TITLE: Effects of an Individualized Exercise Program Plus Behavioral Change Enhancement Strategies for Managing Fatigue in Older People Who Are Frail: Protocol for a Cluster Randomized Controlled Trial

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Background. Although the evidence suggests that general fatigue is a strong indicator of rapid aging, frailty, and disability, general fatigue is undertreated in gerontological care.

Objective. The aim of this study is to investigate whether an individualized exercise program with and without behavioral change enhancement (BCE) strategies for older people who area frail and have general fatigue can reduce their fatigue and symptoms of frailty.

Design. A 3-arm, single-blind, cluster randomized controlled trial registered with ClinicalTrials.gov (NCT03394495) will be conducted.

Setting. The study will be conducted in a community setting.

Participants. Two hundred eighty-five community-dwelling older people with general fatigue will be recruited from 12 district community health centers.

Intervention. People from each center will be randomized to 1 of 3 groups. The combined group will receive a 16-week combined intervention consisting of individualized exercise training and the BCE program plus 2 booster sessions at 2 and 6 months after the program. The exercise group, will receive exercise training and health talks only. The control group will receive health talks only.

Measurements. Outcome measures will be collected at baseline, at the midpoint (week 8) of the program, and then at 1 week, 6 months, and 12 months after the end of the program. The primary outcome, level of fatigue, will be measured using the Multidimensional Fatigue Inventory. Secondary outcomes will include the participants' frailty status, strength, mobility, exercise self-efficacy, and habitual physical activity.

Limitations. A self-reported level of fatigue will be used.

Conclusions. The effect of exercise and BCE strategies on general fatigue among older people who are frail is not known. This study will be a pioneering interventional study on how general fatigue among older people who are frail can be managed and how fatigue-related frailty can be prevented or minimized.

Many older people experience general fatigue with no specific known cause. This type of fatigue has been reported in 27% to 53% of community-dwelling older people worldwide.[1] Although different countries use different criteria to define older people, in developed countries the age of 70 years[2] and over is increasingly being used as the criterion, and that is the definition that will be employed in this study. General fatigue is partly caused by age-related biophysiological changes, such as reduced muscle strength and mass, leading to decreased muscle endurance. This, together with a gradual decline in cardiovascular and pulmonary functions, also leads to a reduction in the maximal heart volume and to a decrease in the vital capacity and expiratory volume of older people. These changes predispose older people to reduce their rate of oxygen consumption during activities.[3] A decrease in the production of energy, or an inability to cope with an increase in the utilization of energy, presents as general fatigue in older people when they perform even mild daily activities. This phenomenon could be part of the transition to a final common pathway of frailty and disability.[3] The operational definition used in this study refers to the most severe level of fatigue – exhaustion – experienced by older people for at least 3 days, which might not be relieved by rest, leading to a decreased capacity to engage in everyday physical and mental activities.[4]

Empirical evidence shows that general fatigue is prevalent among older people and can predict frailty and disability in the long term. Longitudinal studies have shown that older people with self-reported general fatigue have more restricted activities,[5] poorer physical function, slower gait speed, and disability,[5,6] increased utilization of home-help and hospital services,[7] and even a higher risk of mortality in the long

term (ie, 3–5 years).[8] For example, a longitudinal study of 420 older women who were not frail found that women with exhaustion were 3 to 5 times more likely to be frail and disabled 7 years later (at which time 80% of them developed frailty) when compared with those without exhaustion.[9] In fact, exhaustion, together with unintentional weight loss, low levels of activity, a slow walking speed, and a decreased grip strength are the 5 phenotypes of frailty. Older people who are frail are defined as those who have 3 or more characteristics of the 5 phenotypes of frailty.[10] This physiological state of increased vulnerability to stressors results from a decrease and possible dysregulation of reserves in multiple physiological or biological systems.[9,11–14]

Physical exercise has already been demonstrated to have beneficial effects on older people who are frail in terms of improving their fall rates, gait ability, and functional and physical performance in balance and strength.[15] However, there is little in the current literature on how to evaluate the effects of exercise interventions or other types of interventions on the general fatigue experienced by older people who are frail,[16] with the exception of a pilot study reported by our team.[17] Thus, the effects of physical exercise on managing general fatigue among older people remain unknown. This may also indicate that the management of fatigue has yet to receive adequate attention in gerontological care.[18]

The deconditioning model[19] holds that older people with general fatigue might avoid exercise due to the fear that physical overexertion might induce muscle pain or weakness. This explains why older people frequently cite fatigue as a cause of their nonadherence to or withdrawal from exercise programs.[16,20] Their inability to function at previous levels may lead to frustration and to low motivation and

self-efficacy in carrying out their daily activities, thus becoming a major barrier to their engagement in regular exercise.[21,22] However, avoiding exercise exacerbates fatigue-related physiological symptoms (eg, reduced physical endurance, mobility, and cardio-respiratory functions). These physiological changes that result from deconditioning and avoiding physical activity can lead to a self-perpetuating vicious cycle of fatigue.

Fortunately, the evidence suggests that patients with disease-induced fatigue feel less exhausted and more energetic as a result of engaging in regular exercise.[19,20] Recent studies have shown that among people who consistently feel exhausted, those who are willing to gradually exceed their perceived energy limits and recondition their bodies by participating in exercise programs gradually experience less fatigue.[19,23,24] Although the causal pathways for different types of fatigue are not the same, the self-perpetuating vicious cycle of fatigue explained under the deconditioning model is similar among people with different types of fatigue.[25] In addition, exercise targeting the muscle strength, mobility,[26,27] and cardio-respiratory fitness[28] of older people can improve functional capacity, and may improve their perception and condition of fatigue.[29]

However, older people can only obtain all of the benefits of exercise after they have engaged in regular exercise at their individual attainable level for at least 3-5 months.[30] Oversensitivity to physical responses such as mild muscle tiredness after exercise may lead to the avoidance of physical activity; thus, high dropout rates were reported among participants with fatigue in the exercise groups.[23,24] If the

prescribed exercise levels are beyond their physical and psychological capabilities, this may also lead to exhaustion, causing participants to drop out. To overcome this problem, it is suggested that behavioral change enhancement strategies focusing on enhancing motivation be given alongside an exercise program for those with experience of fatigue.[24,31–33]

The health action process approach model divides the process of behavioral change into 2 phases: motivation and volition.[34] The motivation phase refers to the goal initiation phase. Self-efficacy, outcome expectancies, and increased risk awareness are the 3 attributes that motivate individuals to form an intention or goal to change their unhealthy lifestyle for a healthy lifestyle. The volition phase refers to the process of implementing intentions into actual behavior through careful planning and action execution. The empirical evidence shows that the health action process approach model used alongside exercise interventions can promote adherence to exercise regimens among those undergoing orthopedic rehabilitation[35] and cardiac rehabilitation,[36,37] and among older patients with sedentary lifestyles.[38]

The pilot controlled trial of a combined behavioral change enhancement (BCE) and exercise program conducted by the first author (JYWL) and her team was the first trial of general fatigue in older people.[17] Eighty-five older people who are frail and have fatigue will be assigned to receive exercise combined with the BCE intervention (COMB group), exercise only (EXER group), or usual care (control group). The pilot study was not powered to identify significant changes in outcome measurements. However, the observed effect size of the change in fatigue levels between the COMB group and the other 2 groups was 0.21, suggesting that the intervention had a mild to moderate effect

(please refer to the sample size section for details). This pilot study showed that the combined exercise training and BCE program has the potential to strengthen the participants' engagement in daily exercises, as reflected by their significantly higher self-reported participation in exercise and higher attendance rate in all of the training sessions ($F_{2,76}$ = 5.64; P < .01) when compared with the other 2 groups. Not surprisingly then, a trend of greater improvement in physical endurance (such as gait speed, hand grip strength, balance, and mobility) was observed in the COMB group than in the other 2 groups.

This article outlines a fully powered cluster randomized controlled trial with the aim of investigating the effects of an individualized exercise program with and without BCE strategies on fatigue, physical endurance, exercise self-efficacy, and habitual physical activity, while reducing symptoms of frailty, in community-dwelling older people who are frail and have general fatigue. It is hypothesized that participants who receive a combined intervention of exercise and the BCE intervention will have significantly better outcomes than the other 2 groups, as their exercise self-efficacy will have improved after the BCE program. Thus, they will be more capable of adhering to the exercise regimen, leading to positive outcomes.

[H1]Methods

[H2]Study Design

A single-blind, 3-arm, cluster randomized controlled trial is proposed to examine the effect of a 16-week individualized exercise program with or without BCE strategies for older people who are frail and have general fatigue, compared to a control (health education) program.

[H2]Study Settings

Eligibility criteria for district community health centers are those that are funded by the Hong Kong government and under the supervision of the Social and Welfare Department of Hong Kong, and that meet a specific set of standard regulations and criteria on environment and practices. The 12 community centers that have agreed to take part in this proposed project were recruited through a convenience sampling method. They provide similar types of community care and social support services for community-dwelling older people, and thus were invited to be the collaborators in this study.

[H2]Participants

Community-dwelling older people who are frail and have a nonspecific cause of general fatigue will be recruited through participating community centers. Table 1 shows the eligibility criteria used for detailed sample selection.

[H3]Sample size estimation, recruitment procedures, random allocation, and allocation concealment. The changes in the mean fatigue scores were −0.58, −5.16, and −2.66 for the control, EXER, and COMB groups respectively, from before testing to immediately after the intervention in the pilot study. The Cohen *d* effect sizes for the EXER and COMB groups were 0.51 and 0.23, respectively, whereas the overall effect size was 0.21. As no similar cluster randomized controlled trial has been reported in the literature and the cause of general fatigue is heterogeneous, we assumed that an ICC would be low (0.01) within each cluster.[39] Based on an effect size of 0.21 in the pilot study, and 4 clusters (community centers) per group with an ICC of 0.01, a significance level (α) of .05, and a power (1 − β) of 0.8 for a 2-sided test, the sample size was calculated to be 76 participants per group. For a long-term follow-up of 12 months, 285 participants (95 per group) will be recruited after considering an attrition rate of 20%. All centers will be assigned a number from 1 to 12. Using a computer-generated random numbers list, a biostatistician not affiliated with this study will randomize the centers into the control, EXER, or COMB group. To avoid selection biases, the allocation to the study groups will be concealed from the researchers until the recruitment of the sample and the baseline assessment have been completed.

[H3]Sample recruitment plan. We estimate that about 25% to 50%[2,6,40] of the 8710 members (total number of all members) of the 12 centers will be eligible to participate. With the high recruitment rate (87.2%) and low overall attrition rate (7.1%) in our pilot study, we are confident

that a sufficient number of participants can be recruited in 15 to 18 months. Should we be unable to recruit a sufficient number of participants according to our schedule, we will approach additional centers to take part in this study.

[H2]Interventions

The COMB group will receive a 16-week program with a combination of exercise and the BCE program, plus 2 booster BCE sessions to be held at 2 and 6 months after the program (Fig. 1). Another 16-week program with a combination of exercise and health talks will be arranged for the EXER group, whereas participants in the control group will attend only the health talks with no other intervention. Two added health talks will be arranged at 2 and 6 months after the program for the EXER and the control groups. To understand the change in the fatigue level as well as in other physio-psychosocial parameters of this particular group of older people, a control group with no treatment except health talks was employed in this study. In addition, to control the group and social interaction effects of the BCE program for the COMB group, the number and timing of the health talks for the other 2 groups will be similar to those in the BCE sessions. The number of contact hours will be exactly the same between the COMB and the EXER groups, but the contact hours for the control group will only

involve health talks. All face-to-face sessions will have ≤10 participants to maintain good interactions between the participants and the exercise instructor, BCE facilitator, or health talk speakers.

[H3]BCE program in the COMB group. This program is aimed at motivating the participants to develop the intention to actively manage their fatigue; and to encourage them to gradually exceed the perceived limits of their energy and to recondition their bodies by participating in exercise according to their individual exercise regimens. The BCE program was designed based on the health action process approach model. It consists of 3 phases with 6 face-to-face 1-hour sessions plus 2 booster BCE sessions at 2 and 6 months. The first 3 weekly sessions will be arranged during the goal initiation and planning phases. The remaining 3 sessions and 2 booster sessions will be offered once per month in weeks 4, 8, and 12 during the program and at 2 and 6 months after the program during the action execution phase (Tab. 2).

[H3]Exercise intervention in the EXER and COMB groups. A weekly 45- to 60-minute center-based exercise program, designed according to the American Heart Association's recommendations on exercise for older people[41] will be arranged from weeks 4 to 16 during the execution phase. This program will consist of balance training, such as sideways walking (15–20 minutes); resistance exercises, such as using resistance bands to improve muscle strength in both the upper and lower limbs (10–20 minutes); aerobics training, such as walking (10 minutes), with 10 minutes of warm-up and cool-down exercises at the beginning and at the end. All of the participants will receive circuit

training with set exercises, but the dosage of different components will be tailor-made for each participant on the basis of his or her physical condition. To prescribe an appropriate dosage of exercises, a physical therapist will assess each participant's physical condition in week 4 (ie, the first week of the exercise program), and subsequent monthly assessments will be held in weeks 8 and 12. The dosage of exercises will gradually increase by increasing the number of repetitions, the duration of the exercises, and also by using progressively heavier wrist and ankle weights, with perceived exertion maintained at approximately 12 to 14 on the Borg Rate of Perceived Exertion Scale,[26,42] based on the participants' progress. An online video and a pamphlet describing the different types of exercises used in this program will be disseminated to all participants to encourage them to continually practice their exercises at home for approximately 30 minutes at least 3 times per week. Therefore in total, participants are expected to undertake a minimum of 150 minutes of exercise each week (supervised or home based independent practice), based on the recommendation of the American Heart Association.[40]

To ensure that both instructors deliver the BCE program and exercise training according to the protocols, checks will be conducted weekly to monthly during the intervention period based on the BCE program/exercise training checklists. The first author (J.Y.W.L.) or a well-trained research assistant will conduct real-time observations of the BCE/exercise class, and evaluate the class activity against the checklists. A fidelity rate of >90% will be considered an indication that the BCE/exercise instructors have delivered the intervention as detailed in the study protocols, and is consistent with recommendations from the National Institutes of Health Behavior Change Consortium.[43]

[H2] Control Condition

Participants in the control and EXER groups will attend center-based health talks on the management of different health issues with the exception of fatigue. The number and timing of the health talks will be similar to those in the BCE sessions in the COMB group. A research assistant who will not be involved in other procedures of this study will run the health talks.

[H2]Assessment

Outcome measures will be collected at baseline (T0), midpoint (T1) (week 8) of the program, and then at 1 week (T2), 6 months (T3), and 12 months (T4) after the program. The data collection will be conducted by a trained research assistant who will be masked with regard to the group allocation.

The following sociodemographic data will be collected: age, sex, marital status, exercise habits, living conditions, level of education, and participants' health-related information, including cognitive status and medications. Additionally, their levels of comorbidity will be assessed using the Chinese version of the Charlson Comorbidity Index. The score on this index is the sum of the comorbidity and age scores, in which

scores of 0, 1 or 2, 3 or 4, and >5 represent the comorbidity level as none, low, medium, and high, respectively.[44] The health services utilization of the participants in the past 12 months and during the study period, such as the number, duration, and causes of hospital admissions and scheduled or nonscheduled clinical visits, will be collected during each measurement time point and will be treated as a covariate if needed.

Table 3 provides details of the measures to be used for this study. The primary outcome is the level of fatigue, which will be measured using the Chinese Multidimensional Fatigue Inventory,[45] which was initially validated among 385 Chinese patients with cancer. Secondary outcomes include the participants' frailty status, physical strength, mobility, exercise self-efficacy, and habitual physical activity.

[H2]Study Procedure

Potential participants will be referred to the research team by the 12 community centers. All potential participants will be screened for their eligibility to participate in this study. After their written informed consent is obtained, the participants will be interviewed to obtain their health and sociodemographic data and baseline assessments. After that, people from the 12 community centers will be randomized to the control, EXER, or COMB group. The participants from each center will be placed in their center's corresponding group to avoid contamination effects across participants. (Fig. 2).

[H2]Data Analysis

SPSS version 25.0 (IBM SPSS, Chicago, IL, USA) will be used to analyze the data. An intention-to-treat analysis will be adopted. Descriptive statistics will be generated for the demographic data. Normality assumptions for the variables will be checked. The baseline characteristics of the participants in the 3 groups will be compared using analysis of variance for the continuous variables, a chi-square test for the categorical variables, and the Kruskal-Wallis test for the ordinal variables. Mixed-effects modeling will be used to measure changes in the outcome assessments at the midpoint (week 8) and at the 3 postintervention tests (1 week, 6 months, and 12 months after the intervention) among the 3 groups, followed by the application of a Helmert contrast test (if any results are found to be significant).[46] Another mixed-effects modeling approach will be used to measure the participants' attendance rate in the weekly exercise sessions and their adherence to the home exercise during the program and the follow-up period between the EXER and the COMB groups. Any pretest outcome scores, demographic information, data on health conditions, comorbidity index, health service utilization, dosages of exercise recommended by the physical therapist, and participation in other exercise programs during the study period, indicating significant differences between groups, will be treated as covariates as needed. Multiple imputations will be adopted to manage missing data. A P value of $<.05$ will be considered

statistically significant. We hypothesize that exercise self-efficacy and exercise participation are the 2 major factors affecting the primary outcome (ie, fatigue). A subgroup analysis will be conducted to determine whether there are any differences across all measurement time points on the participants' exercise self-efficacy and exercise participation, and how these 2 factors might affect the participants' fatigue level at different time points.

[H1]Ethics

Ethics approval for the study has already been obtained from the Human Subjects Ethics Review Committee of The Hong Kong Polytechnic University (application number: HSEARS20160114001). Written informed consent will be obtained from all participants, after they have been given an explanation of the study. We will assure the participants that they can withdraw from the study at any time without penalties. The principle of protecting research participants in accordance with the Helsinki Declaration will be observed. All research personnel involved will work closely together to monitor the occurrence of untoward effects on the participants. Standard guidelines for managing adverse events will be used. For example, a target heart rate will be identified for each participant. Those at the beginner level will be advised not to exceed 50% to 60% of their target heart rate, with the figure being 60% to 70% for those at the intermediate level. The physical therapist and the first author (J.Y.W.L.), who is a registered nurse, will give individual participants advice on an ad hoc basis to ensure their safety.

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[H1]Discussion

[H2]Potential Impact and Significance of the Study

This study protocol describes a pioneering interventional study investigating how general fatigue among older people who are frail can be managed. Given that fatigue is a common initial sign of frailty and disability,[3,9] we hypothesize that general fatigue is a factor that can be modified to prevent older people from developing frailty or disability. The findings will shed light on how frailty and disability can be prevented or alleviated. If general fatigue can be reduced with our intervention, some participants may rebound to prefrail or even nonfrail status. This will provide scientific evidence that frailty can be reversed through the early screening of warning signs (ie, self-reported fatigue) and then by implementing the appropriate interventions.

Older people with frailty or disability will consume a disproportionate share of health care and community resources. Although reducing

fatigue is an important goal in improving the physical endurance of older people, its benefits to older people (and society in general) will be further enhanced if fatigue reduction can result in or be accompanied by a healthy lifestyle, increased social participation, reduced service utilization, and the maintenance or renewed uptake of activities of daily living—in short, improved independence. If successful, this combined intervention is likely to reduce the financial burden in health and community care for older people who are frail.

[H2]Strengths and Weaknesses of the Study

The strength of our study is that it is a cluster randomized controlled trial with sufficient power to determine the efficacy of the combined intervention. All participants will be followed up for 1 year to determine the long time effects of this intervention. An individualized and client-centered approach is highlighted in the design of this combined intervention, for example, the design of the exercise regimen will be based on a participant's own physical condition; and they will be guided to establish their goals and action plan to manage fatigue. The uniqueness and potential sustainability of the intervention will contribute to the long-term impact of this study. If the present program is demonstrated to be effective for enhancing the physical fitness of the participants and maintaining it beyond the program period due to the enhancement of their self-efficacy, then this intervention will be highly sustainable in the community.

Two potential weaknesses of the study are a reliance on the participants to report their level of fatigue and their adherence to practicing the exercises at home. However, fatigue is a subjective feeling and no objective measurement is available for measuring of fatigue levels. Expectation bias or response bias may occur when participants are aware of the study's objective and thereby attempt to please the researchers. To minimize this bias, an independent assessor who is not acquainted with the participants will be responsible for outcome assessments. To improve participants' adherence to the task of completing the exercise diary, a research assistant will call the participants during the follow-up period every 2 weeks to remind them to accurately record their exercise pattern. In the future, consideration may be given to using an accelerometer to measure the amount of time that the participants spend daily on activities of moderate to vigorous intensity to indicate their adherence to practicing their exercises at home. This data can be correlated with the participants' subjective fatigue levels to see how fatigue affects the daily life of the participants. Another potential limitation is that the progress that the participants make in their exercises can only be monitored by the physical therapist once per month. Although it is unlikely that older people who are frail and have fatigue will make quick progress, we cannot exclude the possibility that some participants may progress more quickly in a month than others, and require more frequent follow-ups. Thus, we also encourage the participants to revise their exercise goal regularly according to their own achievements. In addition, we suggest that in future studies more frequent reviews and prescriptions of the exercises by physical therapists may improve the rate at which participants progress in their exercises. An additional weakness of this study is that the participants will be aware of their

received interventions. By using clusters, participants from each center will be placed in their center's corresponding group, thus avoiding contamination effects across participants. Finally, the control group will have fewer contact hours than the COMB and EXER groups, as having the same number of contact hours could confound the findings.

[H2]Contribution to Clinical Practice

This article details a study protocol of a combined intervention that is systematic, comprehensive, and tailor-made to address general fatigue in older people who are frail. It has the potential to be adopted in community settings, as no sophisticated equipment or skills are involved.

Author Contributions and Acknowledgments

Concept/idea/research design: J.Y.W. Liu, P.P.K. Kor, W.T. Chien, P.M. Siu, K.D. Hill
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J.Y.W. Liu developed the original concept, drafted the protocol, wrote the final manuscript, and will be accountable for the quality control aspect of the study throughout the trial; P.P.K. Kor, together with J.Y.W. Liu, will be responsible for leading and supervising the daily operations of the project. W.T. Chien contributed to updating and designing the behavioral change enhancement (BCE) intervention. He will assist in training the research assistant to facilitate the BCE sessions. K.D. Hill assisted with the development of the assessment battery and the exercise program and will play an active advisory role in all aspects of the implementation and dissemination of the project. P.M. Siu will support J.Y.W. Liu in monitoring the implementation and daily progress of the exercise intervention. They will also assist in training the research assistant to carry out the exercise intervention and physical assessments of the participants. P.L. Lee will be responsible for analyzing the data. All of the authors read and approved the final manuscript.

Ethics Approval

Ethics approval for the study has been obtained from the Human Subjects Ethics Review Committee of The Hong Kong Polytechnic University (application number: HSEARS20160114001). Written informed consent will be obtained from all participants after they have been given an explanation of the study. The authors will assure the participants that they can withdraw from the study at any time without penalties. The authors also will ensure that the principle of protecting research participants in accordance with the Declaration of Helsinki is observed.

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Clinical Trial or Systematic Review Registration

The study related to this protocol is registered at ClinicalTrials.gov (NCT03394495).

Disclosure

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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Table 1.
Eligibility Criteria[a]

Inclusion Criteria	Exclusion Criteria
Are community-dwelling people ≥70 y old	Have any disease in which fatigue is a dominant symptom (such as neurodegenerative diseases, cancer, and end-stage renal failure cachexia)
Are able to communicate in Cantonese to ensure that they understand instructions	Have been hospitalized for ≥5 d in the preceding 3 mo; this situation may lead to muscle wasting due to recent bed rest or reduced activity levels during hospitalization
Are able to walk with or without an assistive device and able to complete the Timed "Up & Go" Test with no specific cutoff point to ensure that their mobility and balance are good enough to participate in the exercise training	Have undergone major surgery (such as total joint replacement and major abdominal surgeries) in the last 6 mo
Are in a frail state (3 or more of the 5 items listed below, with the exhaustion item being 1 of the 3),[b] as determined using the Fried Frailty Index[10]: Unintentional loss of 10% of body weight in the past year Exhaustion, determined by a "yes" response to either "I felt that everything I did was an effort" or "I could not get going in the last week" Slow walk time, with an average walking speed in the lowest quintile, stratified by median body height Reduced grip strength, with maximal grip strength in the lowest quintile, stratified by body mass index quartile Score on the Chinese Version of the Physical Activity Scale for the Elderly in the lowest quintile (ie, ≤30 for men and ≤27.7 for women)	Have been diagnosed with major depression, entailing frequent adjustments of their antidepressants to control unstable depressive moods, to avoid recruiting people with depression-induced fatigue; however, a consistent feeling of fatigue may be manifested as a depressed mood; thus, the participants' mood will be assessed using the Chinese Geriatric Depression Scale[47]
	Have reported that they regularly perform moderately intense exercise (such as hiking and Tai Chi) for ≥3 h/wk
	Are terminally ill
	Are confined to bed or restricted by the permanent use of a wheelchair

[a]The principal investigator will train a research assistant on how to use all of the instruments for screening, with reference to the latest user guidelines for the instruments. The inter- and intrarater reliabilities will be evaluated with the ICC. Acceptable levels of reliability (ICC ≥ 0.9) will be established by comparing the scores rated by the research assistant and the principal investigator prior to participant recruitment.

[b]The presence of ≥3 items indicates frailty, and a "yes" response to either of the exhaustion questions indicates exhaustion.

Table 2.

Health Action Process Approach–Based Behavioral Change Enhancement Program Protocol[a]

Phase[b]	Aims	Session(s)	Contents
Goal initiation	To establish the intention to adhere to strategies that address issues related to fatigue To understand the expected outcomes of the program To increase awareness of the negative impacts of unmanaged fatigue To strengthen self-efficacy	1	To encourage the participants to share their experiences with fatigue To explain the expected outcomes of the program and how these outcomes can match the personal goals of the participants To introduce the participants to the impacts of unmanaged fatigue on physical and psychosocial well-being To introduce the participants to the deconditioning model of fatigue (ie, avoiding physical activity exacerbates fatigue-related physical symptoms) To discuss the participants' intention to complete the program
		2	To introduce the connection between exercise and fatigue To understand the expected outcomes resulting from regular exercise in older people To recognize correct or incorrect beliefs about exercise for older people To recognize and overcome barriers to staying or becoming physically active To identify the negative impacts of leading a sedentary lifestyle
Plan formulation	To create an action plan and coping plan for adhering to the exercise regimen To set subgoals	3	To evaluate the participants' current preferences relating to exercise To set achievable subgoals with the participants on the basis of their physical and cognitive abilities To reassure the participants that the final goals will be divided into several achievable subgoals according to their progress throughout the program To create a detailed action plan of when, where, and how to practice the desired action To identify an alternative coping plan
Action execution	To encourage action execution To continue strategies that can enhance the participants' self-efficacy, including: Obtaining performance accomplishments Generating social persuasion Gaining vicarious experience Perceiving the positive physiological and emotional responses of engaging in regular exercise	4–6	To self-evaluate levels of adherence to the action plan and the achievement of the subgoals, so as to let the participants experience success by achieving the (sub)goals To provide positive feedback and encouragement from peers and the behavioral change enhancement facilitator To observe peers with similar physical and psychological difficulties related to fatigue adhering to the action plan, so as to provide participants with chances to learn about the successful experiences of their peers during the sharing sessions To continue to refine the subgoals and the action and coping plans according to progress, if necessary To promote positive perceived responses (such as vitalization-enjoyment and improved endurance) after exercise To guide the participants to develop their own plan for the sustainability of their actions in the future To include all of the participants in the final session (session 6) and encourage them to continue the action in the future
		Booster (sessions at months 2 and 6)	To recap all strategies used during action execution in previous sessions, so as to reinforce the participants' self-efficacy To review and modify long-term goals, action plans, and exercise regimens To practice exercises together To share experiences and thoughts related to: Participation in regular exercise Fatigue management

[a]The 2 expected outcomes are that the participants will demonstrate a sense of self-control and confidence in managing their fatigue-related health issues and that they will agree to gradually exceed their perceived energy limits and recondition their bodies through participation in exercise according to their own exercise regimen. The maximum group size will be 10.

[b]The aims of the 3 phases are as follows. Phase 1 (goal initiation) is aimed at motivating the participants to actively manage their fatigue. Embedded in the contents will be 3 attributes (ie, increased risk awareness, enhanced self-efficacy, and awareness of outcome expectancies) designed to motivate individuals to modify their behaviors.[34] Phase 2 (plan formulation) is aimed at guiding the participants in transforming their (sub)goals into detailed individualized action plans. Action plans foster goal achievement by helping the participants to get ready to start. The participants' current exercise preference will be evaluated to ensure that the identified subgoals will not exceed their functional capabilities. A plan for coping will also be formed with reference to anticipated barriers, and alternative plans will be generated to overcome those barriers. Both plans and (sub)goals will be modified on the basis of the participants' progress. Phase 3 (action execution and booster sessions) are aimed at encouraging the participants to continually execute the action plans. The following 4 strategies to strengthen the participants' self-efficacy will be used in all of these sessions: obtaining performance accomplishments through experiences of success in goal achievement; generating social persuasion through regular sensible feedback and encouragement by the behavioral change enhancement facilitator; gaining vicarious experiences through peer sharing; and perceiving the positive physiological and emotional responses of engaging in regular exercise.[48,49]

Table 3.

Summary of Measures and Assessments[a]

Measure	Outcome	Instruments	Descriptions
Primary	Fatigue	Chinese Multidimensional Fatigue Inventory (CMFI-20)[45]	This instrument was validated on 385 local patients with cancer. A factor analysis revealed that it contains 3 factors (ie, physical, mental, and spiritual) with factor loading ranging from 0.52 to 0.75. The Cronbach α was between 0.7 and 0.8 for scores on the 3 domains of the CMFI-20 and the total CMFI-20 score. These data support the view that the CMFI-20 is a reliable and valid instrument.
Secondary	Physical ability	30-s chair stand test[50]	To test a person's lower-limb strength.
		Handheld Jamar Hydraulic Hand Dynamometer[42]	To test a person's upper-limb strength.
		Timed "Up & Go" Test[51]	To assess a person's mobility.
		Gait speed (4.5-m walk)	To assess a person's mobility.
		2-min walking test[52]	To assess a person's overall physical endurance.
	Exercise self-efficacy	Chinese Self-Efficacy for Exercise Scale (CSEE)[8,53]	To assess the participants' self-confidence in their ability to exercise in a variety of circumstances (eg, when feeling tired). It was validated on 192 Chinese older people. Discriminant validity was shown by the CSEE total score, which significantly differentiated between individuals with and individuals without regular exercise. The Cronbach α of 0.75 showed an acceptable level of internal consistency.
	Exercise adherence[b]	Exercise diary	The assessment will be based on the participants' attendance in the weekly exercise training sessions and, for the combined and exercise groups, using an exercise diary. The diary will be used to record the dosage of exercise recommended to the participants by the physical therapist and the participants' adherence to the home exercise. The participants will be instructed to record the frequency and duration of each type of exercise that they practiced at home during the previous week. They will

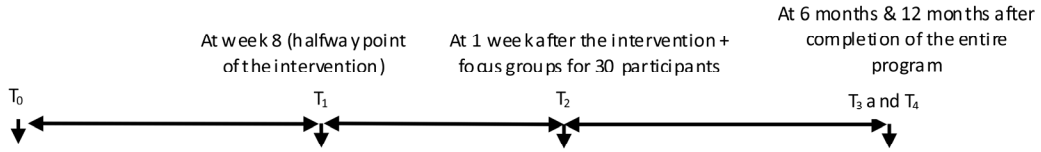
			also be asked to rate their overall level of adherence to the exercise regimen on an 11-point scale (from 0 [nonparticipation] to 10 [full participation]) on the basis of the following question: "Did I comply with the exercise regimen in the past 7 days?" This information will be collected weekly during the exercise program and will continue to be collected biweekly during the 12-mo follow-up period. A research assistant will call the participants by phone every 2 weeks during the follow-up period to remind them to record their exercise participation.
	Frailty status	Fried Frailty Index[10]	Including 5 criteria[c]: An unintentional loss of 10% of body weight in the past year. Exhaustion, determined by a "yes" response to either "I felt that everything I did was an effort" or "I could not get going in the last week." A slow walk time, with an average walking speed in the lowest quintile, stratified by median body height. Reduced grip strength, with maximal grip strength in the lowest quintile, stratified by the body mass index quartile. Score on the Chinese Version of the Physical Activity Scale for the Elderly (PASE-C) in the lowest quintile (ie, ≤30 for men and ≤27.7 for women).
	Physical activity level	Chinese Version of the Physical Activity Scale for the Elderly (PASE-C)[54]	A 10-item scale to measure self-reported occupational, household, and leisure activities for the last week. Its total score is calculated by multiplying the amount of time spent in each activity (h/wk) by the weight of the preset item. The PASE-C has been shown across different studies to be a reliable and valid instrument.[55,56]
	Depressive mood	Chinese Geriatric Depression Scale (C-GDS)[47]	A 15-item scale to measure the presence of depressive symptoms. Scores of 0–4, 5–9, and 10–15 indicate normal, mild, and moderate to severe depressive moods, respectively. The C-GDS is commonly used in both clinical and research settings and has been shown to have good reliability and validity.[47,57]

[a]All outcome measures will be collected at baseline (T0), the midpoint (T1) (week 8) of the program, and then at 1 wk (T2), 6 mo (T3), and 12 mo (T4) after the program.

[b]Information on exercise adherence among participants in the combined and exercise groups will be monitored weekly via an exercise diary.
[c]The presence of ≥3 criteria indicates frailty, and a "yes" response to either of the exhaustion questions indicates exhaustion.

Figure 1.

Overview of the combined intervention. HAPA = health action process approach.



Week		1-2	3	4-16	2 and 6 months after completion of the entire program
HAPA Phase		Phase 1 Goal Initiation	Phase 2 Plan Formation	Phase 3 Action Execution	
Intervention Component	Behavioral Change Enhancement Program	2 sessions	1 session	3 sessions: 1 session per month in weeks 4, 8, and 12 (ie, the first week of each month in the action execution phase)	2 booster sessions: 1 session 2 months after completion of the entire program and 1 session 6 months after completion of the entire program
	Exercise			12-week center-based exercise program of balance training, resistance exercises, and aerobic training Physical therapist tailor-made individualized home-based exercise regimens for the participants on the basis of individual physical assessments at weeks 4, 8, and 12	Continue to regularly practice the exercises at home

Figure 2.

CONSORT diagram of the cluster randomized controlled trial. The exercise (EXER) group will receive exercise training and health talks only; the combined (COMB) group will receive the 16-wk combined intervention consisting of individualized exercise training and the behavioral change enhancement program plus 2 booster sessions at 2 and 6 mo after the program. *Baseline and outcome assessments: fatigue, physical endurance, exercise self-efficacy, Fried Frailty Index, habitual physical activity, depressive mood, and exercise adherence (only for the exercise [EXER] group and the combined [COMB] group). HAPA = health action process approach.