**Abstract**  
Physical inactivity contributes to type II diabetes, cardiovascular disease, depression, dementia, and cancer, defined as the “diseasome of physical inactivity”; however, there is no exercise training regimen broadly available in the field to prevent such diseasome. The reasons are that there is no database on the effects of exercise training according to interindividual variations in physical fitness, disease, and genetic background. The authors have developed interval walking training, a portable calorimeter, and the e-Health Promotion System, which enables one to develop a database to provide the most appropriate exercise prescription for individuals to prevent diseasome. Also, it will enable exercise prescriptions to evolve to the level of the current nutritional prescription system which is broadly used in hospitals and health centers by dieticians and nurses and supported by national health insurance.

**Keywords**: lifestyle-related disease, diseasome, exercise prescription, interval walking training, IT network, genomes

**Introduction**

Physical fitness decreases gradually and unconsciously with aging, similar to a person on a raft floating downstream. This decrease in physical fitness has been suggested as a fundamental and common cause of many age-associated diseases: hypertension, hyperglycemia, obesity, and dyslipidemia; and exercise training has been recommended for their prevention. To attain these effects, exercise training should be performed with a subjective feeling of “somewhat hard” intensity for more than 30 min per day, if possible, every day, similar to trying to paddle the raft back upstream; however, it may be difficult for many people to accomplish this. Against this difficulty, we have developed an interval walking training system broadly available to middle-aged and older people according to the American College of Sports Medicine (ACSM) guidelines. Here, we review the ACSM exercise prescription, and report the effects of interval walking training on physical fitness and lifestyle-related diseases.

**Physical fitness with aging**

Physical fitness peaks in our twenties and, thereafter, it gradually decreases by 5-10% per decade. When it has decreased to less than 25% of the peak level, we are not able to live independently. We call this as the functional disability threshold. Indeed, it has been suggested that the cross-sectional area of the thigh muscle in our eighties decreases to ~50% of what it was in our twenties. In addition, maximal aerobic capacity (VO_{2max}) in our twenties is ~45ml/kg/min (0.23kcal) but decreases to ~30ml/kg/min (0.15kcal) in our sixties, and further decreases to ~10ml/kg/min (0.05kcal) in our eighties. These decreases in physical fitness have been suggested to be caused by senile muscle atrophy, called sarcopenia, which is thought to be caused by similar genetic mechanisms of aging that cause increased gray hair and wrinkles.

**Physical fitness and age-associated diseases**

It is interesting that health care costs increase with the decrease in physical fitness with aging. Pedersen has suggested that the cross-sectional area of the thigh muscle in our eighties decreases to ~50% of what it was in our twenties. In addition, maximal aerobic capacity (VO_{2max}) in our twenties is ~45ml/kg/min (0.23kcal) but decreases to ~30ml/kg/min (0.15kcal) in our sixties, and further decreases to ~10ml/kg/min (0.05kcal) in our eighties. These decreases in physical fitness have been suggested to be caused by senile muscle atrophy, called sarcopenia, which is thought to be caused by similar genetic mechanisms of aging that cause increased gray hair and wrinkles.
mental cause of these diseases is low muscle metabolism and, therefore, these diseases are known as “diseasomes of physical inactivity”. Moreover, since the syndrome is spread throughout communities where people share similar lifestyles, it may be regarded as a type of infectious disease. Accordingly, a community-based exercise prescription system to prevent this is recommended.

**Exercise training based on individual physical fitness**

Exercise training is the most effective strategy to prevent the deterioration of physical fitness with aging but it should be prescribed according to trainees’ individual fitness levels. For example, before starting training to increase muscle strength (resistance training), trainees have to have the muscle strength of their target joints determined by trainers in a gym by measuring the maximal dumbbell weight that they can lift once, called one repetition maximum (1RM). Then, they are recommended to lift a dumbbell weight of 50-80% 1RM, at >1 set of 3-15 times/day, 2-3 days/week. In addition, they are recommended 1) to have a no-training day between the training days, 2) not to perform the training more than 3 days/week, and 3) to increase the dumbbell weight gradually to the target level over 1-2 months to prevent any muscle injuries due to over training.

On the other hand, if trainees have no access to machines and trainers’ services in a gym, they can perform push-ups and squats using their body weight and resistance exercise using a rubber band to increase muscle strength. They are recommended to perform training at a frequency that they feel to be “hard” for a set, 1-2 sets/day, 3-7 days/week. The frequency of “hard” is 2-3 times below the maximal frequency or the rate of perceived exertion (RPE) of 15-16. The RPE, also called the Borg Scale, is defined as 6 points for “very very light” and 20 points for “very very hard”. Whether one uses machines or not, the thigh muscle strength of the target joint is expected to increase by 10-110% after following the above resistance training regimen for 3-6 months.

Similar to resistance training, before starting training to increase aerobic capacity (aerobic training), trainees have to have their capacity checked by professional trainers in a gym by measuring the oxygen consumption rate during graded exercise on a cycle ergometer or treadmill. In cycle ergometer exercise, the intensity is increased by 60 watts every 3 min from 0 watts to the maximal level at which the trainee is exhausted, during which period the oxygen consumption rate, carbon dioxide production rate, and heart rate are measured. It was determined that the exercise intensity had reached the maximal level when 3 of the 4 criteria were fulfilled: 1) the trainee cannot continue to pedal at a given rhythm of 60 cycles/min, 2) the heart rate reaches the age-predicted maximal heart rate (220 – age, measured in beats/min), 3) the respiratory quotient has increased to more than 1.1, and 4) the oxygen consumption rate does not increase despite increased exercise intensity.

On the other hand, if trainees have no access to machines and trainers’ services in a gym, they are able to roughly estimate their maximal aerobic capacity by using the “12-min running test”, “20-m shuttle run test” or “walking or running at a given RPE”. For example, using RPE, trainees walk or run on flat ground for 3 min with the subjective feeling of “somewhat hard,” equivalent to 13 points of RPE, the distance is measured, the speed (m/min) is calculated, the oxygen consumption rate is determined from Table 1, and then maximal aerobic capacity is estimated by multiplying the value by 1.54 (20/13).

After determining VO₂max, whether with machines or not, trainees may exercise at the intensity of 60-70% VO₂max, 30-60 min/day, 4-7 days/week. They may start exercise at 50% VO₂max for the first month, and then gradually increase the intensity to 60% for the 2nd month, and end at 70% VO₂max for the 3rd month; but they should not exceed 85% VO₂max. When they perform exercise training using machines for this purpose, for example, using a cycle ergometer, it is easy to determine the intensity; however, when they perform other styles of exercise, such as swimming, tennis, and cycling in the field, it is difficult to know the intensity. In that case, they can determine the target intensity by monitoring the heart rate during exercise. The target heart rate during exercise can be calculated from the equation [target heart rate = (age-predicted peak heart rate – heart rate at rest) x (0.6-0.7) + heart rate at rest], equivalent to the 80-90% age-predicted heart rate.

If they perform the exercise at this intensity, equivalent to 13 points of RPE, 30-60 min/day, 4-7 days/week, for 3-6 months, their VO₂max is expected to increase by 10-20%. When the energy expenditure per day is converted to calories, it is the equivalent of 300-600 kcal for trainees in their twenties, 200-400 kcal for those in their sixties, and 50-100 kcal for those in their eighties; and the energy expenditure per week is 1200 kcal, 800 kcal, and 200 kcal, respectively.

**Interval walking training**

The exercise regimens stated above have been thought to prevent age-associated diseases: hypertension, hyperglycemia, obesity, and dyslipidemia; however, it might be difficult for middle-aged and older people to perform such exercise training regimens at a given intensity regularly. We recently found in middle-aged and older people that 1) not only maximal aerobic capacity but also thigh muscle strength increased after aerobic exercise training for 5 months using a cycle ergometer and 2) that we were able to estimate maximal aerobic capacity by graded walking in the field without using machines such as a treadmill and cycle ergometer. Accordingly, we have applied these findings to exercise prescription with "in-
Table 1. Estimation of VO$_{2\text{max}}$ and maximal workload from the measurements in the field.

<table>
<thead>
<tr>
<th>VO$_{2\text{max}}$ (ml/kg/min)</th>
<th>12-min running distance, m</th>
<th>20-m shuttle run, frequency</th>
<th>Cycling intensity, watts/kg</th>
<th>Running speed, m/min</th>
<th>Walking speed, m/min</th>
<th>Maximal work load, kcal/kg/min</th>
<th>Maximal work load, METs</th>
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VO$_{2\text{max}}$ (ml/kg/min) = 12-min running distance (m) x 0.021 – 7.233
= 20-m shuttle run (frequency) x 0.225 + 26.07
= Running speed (m/min) x 0.119 +3.5
= Walking speed (m/min) x 0.103 +3.5 (<99m/min)
= [Walking speed (m/min) x 0.392-28.2] +3.5 (>100m/min)
Maximal work load (kcal/kg/min) = VO$_{2\text{max}}$ (ml/kg/min) x 0.005
Maximal work load (METs) = VO$_{2\text{max}}$ (ml/kg/min)/ 3.5

Interval walking training (IWT)” for middle-aged and older people in the field, named the Jukunen Taikudaigaku Project, starting in 1997 and since then, we have accumulated a database regarding the effects of IWT on physical fitness and the indices of lifestyle-related diseases. This project has been organized by the Non-Profit Organization of Jukunen Taikudaigaku Research Center (JTRC) since 2005, and detailed information on the project is given by their web site10) As in Fig. 1, the project has four features as follows:

1) Interval walking training (IWT)

Before starting training, peak aerobic capacity (VO$_{2\text{peak}}$) for walking was determined in individual participants. Accordingly, they walked at subjectively slow, intermediate, and fast speeds for 3 min each, during which time energy expenditure and heart rate were measured every 5 sec by triaxial accelerometry and by the near infrared ear pick-up method (JD Mate: Kissei Comtec, Matsumoto), respectively, and the values for the last 30 sec of fast walking were averaged and adopted as VO$_{2\text{peak}}$ and HR$_{\text{peak}}$.

After this, participants were instructed to repeat IWT at their preferred time and place at low and high intensity walking alternately at the target levels of ~40% and ≥70% VO$_{2\text{peak}}$, respectively, for 3 min each, ≥4 days/week$^1$, for 12 weeks. During IWT, energy expenditure was monitored with a tri-axial accelerometer (JD Mate) carried on the mid-clavicular line of the right or left waist. A beeping signal from the device alerted participants when a change of intensity was scheduled and another sound let them know when the intensity of fast walking had reached the target level. Participants visited a local community office every 2 weeks, and data from the tracking devices were transferred to a central server computer. Then results were sent back to participants and they received instructions from trainers.

As a result, we found that VO$_{2\text{peak}}$ increased by ~10% and knee extension and flexion forces increased by 17% and 13%, respectively, while systolic and diastolic pressure decreased by ~10mmHg and ~5 mmHg, respectively,
after 5 months of training. On the other hand, standard walking training of moderate intensity continuous walking at 40% VO$_{2\text{peak}}$ for 60 min/day, 4 days/week, for 5 months, produced only minimal results similar to those of persons remaining sedentary during the same period$^{11}$. Moreover, we found in the study that VO$_{2\text{peak}}$ was significantly correlated with isometric knee extension force ($R^2 = 0.49, P<0.0001$), suggesting that thigh muscle strength is a key determinant for VO$_{2\text{peak}}$ in subjects of this age. Furthermore, these results indicate that increased VO$_{2\text{peak}}$ induces a marked reduction in blood pressure.

Recently, using these techniques, we examined the effects of IWT on physical fitness and the indices of lifestyle-related diseases (LSD) in 198 men and 468 women aged ~65 years old$^{12}$. They performed IWT, ~60 min/day, ~4 days/week, for 4 months on average. We assessed the scores of LSD before and after IWT according to the criteria in the health care guideline for Japanese by the government (Health Insurance Bureau, Ministry of Health, Labor, and Welfare, Japan 2007); 1) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, 2) triglyceride ≥150 mg/dl or blood high density lipoprotein cholesterol ≤40 mg/dl, 3) blood glucose ≥100 mg/dl, 4) BMI ≥25 kg/m$^2$; therefore, the full score was 4 points when all criteria were met.

To analyze the results, we divided the subjects into 3 groups according to VO$_{2\text{peak}}$ in women (Fig. 2-A) and men (Fig. 2-B). The LSD scores decreased as VO$_{2\text{peak}}$ increased and, moreover, when VO$_{2\text{peak}}$ increased after training, the LSD score decreased in both genders. Furthermore, when
looking at the LSD score for each criterion in women (Fig. 3-A) and men (Fig. 3-B), the hypertension score was 0.7-0.8, suggesting that 70-80% of subjects met the criterion in both genders. Similarly, 40-60% and 20-50% of subjects had hyperglycemia and high BMI, respectively, in both genders. After training, subjects meeting each criterion showed a decrease of 5-30% in hypertension, 10-40% in hyperglycemia, and 10-30% in high BMI, but with no significant reduction in blood lipids. These results suggest that increased \( \text{VO}_2\text{peak} \) decreased blood pressure, blood glucose, and BMI in that order while the effects on blood lipids were modest.

2) Three-dimensional accelerometry

The authors have developed a new portable calorimeter with which energy expenditure can be precisely measured even when walking on inclines\(^3\). First, \( \text{VO}_2 \) was measured by respiratory gas analysis and vector magnitude (VM, G) from triaxial acceleration in middle-aged and older men and women aged ~63 years during graded walking on a treadmill while the incline was varied from -15% to +15%. Participants walked at subjectively slow, moderate and fast speeds on level and uphill inclines and, in addition, at their fastest speed at 0% incline. Similarly, they then walked on downhill inclines for 3 min each. The regression equation to estimate \( \text{VO}_2 \) from VM and the theoretical vertical upward speed (\( \text{Hu} \), m/min) and downward speed (\( \text{Hd} \), m/min) for the last 1 min of each trial as was determined as \( \text{VO}_2 = 0.0044\text{VM} + 1.365\text{Hu} + 0.553\text{Hd} \).

\[
\text{VO}_2 = 0.0044\text{VM} + 1.365\text{Hu} + 0.553\text{Hd}
\]

**Fig. 2** Total lifestyle-related disease (LSD) score and peak aerobic capacity for walking (\( \text{VO}_2\text{peak} \)) before and after interval walking training in women (A) and men (B). When the subjects were divided equally into 3 groups according to \( \text{VO}_2\text{peak} \), the score was lower in higher \( \text{VO}_2\text{peak} \) groups. After interval walking training for 4 months, the score decreased as \( \text{VO}_2\text{peak} \) increased in every group. From [12].

**Fig. 3** Lifestyle-related disease (LSD) score for each criterion; hypertension, hyperglycemia, high BMI, and dyslipidemia, in women (A) and men (B). When the subjects were divided equally into 3 groups according to \( \text{VO}_2\text{peak} \) before training, the score was higher in the order of hypertension, hyperglycemia, high BMI, and dyslipidemia in every group. After training, all scores except for dyslipidemia decreased by 10-40%. From [12].
Second, to validate the precision of the equation, VM and altitude changes were measured - with a portable device (JD Mate) equipped with a triaxial accelerometer and a barometer - in middle-aged and older subjects walking on an outdoor hill, and the estimated VO₂ by the equation stated above was compared with the value simultaneously measured by respiratory gas analysis. It was found that the estimated VO₂ (γ) from the equation was identical to the VO₂ measured by respiratory gas analysis during walking on an outdoor hill. Thus, the authors were able to develop a device for estimating VO₂ precisely during walking regardless of the geography. Moreover, subjects can perform high-intensity exercise training ≥70%VO₂peak not only by fast walking on a flat surface but also by slow or moderate walking on inclines or stairs.

3) e-Health Promotion System

Another reason hindering the extension of a nationwide exercise prescription for individuals is the cost for trainers. To solve this problem, the authors have been developing the e-Health Promotion System, as shown in Fig. 11. The participants in the program visit local health care institutes near their homes - a local community office and a drug store, every 2 weeks, to transfer their walking records from the JD Mate to a central server computer, and receive a trend graph of their achievements. Based on records from the DB regarding the effects of IWT on physical fitness over a 5-month period, the indices of LSD in 4,000 subjects, and other data, the staff (nurses, dietitians, pharmacists or trainers) give the participants exercise and nutritional prescriptions. If participants have a computer in their own home, they are able to receive the same service over the Internet without going out.

4) Individual genomic variance

Recently, the authors started to analyze individual genomic variance in relation to inter-individual variation in response to IWT14,15. Masuki et al.15) assessed whether single nucleotide polymorphism rs1042615 of the vasopressin V1a receptor altered the indices of LSD in subjects; and, if so, whether it also altered the effects of IWT. CC, CT, and TT carriers of rs1042615 (42, 118, and 64 men; 113, 263, and 154 women, respectively) performed IWT, ≥4 days/wk, for 5 months. Before IWT, BMI and diastolic blood pressure for men were both higher in TT than in CC; however the differences disappeared after IWT despite similar training achievement between groups. Moreover, after IWT, BMI and DBP decreased more in TT than in CC with a greater decrease in low-density lipoprotein (LDL) cholesterol in TT than CC. The decreases in DBP and LDL cholesterol were still greater in TT even after adjustment for their pre-training values. On the other hand, for women, these parameters before IWT and changes after IWT were similar between CC, CT, and TT. Thus, polymorphism rs1042615 of the V1a receptor altered BMI and DBP in middle-aged and older men, and the training-induced responses of DBP and LDL cholesterol; whereas women did not show any of these responses. These results suggest that single nucleotide polymorphism rs1042615 of the vasopressin V1a receptor was involved in inter-individual variance in responses to IWT in middle-aged and older men.

According to the outcome of these studies, a computer program is being developed to predict the effects of IWT on physical fitness and the indices of LSD according to not only physical, but also genetic characteristics of participants before training. If the program becomes available to staff in the field, they will be able to give participants more individual exercise prescriptions even though they are not specialized in this subject. This would increase the number of participants in IWT.

**Future direction of exercise prescription in the field**

In Japan, nutritional prescriptions to prevent lifestyle-related diseases have been widely given in hospitals and health centers by dietitians and nurses sponsored by health insurance; however, the use of exercise prescriptions has not reached this level. The success of nutritional prescriptions may be partially because dietitians have successfully determined the minimal requirement of individual nutrients for our daily life and presented the standards in physical/chemical units based on the recommended daily allowance (RDA). On the other hand, since there are so many styles of exercise, and since less attention has been paid to measuring energy expenditure in a large population of people in the field, it has been difficult to prescribe exercise training based on the cost vs effect relationship; however, as stated above, if the target of exercise expenditure (exercise intensity) for all types of exercise is determined according to individual physical fitness level, and exercise intensity and energy expenditure during training are monitored in the field, it may enable the promotion of exercise prescriptions to the same level as nutritional prescriptions supported by national health insurance.

In summary, interval walking training and the related system explained above, which has been developed based on ACSM guidelines, have enabled exercise prescriptions for individual physical fitness to become broadly available in middle-aged and older people. If a sufficiently large database can be built on the cost and effect relationship of such training, it will make it possible for exercise prescriptions to be supported by health insurance, as are nutritional prescriptions in Japan.
Acknowledgments

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