuya M, Sugimoto K, Suzuki T, Watanabe Y, Kamibayashi K, Kurihara T, et al. Chapter 3 prevention of sarcopenia. *Geriatr Gerontol Int* 2018;**18**:23–27.
21. Arai H, Wakabayashi H, Yoshimura Y, Yamada M, Kim H, Harada A. Clinical guidelines for sarcopenia, Chapter 4 treatment of sarcopenia. *Geriatr Gerontol Int* 2018;**1**:28–44.
22. Watanabe Y, Hirano H, Arai H, Morishita S, Ohara Y, Edahiro A, et al. Relationship between frailty and oral function in community-dwelling elderly adults. *J Am Geriatr Soc* 2017;**65**:66–76.
23. Feinberg MJ, Ekberg O. Videofluoroscopy in elderly patients with aspiration: importance of evaluating both oral and pharyngeal stages of deglutition. *AJR Am J Roentgenol* 1991;**156**:293–296.
24. Kikutani T, Enomoto R, Tamura F, Oyaizu K, Suzuki A, Inaba S. Effects of oral functional training for nutritional improvement in Japanese older people requiring long-term care. *Gerodontology* 2006; **23**:93–98.
25. Ministry of Health, Labour and Welfare. Manual for prevention of long-term care in elderly (Revised) in 2012 (Report in Japanese). 2012. http://www.mhlw.go.jp/topics/2009/05/dl/tp0501-1_1.pdf. Accessed 25 April 2018.
26. Yamada Y, Nanri H, Watanabe Y, Yoshida T, Yokoyama K, Itoi A, et al. Prevalence of frailty assessed by Fried and Kihon checklist indexes in a prospective cohort study: design and demographics of the Kyoto-Kameoka longitudinal study. *J Am Med Dir Assoc* 2017;**18**:733.e7–733.e15.
27. Watanabe Y, Yamada Y, Yokoyama K, Yoshida T, Yoshinaka Y, Yoshimoto M, et al. Comprehensive geriatric intervention program with and without weekly class-style exercise: research protocol of a cluster randomized controlled trial in Kyoto-Kameoka Study. *Clin Interv Aging* 2018;**13**:1019–1033.
28. Pruitt SL, Leonard T, Murdoch J, Hughes A, McQueen A, Gupta S. Neighborhood effects in a behavioral randomized controlled trial. *Health Place* 2014;**30**:293–300.
29. Tanimoto M, Ishii N. Effects of low-intensity resistance exercise with slow movement and tonic force generation on muscular function in young men. *J Appl Physiol* 2006;**100**:1150–1157.
30. Watanabe Y, Tanimoto M, Oba N, Sanada K, Miyachi M, Ishii N. Effect of resistance training using bodyweight in the elderly: comparison of resistance exercise movement between slow and normal speed movement. *Geriatr Gerontol Int* 2015;**15**:1270–1277.
31. Kimura M, Mizuta C, Yamada Y, Okayama Y, Nakamura E. Constructing an index of physical fitness age for Japanese elderly based on 7-year longitudinal data: sex differences in estimated physical fitness age. *Age (Dordr)* 2012;**34**:203–214.
32. Yamada Y, Watanabe Y, Ikenaga M, Yokoyama K, Yoshida T, Morimoto T, et al. Comparison of single- or multifrequency bioelectrical impedance analysis and spectroscopy for assessment of appendicular skeletal muscle in the elderly. *J Appl Physiol* 2013;**115**:812–818.
33. Watanabe Y, Yamada Y, Yoshida T, Matsui T, Seo K, Azuma Y, et al. Relationship between physical fitness at the end of preseason and the in-season game performance in Japanese female professional baseball players. *J Strength Cond Res* 2017;**33**:1580–1588.
34. Watanabe Y, Yamada Y, Fukumoto Y, Ishihara T, Yokoyama K, Yoshida T, et al. Echo intensity obtained from ultrasonography images reflecting muscle strength in elderly men. *Clin Interv Aging* 2013;**8**:993–998.
35. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;**39**:142–148.
36. Yamada Y, Schoeller DA, Nakamura E, Morimoto T, Kimura M, Oda S. Extracellular water may mask actual muscle atrophy during aging. *J Gerontol A Biol Sci Med Sci* 2010;**65**:510–516.
37. Boussuge PY, Rance M, Bedu M, Duche P, Praagh EV. Peak leg muscle power, peak VO2 and its correlates with physical activity in 57 to 70-year-old women. *Eur J Appl Physiol* 2006;**96**:10–16.
38. Watanabe Y, Ikenaga M, Yoshimura E, Yamada Y, Kimura M. Association between ultrasonography echo intensity and attenuation of computed tomography in young and older adults. *Clin Interv Aging* 2018;**13**:1871–1878.
39. Yamada Y, Yokoyama K, Noriyasu R, Osaki T, Adachi T, Itoi A, et al. Light-intensity activities are important for estimating physical activity energy expenditure using uniaxial and triaxial accelerometers. *Eur J Appl Physiol* 2009;**105**:141–152.
40. Yamada Y, Yokoyama K, Noriyasu R, Osaki T, Adachi T, Itoi A, et al. Erratum to: calculation of total energy expenditure in publications on physical activity energy by Yamada et al. in 2009 and 2013. *Eur J Appl Physiol* 2016;**116**:1279–1280.
41. Murakami H, Kawakami R, Nakae S, Nakata Y, Ishikawa-Takata K, Tanaka S, et al. Accuracy of wearable devices for estimating total energy expenditure: comparison with metabolic chamber and doubly labeled water method. *JAMA Intern Med* 2016;**176**: 702–703.
42. Ministry of Health, Labour and Welfare. Exercise and Physical Activity Reference for Health Promotion 2006. 2007. http://www.nibiohn.go.jp/eiken/programs/pdf/epar2006.pdf. (Translated). Accessed 25 April 2018.
43. Ministry of Health, Labour and Welfare. Physical Activity References for Health Promotion 2013 (Report in Japanese). 2013. http://www.nibiohn.go.jp/eiken/info/pdf/sintai2013.pdf. Accessed 25 April 2018.
44. Murakami H, Tripette J, Kawakami R, Miyachi M. "Add 10 min for your health":

the new Japanese recommendation for physical activity based on dose–response analysis. *J Am Coll Cardiol* 2015;**65**: 1153–1154.

45. Miyachi M, Tripette J, Kawakami R, Murakami H. "+10 min of physical activity per day": Japan is looking for efficient but feasible recommendations for its population. *J Nutr Sci Vitaminol* 2015;**61**:S7–S9.
46. Chaitman BR, Pepine CJ, Parker JO, Skopal J, Chumakova G, Kuch J, et al. Effects of ranolazine with atenolol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina: a randomized controlled trial. *JAMA* 2004;**291**:309–316.
47. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA* 2007;**297**:2081–2091.
48. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The physical activity guidelines for Americans. *JAMA* 2018;**320**:2020–2028.
49. Kamada M, Shiroma EJ, Buring JE, Miyachi M, Lee IM. Strength training and all-cause, cardiovascular disease, and cancer mortality in older women: a cohort study. *J Am Heart Assoc* 2017 Oct 31;**6**:pii: e007677.
50. Stamatakis E, Lee IM, Bennie J, Freeston J, Hamer M, O'Donovan G, et al. Does strength-promoting exercise confer unique health benefits? A pooled analysis of data on 11 population cohorts with all-cause, cancer, and cardiovascular mortality endpoints. *Am J Epidemiol* 2018 May 1;**187**:1102–1112.
51. Tsuzuku S, Kajioka T, Endo H, Abbott RD, Curb JD, Yano K. Favorable effects of non-instrumental resistance training on fat distribution and metabolic profiles in healthy elderly people. *Eur J Appl Physiol* 2007;**99**: 549–555.
52. Tsuzuku S, Kajioka T, Sakakibara H, Shimaoka K. Slow movement resistance training using body weight improves muscle mass in the elderly: a randomized controlled trial. *Scand J Med Sci Sports* 2018;**28**:1339–1344.
53. Tanimoto M, Arakawa H, Sanada K, Miyachi M, Ishii N. Changes in muscle activation and force generation patterns during cycling movements because of low-intensity squat training with slow movement and tonic force generation. *J Strength Cond Res* 2009;**23**:2367–2376.
54. Melanson EL. The effect of exercise on non-exercise physical activity and sedentary behavior in adults. *Obes Rev* 2017 Feb;**18**:40–49.
55. Nanri H, Yamada Y, Yoshida T, Okabe Y, Nozawa Y, Itoi A, et al. Sex difference in the association between protein intake and frailty: assessed using the Kihon Checklist Indexes among older adults. *J Am Med Dir Assoc* 2018;**19**:801–805.
56. Yamaguchi M, Yamada Y, Nanri H, Nozawa Y, Itoi A, Yoshimura E, et al. Association between the frequency of protein-rich food intakes and Kihon-Checklist Frailty Indices in older Japanese adults: the Kyoto-Kameoka Study. *Nutrients* 2018;**10**:E84.
57. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the. *J Cachexia Sarcopenia Muscle*: update 2017. J Cachexia Sarcopenia Muscle 2017;**8**:1081–1083.