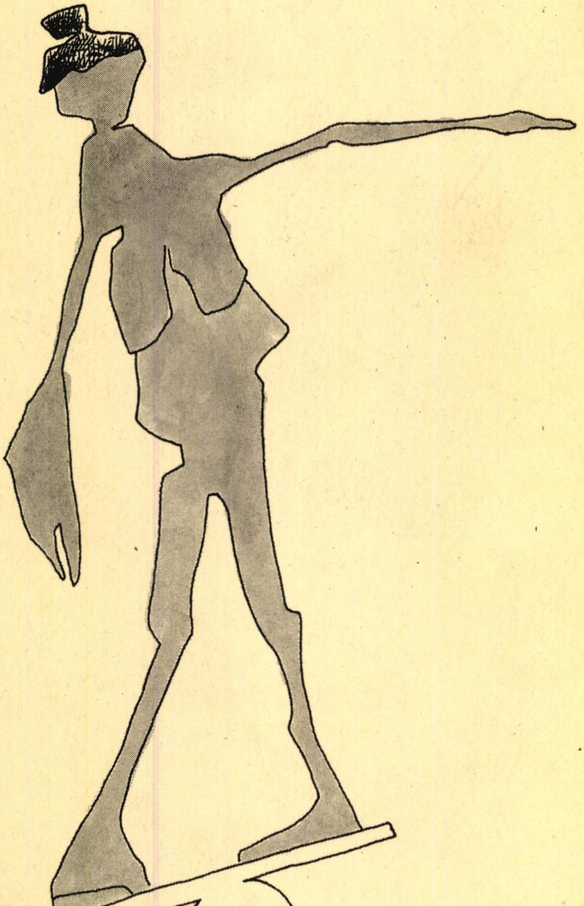
Aging in balance

Physical exercise and nutrient dense foods for the vulnerable elderly



Marijke Chin A Paw

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Stellingen

1. Stilstand leidt tot achteruitgang *(dit proefschrift).*

2. Krachttraining dient de spier; functionele training de gehele mens *(o.a. dit proefschrift).*

3. Wat je waarneemt is niet altijd meetbaar *(dit proefschrift).*

4. Lobi na dresi *(Aandacht geneest, Surinaams gezegde).*

5. Plantaardige voeding is aardig voor plant, mens en dier.

6. 'Those who cannot find time for exercise will most certainly find time for illness' *(unknown).*

7. Non multa sed multum *(Niet het vele is goed maar het goede is veel, uit de lessen van Opa van der Sloot).*

8. True enjoyment comes from activity of the mind and exercise of the body *(Humboldt).*

9. Desoriëntatie is het verlies van het Oosten *(S. Rushdie).*

10. Dans speelt met de zwaartekracht van passiviteit.

11. De 'ritualiteit' van de Oosterse keuken balanceert en activeert lichaam en geest.

12. Het is wetenschappelijk bewezen dat een hommel gegeven het zware gewicht van zijn lichaam en het geringe draagvlak van zijn vleugels onmogelijk kan vliegen. De hommel weet het echter niet en vliegt *(G. Burssens).*

Stellingen behorende bij het proefschrift *'Aging in balance: physical exercise and nutrient dense foods for the vulnerable elderly'*
Marijke Chin A Paw, Wageningen 19 oktober 1999

The study presented in this thesis was funded by the Dutch Dairy Foundation on Nutrition and Health, in Maarssen, The Netherlands. The intervention study was additionally supported by the Dutch Health Research Council, The Hague, The Netherlands, grant number 28-2748. The study was part of the research program of the Graduate School VLAG.

Financial support by the Wageningen University and the Dutch Dairy Foundation on Nutrition and Health for the printing of the thesis is gratefully acknowledged.

Chin A Paw, Marijke

Aging in balance - Physical exercise and nutrient dense foods for the vulnerable elderly. Thesis Wageningen Universiteit – With ref. – With summary in Dutch
ISBN 90-5808-125-7

Illustrations Lars van Es

Printing Ponsen & Looijen bv, Wageningen, The Netherlands

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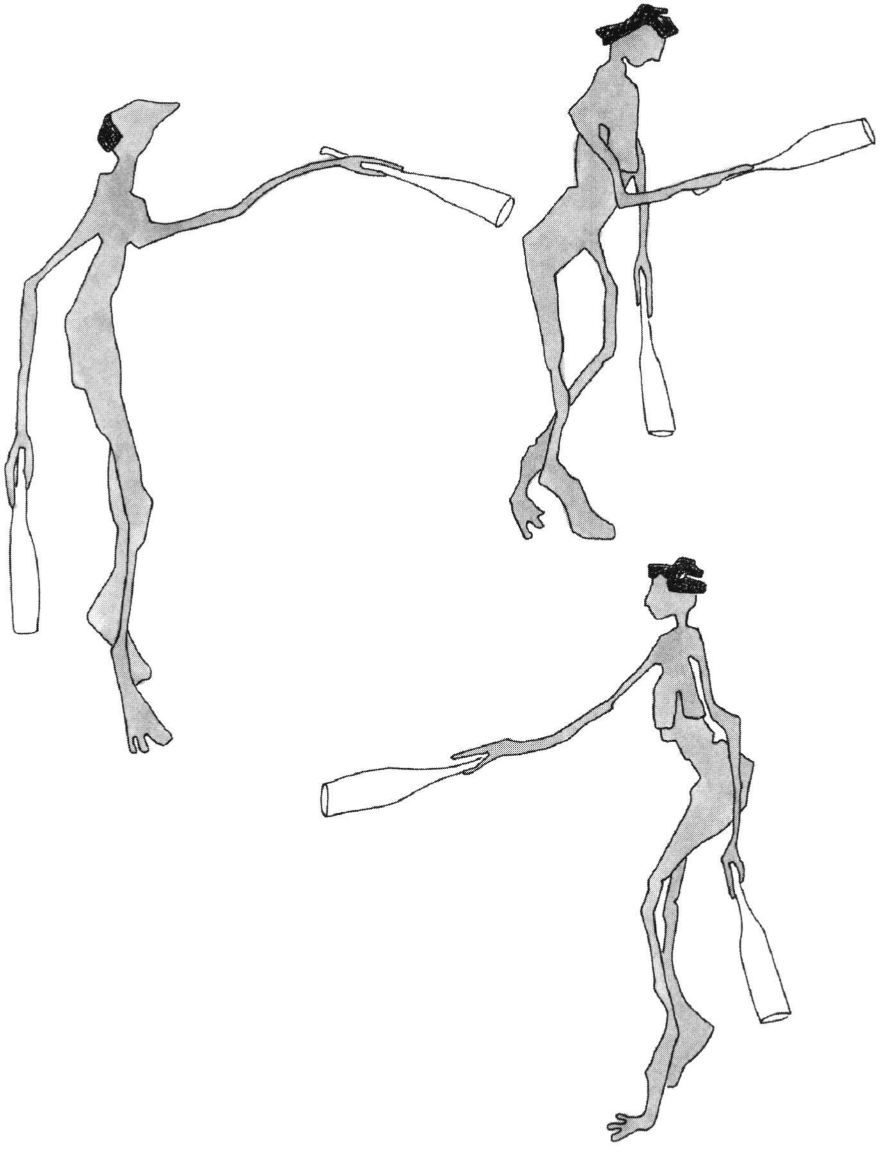


Life expectancy in the Western world has shown an impressive increase during this century. In 1994 the average life expectancy in the Netherlands was 74.6 years for men and 80.3 years for women. Not all of these years are expected to be spent in *good health*, though: in 1994 the number of years in perceived good health (healthy life expectancy) was 60.1 years for women and 60.3 years for men.[1] The number of years without disabilities (disability-free life expectancy) was 62.7 for women and 60.8 for men.[1] Health status is thus not optimal in the remaining years. This has led to a growing awareness of the fact that prevention and health care for elderly people should aim not only to prolong life but to improve its quality as well.

Two promising strategies for improving the quality of life or health status of older adults are physical exercise and nutrient supplementation. Both regular physical activity and an adequate dietary intake are recognized as essential and mutually interacting factors for optimal health. Because of their limited reserves, resulting in an increased susceptibility to disability and dependency, frail older persons are at an increased risk of a decline in quality of life. For this reason they may particularly benefit from preventive interventions related to physical activity and diet. The design of possible preventive interventions deserves special attention due to the frailty element: programs need to be tailored to specific needs and capabilities.

This thesis focuses on the effectiveness of a specifically designed exercise and nutritional program. The effects of these programs on functional status, psychological well-being and social contacts have been studied in a large scale randomized controlled trial. Effects on immune response are also addressed. The complementary thesis of Nynke de Jong describes the effects of both interventions on nutritional and biochemical health indices.[2]

This introduction briefly explains the concept of frailty, the preventive interventions and the different outcome measures. The rationale of the thesis, the design of the intervention study and the outline of the thesis will also be addressed.

Physical frailty

The term *frailty* is frequently used in geriatric medicine and gerontology to describe situations in which aging, disease and other factors such as a lack of physical activity and inadequate nutrition make some people vulnerable (see Figure 1.1). There is no generally accepted definition or standardized criteria to identify frailty.[3;4] The term is often used to denote people living in institutions or those with an impaired functional status. This muddles the distinction between frailty and functional dependence. Others regard frailty as a *precursor state* to disability and dependence on others for daily activities: *a state of reduced physiologic reserve associated with an increased susceptibility to disability.*[5] This definition includes those who are already dependent on others as well as those who are at a high risk of becoming dependent. Frailty can thus be seen as a position on a continuum from sturdy and robust at one end to a little frail, moderately frail and very frail at the other.[6] This position is not static: for some people frailty might be temporary, for example when following a serious illness or losing a loved one. For others it might be permanent, its degree changing over time.

In order to evaluate preventive interventions it is necessary to identify frailty, preferably at an early stage, before disability and institutionalization have occurred. In this thesis we focus on frail older people who still live at home, but who due to their reduced reserves are at an increased risk of dependency. This group is likely to be underrepresented in general surveys of the elderly because recruitment tends to favor enrollment of healthier, more active and better nourished subjects. A frail population will therefore be more difficult to reach and its recruitment will take more effort and time. Although it would have been easier to study institutionalized elderly, we have chosen to study the potential benefit of intervention on independently-living frail elderly. Most older people live at home and wish to remain doing so. Those 'at risk' of functional dependence, if successfully identified, may particularly benefit from intervention programs meant to prevent or slow down a further decline in function. Improving their functional status may prevent or postpone the need for undesirable and expensive institutionalization and home health care provisions, and is therefore of the utmost relevance.

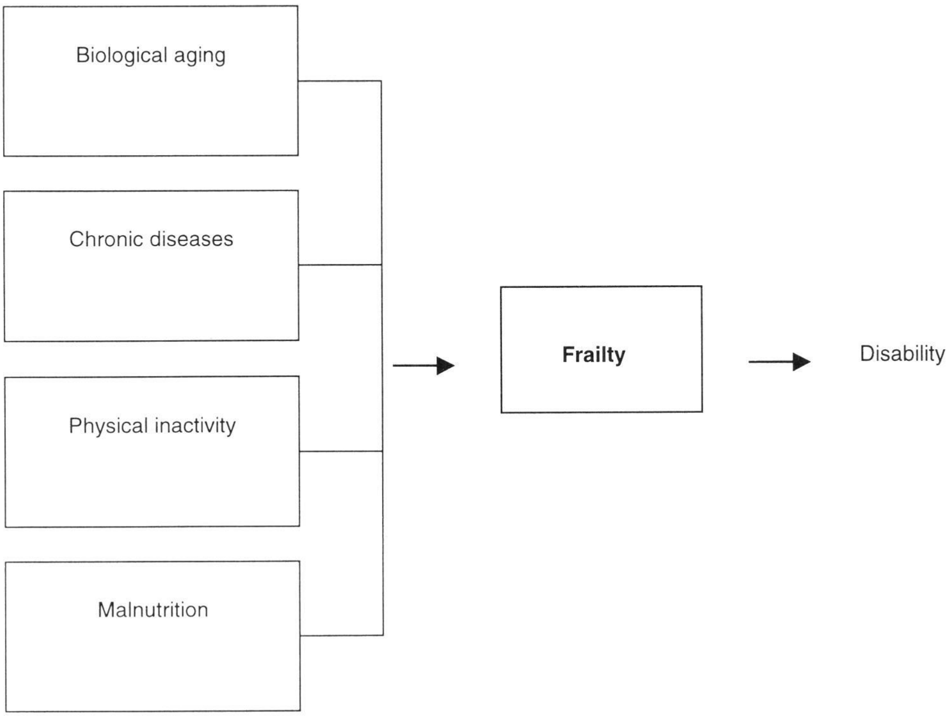


Figure 1.1 Conceptual model of frailty

Causes of frailty

In addition to biological aging and chronic diseases, physical inactivity and dietary inadequacies are the main contributors to physical frailty (Figure 1.1).[5;7] In general, physical activity as well as diversity in types of activity decline with age.[8] In the Netherlands in 1990, 57 percent of people aged 65 and over were considered to be physically inactive during leisure time: this was defined as not participating in sports or other types of physical activity such as walking, cycling or gardening.

Among people aged 35-44 this percentage is 29%.[9] Due to lower energy expenditure, lower activity levels may result in a decrease in food intake, which in turn may result in nutritional inadequacies. Both an inadequate nutritional state and inactivity have been associated with a loss of muscle mass and muscle function, resulting in functional limitations and an even further decline in activity level: a downward process thus evolves.[5;7]

Prevention of frailty

Appropriate exercise or multi-vitamin/mineral supplementation may be effective in preventing or even reversing this downward process of frailty. The combination of both may be even more effective. Figure 1.2 summarizes the hypothesized relation between physical activity, diet and health.

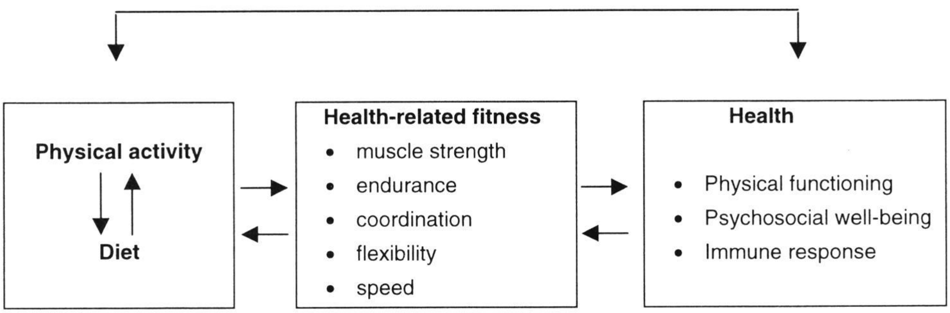


Figure 1.2 Conceptual model for the relation between physical activity, diet and health as studied in the present thesis (based on Bouchard et al)[10]

Physical exercise

The level of physical activity is an important and consistent predictor of disability.[11;12] By improving physical fitness, exercise could ameliorate certain aspects of health status such as physical functioning, psychosocial well-being and immune response. In addition, certain types of exercise are hypothesized to lead to a direct improvement of physical function or well-being (Figure 1.2). An example is the restoration of performance of daily activities such as walking or stooping. Next to these physical mechanisms, exercise could also improve daily functioning and well-being through psychological mechanisms. Subjects are stimulated to lead a more active lifestyle, may improve their self-efficacy and may learn to enjoy physical activity.

As a result, exercise has been advocated as a means of primary and secondary prevention of frailty and disability in later life.[7;12;13] Recent research has demonstrated the trainability of the frail and oldest old,[14-16] but literature on design and feasibility of exercise protocols adapted to a frail population is scarce. In addition, convincing this vulnerable group to initiate and sustain an exercise program is very difficult. Our goal was therefore to develop an exercise program that is not only effective, but also enjoyable and easily accessible. The uniqueness of our program is the focus on skills training, meaning that the specific activities required for independence in daily activities were practiced. These daily activities require sufficient muscle strength to carry, lift, stand and walk, as well as the ability to reach, bend and grasp. Exercises therefore focused on an efficient use of all motor qualities - strength, speed, endurance, flexibility and coordination - which were trained by performing motor actions like walking, kneeling, reaching, standing up from a chair, catching, and kicking. These activities were performed in the context of motor behavior such as games and daily activities. The design of the exercise program is described in detail in *Chapter 4*.

Nutrient dense foods

Low mobility and activity, poor appetite, dietary restrictions and social isolation are frequent characteristics in frail elderly and may lead to a low food intake.[17] Low dietary intake increases the risk of nutrient inadequacies. Reduced absorption, increased excretion, poor utilization and nutrient-drug interactions may further contribute to potential nutritional problems.[18] Nutritional inadequacies have been associated with decreased body strength, immune response and indicators of quality of life.[19;20]

As mentioned before, an inadequate nutritional state is an important contributor to frailty. Due to poor appetite and low dietary intake, sufficient dietary improvement through regular food alone is very difficult.[17] One approach to improve nutrient status in this group may be consumption of nutrient dense foods such as enriched or fortified foods. Since intake is often low for a number of nutrients and the action of many nutrients is complementary, it is more relevant to determine the effects of improving the general micronutrient state than the effects of isolated individual nutrients.

A variety of nutrient dense food products has been developed for the intervention study described in this thesis. Specific products such as dairy desserts and fruit juices were enriched with vitamins and minerals for which elderly people's intake is frequently low. Consumption of two of these products provided 100% of the Dutch recommended daily allowances (RDA) of vitamins D, E, B1, B2, B6, folic acid, B12 and C, and 25-100% of the Dutch RDA of calcium, magnesium, zinc, iron and iodine. Because of their limited mobility, the energy expenditure of frail elderly is generally low. For this reason no extra energy was added. In addition, we also wanted to examine the effects of both interventions on appetite and spontaneous energy intake. We preferred enriched food products instead of vitamin pills because consumption of tasty food products is more attractive than taking yet another tablet. A detailed description of the contents and the product appraisal can be found in the complementary thesis of Nynke de Jong.[2]

Exercise and nutrient dense foods

An interaction between exercise and diet is also imaginable. The effects of exercise may be different, depending on the underlying nutritional state. Conversely, increased energy expenditure through physical activity may improve appetite and dietary intake, thereby reducing the risk of nutritional inadequacies. Simultaneous intervention with both training and nutritional supplementation could provide even greater gains.

Outcome measures

This thesis deals with the effects of the above-mentioned interventions on indicators of health status or health-related quality of life in frail older people. In an aged population quality of life may be a more relevant outcome measure than morbidity and mortality. Quality of life also reflects information on severity and complications of diseases and their impact on daily functioning and well-being. Besides, the most prevalent diseases are often chronic and incurable. There is no standardized and ideal way to measure health-related quality of life. Health-related quality of life is generally considered to comprise three main domains: physical, psychological and social functioning. In the present thesis we focus on physical functioning in the physical domain and on subjective well-being and social contacts in the psychological and social domains. We will also be addressing the effects on cellular immune response (see Figure 1.3).

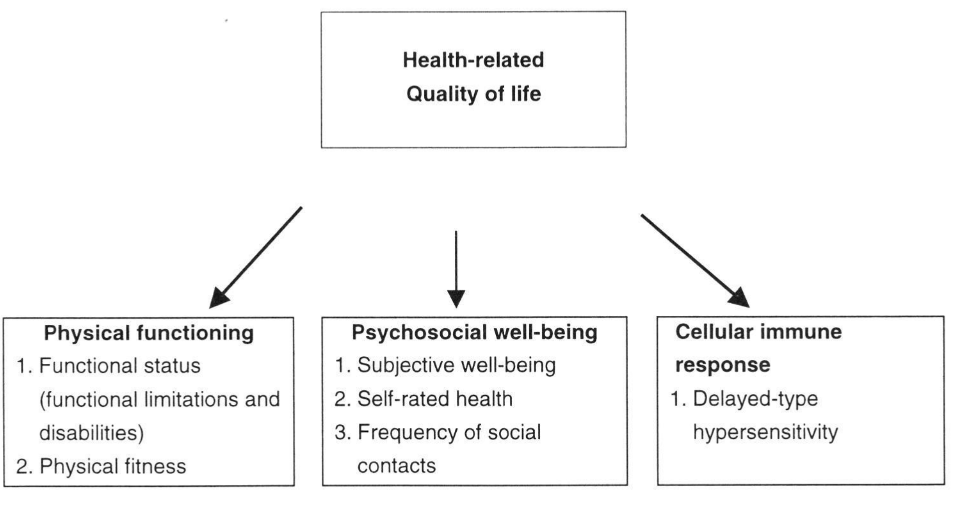


Figure 1.3 Operationalization of quality of life in the present thesis

Physical functioning is often operationalized by assessing physical disability in daily activities. We have also included functional limitations and physical fitness as indicators of physical functioning. Questions on an individual's subjective appraisal of their health and general well-being have been included as indicators of psychological functioning. The frequency of social contacts was assessed as a measure of social functioning. The effects of both interventions on cellular immune response have also been studied. As infectious diseases can have debilitating consequences for the elderly, prevention of the age-related decline in cellular immune response may beneficially affect their quality of life.

With regard to the frailty of the study population we have paid special attention to the applicability of the instruments in this vulnerable population group. We selected several instruments with demonstrated validity, reliability and demonstrated feasibility in an elderly population.

Physical functioning

Two components of physical functioning are addressed: functional status and physical fitness.

Functional status

Functional status refers to a person's ability to perform tasks and fulfill social roles associated with daily living across a broad range of complexity.[21] The ability to perform everyday physical activities is important for the quality of life of older people. In this thesis functional status was measured by physical performance tests and disabilities as reported by the respondents themselves. Both measures seem to have their own contribution to the assessment of functional status.[22] They reflect different steps in the disablement process. This process, as described by Verbrugge,[23] progresses from pathology to impairments, which in turn lead to functional limitations and disabilities.

Functional limitations are defined as restrictions in performing basic physical and mental actions used in daily life. Examples are restrictions in walking, lifting objects, and impaired eyesight, hearing and communication. Limitations are often measured by performance-based tests in which respondents are asked to perform tasks in a standardized or usual manner.

Disability is defined as an experienced difficulty doing activities in any domain of daily life in one's regular manner. Examples are dressing, eating, preparing meals, hobbies and other leisure activities. Disability can be measured in a simple, direct manner with self-reports about the degree of difficulty experienced when performing these activities. Disability refers to the expression of a functional limitation within a social context. Performance-based measures thus reflect functional limitations, whereas self-reported functional status reflects disabilities.[22]

Physical fitness

Fitness is highly associated with functional limitations and may be an important modifier in the subsequent onset of disability.[24] A certain level of physical fitness is required to perform daily physical activities. Physical fitness is defined as *the ability to perform muscular work satisfactorily* and includes the following components: morphologic factors (such as body composition, bone density, flexibility), muscular endurance (power, strength, endurance), motor ability (agility, balance, coordination, speed of movement) and cardio-respiratory capacity (submaximal exercise capacity and maximal aerobic power).[10] In this thesis we focus on several components of fitness: coordination (manual dexterity), speed of movement (reaction time), standing balance, flexibility (of the hip and spine and of the shoulder), and strength (hand grip and leg extension strength). Because of the high respondent burden of tests measuring submaximal exercise capacity and maximal aerobic power, these components were not included.

Until now many studies on exercise and frailty have focused on institutionalized elderly people and examined resistance strength training and muscle strength.[15;16;25] Less information is available on the effects of comprehensive exercise programs on the overall physical performance of independently-living frail individuals. Chandler et al[14] have observed improved chair rise performance as well as mobility tasks but no effects on balance, endurance or disability after 10 weeks of strength training. Because there is such specificity in training effects, improvements in overall physical performance probably require a comprehensive program in which the specific activities required for independence in daily activities are practiced.

This is, to our knowledge, the first controlled trial evaluating the effects of micronutrient supplementation on functional status. Cross-sectional studies suggest correlations between dietary intakes of vitamin B6, magnesium, potassium, and muscle capacity.[26] Two trials on muscle strength that examined supplementation with both macro and micronutrients found no effects on functional measures such as grip strength, gait or stair-climbing power.[15;27]

Psychological and social functioning

Just like frailty, well-being is difficult to operationalize. It may be related to self-esteem, cognitive functioning, personality and mood, including positive affects such as happiness, vigor and morale, and negative affects such as anxiety and depression.[28] The concept of *well-being* refers to more subjective internal states, including how people feel physically and emotionally, how they think about their health, and how they think about themselves and their lives. In this thesis psychological well-being was operationalized as the score on the Dutch Scale for Subjective Well-being of Older persons (SSWO).[29] This scale includes 30 items on health, self-respect, morale, optimism and contacts, and has been developed and validated for elderly persons. Self-rated health, relative health and frequency of social contacts were also assessed. Self-rated health describes how a person perceives his own health.[30] Strong and consistent associations between self-rated health and changes in functional status, health care utilization and mortality have been found.[31-33] Social contacts with family and friends can provide social and instrumental support and thereby contribute to well-being.

There is little experimental evidence of the beneficial effects of physical activity or micronutrient supplementation on subjective well-being, especially in frail elderly people.[28;34;35] Most studies have involved healthy young or middle-aged subjects or anxious or depressed populations, and used vigorous aerobic training, vitamin pills or supplements including both macro and micronutrients. Furthermore, findings are inconsistent partially due to methodological weaknesses such as small sample sizes, short intervention periods and the absence of an adequate placebo or control group.[28]

Cellular immune response

Considerable evidence indicates that aging is associated with an altered regulation of the immune system.[36] As immunocompetence declines, the incidence of infections, cancer and autoimmune disorders increases. Part of the age-related decline may be caused by nutritional deficiencies and/or decreased physical activity.[37;38] Consequently, nutritional or exercise interventions to enhance immune function or prevent its decline could result in a decrease in the incidence and mortality of some diseases and thereby improve quality of life in elderly people.

The effects of regular exercise on immunity in both frail and healthy elderly people are unclear. Cross-sectional studies have found significantly increased natural killer cell activity and T cell function in highly conditioned elderly subjects compared to age-matched untrained controls.[39] Nevertheless, two controlled intervention studies with resistance and cardiovascular training[39;40] failed to find any effects after 12 weeks of these types of training in healthy elderly subjects. Previous studies suggest that supplementation with multiple micronutrients improves cellular immune response in healthy elderly.[41;42] Because nutrient status, physical activity and immune response are impaired in frail elderly, a beneficial effect is more likely to occur and could be of greater clinical importance.

Rationale of the thesis

As more individuals live longer, it is of great interest to determine the effects and feasibility of interventions in improving health, functional capacity and well-being, especially of the most vulnerable segment of the population, the frail and very old. Two preventive interventions with great potential are exercise and micronutrient-enriched foods. Until now most research has been done in healthy or selected groups of frail institutionalized elderly. Frail elderly still living in the community are another vulnerable group at high risk of health deterioration who may particularly benefit from preventive interventions. Further, there is a lack of exercise programs feasible for widespread implementation and long-term adherence in frail populations. Data on such programs are also scarce. The health-related effects of enriched foods have hardly been studied, given the fact that they have become available only recently.

The objectives of this thesis are to investigate:

1. Criteria for the identification of frail elderly people;
2. Effects of a specific exercise and nutritional program on physical functioning, psychosocial well-being and immune response in frail independently-living elderly people;
3. Development of an exercise program for frail elderly people.

Design of the intervention study

The intervention study was a randomized controlled trial based on a two-by-two factorial design that permitted an assessment of the effects of the exercise and nutritional intervention, both independently and combined.

Figures 1.3a and 1.3b depict the study design. Subjects were recruited by mail from senior housing complexes, Meals-on-Wheels programs, home care organizations and general practitioners in the Wageningen area. To stimulate enrollment, study subjects were first invited to attend an informative meeting near their houses. The design of the study and programs was explained and we emphasized that the program was accessible for all mobility levels and that subjects were always free to withdraw. Transport to these meetings was arranged whenever necessary.

Those interested in participating were contacted later by telephone in order to check the following inclusion criteria: age 70 or older, requirement of care services such as home care or Meals-on-Wheels, not participating regularly in physical activities of moderate to high intensity, self-reported BMI below 25 kg/m^2 or involuntary weight loss, non-institutionalized, not having taken multivitamins for the last month, no terminal disease or rapidly deteriorating health status, and the ability to comprehend the procedures of the study (see Figure 1.3a).

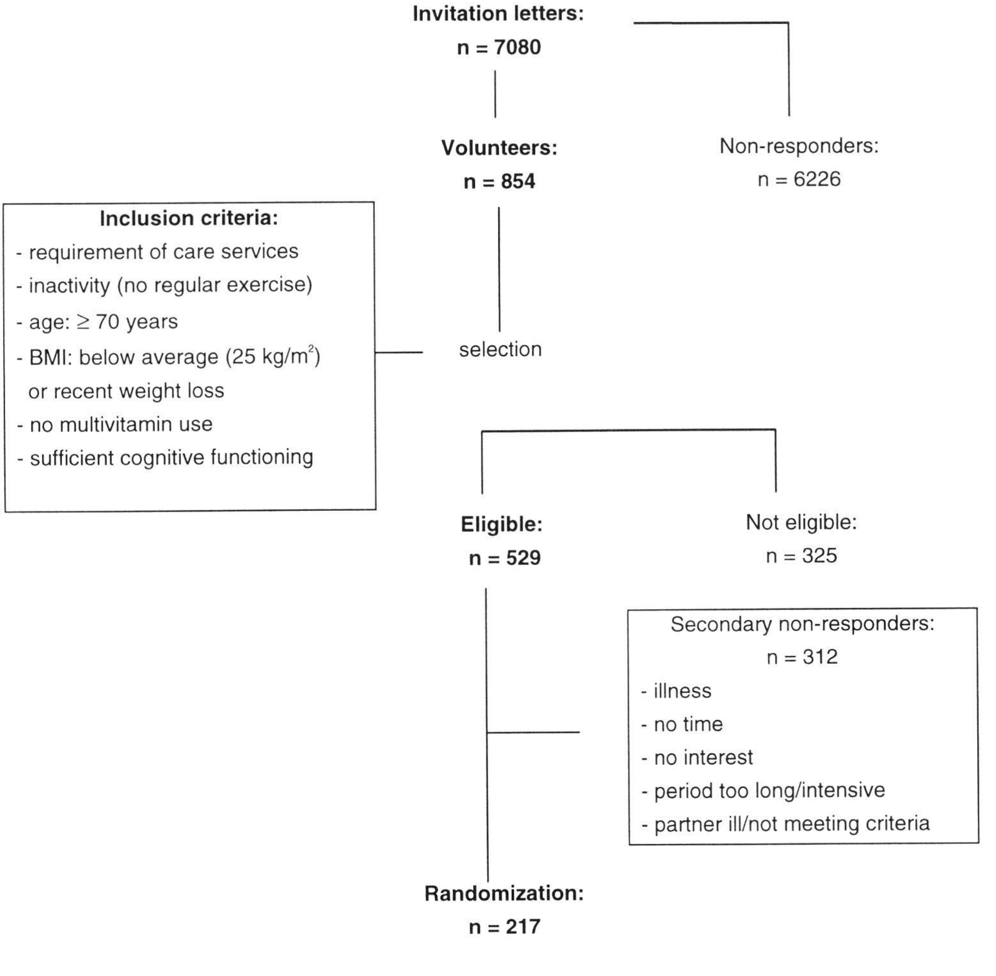


Figure 1.3a Flow chart of the randomized trial

Each participant's general practitioner approved study participation. Subjects were then randomly assigned to one of four groups (see Figure 1.3b):

a) supervised group exercise + regular food products;
b) social program + nutrient dense food products;
c) both: supervised group exercise + nutrient dense food products;
d) control group: social program + regular food products.

To adjust for the effects of socializing and attention, those not randomized to exercise participated in a social program (lectures, games, crafts) once every two weeks for 90 minutes under the supervision of a creative therapist. To prevent disappointment for being assigned to the 'control' instead of 'treatment' program, the social program was introduced as an educational program. Those not assigned to nutrient dense food products received regular products which appeared identical and were of similar energy content but non-enriched. Assignment to enriched or regular products was kept blinded throughout the intervention period. Assignment took place before baseline measurements using sealed envelopes. Couples were randomized together. For logistic reasons subjects were enrolled in the study from January through July (1997).

We hoped to end up with a complete follow-up for 200 participants, 50 in each group. A sample size of 50 subjects in each intervention group is enough to allow us to pick up a difference of 10-25% in the most important outcome variables with $\beta = 80\%$ and $\alpha = 5\%$. As we expected a higher dropout in the intervention groups, a few more subjects were assigned to these groups.

The intervention period was 17 weeks. This period was based on the results of earlier studies that found effects of exercise on muscle strength and of micronutrient supplementation on blood vitamin concentrations after 8 and 12 weeks.[15;43] A longer intervention period (e.g. 1 year or longer) would have been preferable for the study of long-term feasibility, but this was not possible due to practical and financial reasons.

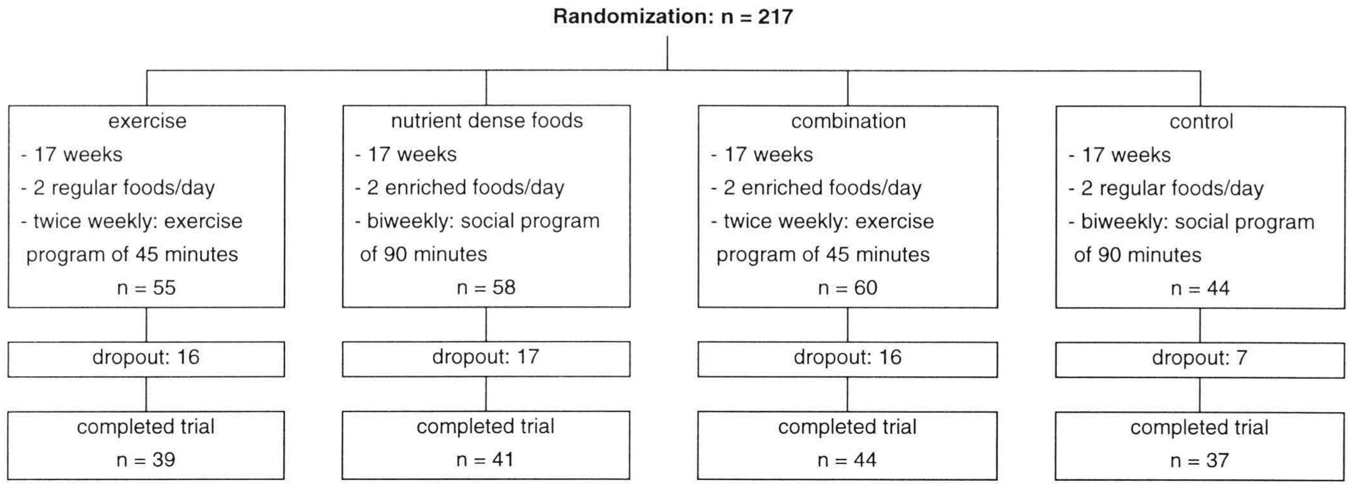


Figure 1.3b Flow chart of the randomized controlled trial.

Outline of this thesis

In this thesis, effects of a 17 weeks exercise program and consumption of micronutrient enriched foods on physical functioning, psychosocial well-being and cellular immune response of frail elderly are addressed.

In order to study effectiveness of these interventions, first possible characteristics for identification of frailty were examined (*Chapter* 2). In data of the Zutphen Elderly Study three different working definitions for selecting a frail elderly population were evaluated (*Chapter* 2.1). Frailty was defined as inactivity combined with 1) low energy intake, 2) weight loss or 3) low body mass index. Differences in health, functioning and diet in 1990 (cross-sectional) and functional decline and mortality in the following 3 years between frail and nonfrail participants, according to the working definitions, were studied. In *Chapter* 2.2 effectiveness of inactivity alone or combined with weight loss, was further studied in the SENECA study, a longitudinal study on nutrition, lifestyle and health of elderly Europeans. Differences in health, functioning and nutritional characteristics between those who were inactive, weight losing or both and the weight stable, active reference group were evaluated.

Chapter 3 describes the effect of the exercise and nutritional intervention on different domains of quality of life. Effects on physical functioning (performance tests and self-report) and fitness are described in *Chapter* 3.1. *Chapter* 3.2 deals with effects on psychological well-being and social contacts. Effects on cellular immune response as measured by delayed-type hypersensitivity skin test response against 7 recall antigens, is described in *Chapter* 3.3.

A more detailed description of the design of the exercise program can be found in *Chapter* 4. Here also the feasibility for implementation in a real life situation will be addressed.

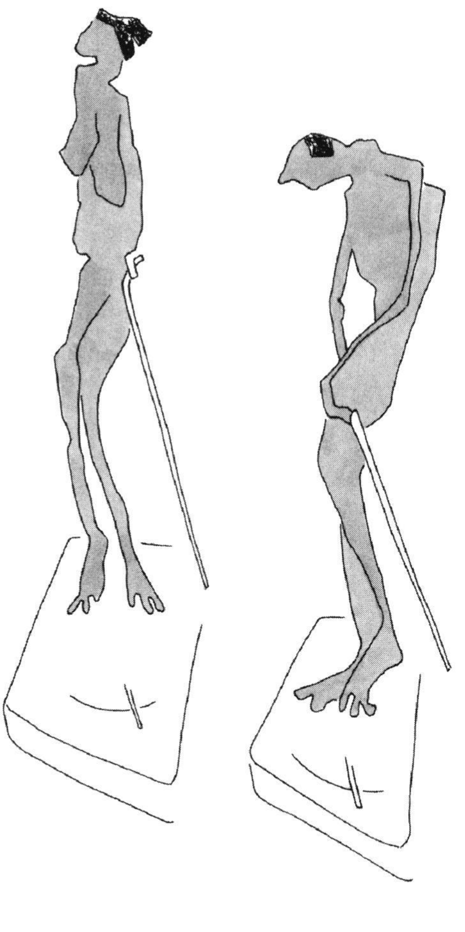
Since *Chapters 2 to 4* were originally written as separate articles for publication in scientific journals some overlap between the chapters exists.

In the general discussion (*Chapter* 5), the main findings are placed in a broader perspective, strengths and limitations of the study are discussed, as well as public health implications and suggestions for further research. Effects of both interventions on nutritional- and biochemical health indices and appraisal of the nutrient dense foods will be addressed in the complementary thesis of Nynke de Jong.[2]

The thesis concludes with a summary, in both English and Dutch.

2

Criteria for identifying frail older persons



2.1

How to select a frail elderly population.

A comparison of three working definitions.

JMM Chin A Paw, JM Dekker, EJM Feskens, EG Schouten, D Kromhout.
Journal of Clinical Epidemiology 1999 (in press).

Abstract

The aim of this study was to compare three different working definitions for selecting a frail elderly population. Frailty was defined as inactivity combined with 1) low energy intake (n = 29), 2) weight loss (n = 26) or 3) low body mass index (n = 26).
In the Zutphen Elderly Study (n = 450 men, aged 69-89) differences in health, functioning and diet for 1990 and functional decline and mortality in the following 3 years between frail and nonfrail participants - according to the working definitions - were studied using logistic regression analysis.
Differences according to the inactivity/weight loss criterion were more pronounced than according to the other two criteria. Inactivity/weight loss was associated with lower subjective health and performance and more diseases and disabilities in 1990. Three-year relative risks of mortality (OR: 4.1, 1.8-9.4) and functional decline (OR: 5.2, 1.04-25.8 for disabilities, OR: 3.7, 0.8-16.2 for performance) were also higher.
Inactivity in combination with weight loss seems to be a practicable working definition for selecting a frail elderly population.

Introduction

Physical frailty represents a large threat to the functioning and quality of life of older people. Many studies have focused on *frail elderly*. Still, criteria used for the selection of these frail elderly are not standardized. The term frail elderly is often used to denote those living in institutions or with an impaired functional status. This muddles the difference between frailty and functional dependence. Buchner and Wagner[5] have defined frailty as a state of reduced physiologic reserve associated with an increased susceptibility to disability. Rockwood et al[3] have defined as frail those who depend on others for the activities of daily living or those who are at a high risk of becoming dependent. Frail elderly people can also be found among non-institutionalized subjects. Preventive strategies and targeted services for frail elderly people require identification of this risk group, preferably before disability and institutionalization have occurred.

Two major determinants of frailty are physical inactivity and malnutrition. Both increase the risk of muscle weakness, which is associated with disability.[5;7;44] The positive effects of physical activity on muscle strength, bone mass and functional independence[11;45] have been demonstrated repeatedly. Inadequate dietary intake and nutritional deficiencies are also important causes of the age-related decline in muscle mass and impaired physiologic functioning.[7;46]

Inactivity and malnutrition interact in their impact on frailty. Inactivity may decrease appetite and thus dietary intake, resulting in malnutrition, muscle disfunction and further inactivity: a downward process thus evolves. Preventing disability and further deterioration requires identification of elderly people at the beginning of this downward process. Possible early markers of frailty may be physical inactivity and low energy intake. Low body mass index (BMI) and weight loss as indicators of a decline in muscle mass may be other early markers of frailty. Both low body weight and weight loss in old age have been associated with poor health and disability.[47]

The aim of the present study was to examine three working definitions of frailty using data from the 1990 survey of an ongoing follow-up study. Frailty was defined as physical inactivity combined with either low energy intake, 5-year weight loss or low BMI. Associations between frailty (according to these three working definitions) and health, functioning, diet (cross-sectional) and decline in functioning and mortality in the following 3 years were studied.

Methods

Study population

The Zutphen Study is a longitudinal study on chronic diseases and risk factors and constitutes the Dutch contribution of the Seven Countries Study.[48] It originally started in 1960 with a cohort of 878 men aged 40-59, living in the town of Zutphen in the Netherlands. In 1985, 555 men were still alive and were invited for a new examination along with an additional random sample of 711 men of the same age

(65-84 years). In 1985, 939 of these men (response rate 74%) were investigated, and this group formed the cohort of the Zutphen Elderly Study. In 1990 and 1993 the survivors (n = 721) were contacted for reexamination. From the 560 men interested in participating, 107 were not living independently anymore, and no information on weight loss was available on 3 of them. The present study population consisted of 450 men who were living independently and whose information on weight loss for the period between 1985 and 1990, and on energy intake and physical activity for 1990, was available.

Examinations

Data were collected according to a standardized protocol.[48]

Selection criteria

Physical activity was assessed with a self-administered questionnaire designed for retired men.[49] This questionnaire has demonstrated a substantial 4-month test-retest correlation ($r = 0.93$; $p < 0.001$), and has been validated against the doubly labeled water method ($r = 0.61$; $p < 0.01$) in a subsample of Zutphen Study participants.[50] The core questionnaire consisted of six questions about the frequency and duration of walking and bicycling in the previous week and the average amount of time spent monthly on hobbies, gardening, odd jobs and sports. Time estimates were converted to minutes per week for each type of activity and summed for the total weekly minutes of activity.

Data on food and beverage intake were collected by the cross-check dietary history method adapted to the Dutch situation.[51;52] This method provides information on the usual food consumption pattern during the 2-4 weeks preceding the interview. The use of vitamin supplements and whether or not the participant followed a prescribed diet were also recorded. Food intake data were encoded and converted into energy and nutrient values using the 1989 release of the Netherlands food table.[51]

Height and weight were measured with participants dressed in underwear only. Body mass index was calculated by dividing weight (kg) by the square of height

(m^2). Subscapular and tricipital skinfold thickness was measured in duplicate with a caliper on the right side of the body.

Functional status

Performance-based functional capacity was evaluated by four performance tests: walking speed, standing balance, chair stands and external shoulder rotation. The tests were adapted from the Established Populations for Epidemiologic Studies of the Elderly (EPESE)[53] and have previously been described in detail.[22] In short, in the test for standing balance the participant was asked to hold a tandem position for 10 seconds. In the test for walking speed participants were asked to walk a distance of 8 feet (2.44 m) in their usual gait. In the chair-stand test, the time required to stand up from a chair five times as quickly as possible was measured. In the test for external shoulder rotation the range of motion of shoulder and arms was assessed. A cut-off point for low performance was defined for each test. A summary score was conducted as the number of tests performed at a low level.[22] A decline in performance was defined as low performance on more tests of these four in 1993 compared to 1990 (the same cut-off points were used in 1990 and 1993). Isometric handgrip strength of the dominant hand was measured with a Martin vigorimeter. The tests were carried out under standard conditions by trained personnel.

Disabilities were assessed as self-reported disabilities in 13 daily activities. The 13 activities were grouped into three dimensions: basic activities of daily living (BADL; e.g., toiletting and dressing), mobility (e.g., walking and climbing stairs) and instrumental activities of daily living (IADL; e.g., housework and cooking).[22] Those who needed help in one or more items in a specific dimension were classified as disabled in this parameter.

Global cognitive function was tested with the Dutch version of the 30-point Mini-Mental State Examination (MMSE).[54] A score of ≤ 25 is indicative of cognitive impairment.[55]

Health-related characteristics

Blood pressure was measured twice on the right arm with subjects in supine position with a random-zero sphygmomanometer. Serum albumin levels were analyzed in an auto-analyzer (SMAC, Technicon, Tarrytown, NY) in the Central Laboratory of Clinical Chemistry of the Academic Hospital in Leiden. Serum total cholesterol determinations were conducted in a standardized lipid laboratory (Division of Human Nutrition and Epidemiology, Wageningen, The Netherlands) following World Health Organization (WHO) criteria. Information on a history of chronic diseases was obtained through a standardized questionnaire and verified with hospital discharge data and written information from the subjects' general practitioner. Information on age, socioeconomic status and smoking status were collected by questionnaire. We also carried out a mortality follow-up. Municipal registries provided information on the participants' vital status until January 1995. None of the men were lost to follow-up.

Statistical analysis

Working definitions

From the physical activity questionnaire, the total amount of activity was calculated in minutes per week.[56] Physical inactivity was defined as less then 210 minutes (lowest quartile) of physical activity per week. Five-year weight changes were calculated by subtracting weight measured in 1990 from weight measured in 1985. Frailty was operationalized as physical inactivity combined with 1) an energy intake of less than 7.6 (lowest quartile) MJ per day, 2) a 5-year weight loss of more than 4 kg (lowest quartile of weight change), or 3) a BMI of less than 23.5 kg/m^2 (lowest quartile) (Figure 2.1.1). Men consuming a prescribed energy-restricted diet were assigned to the nonfrail group.

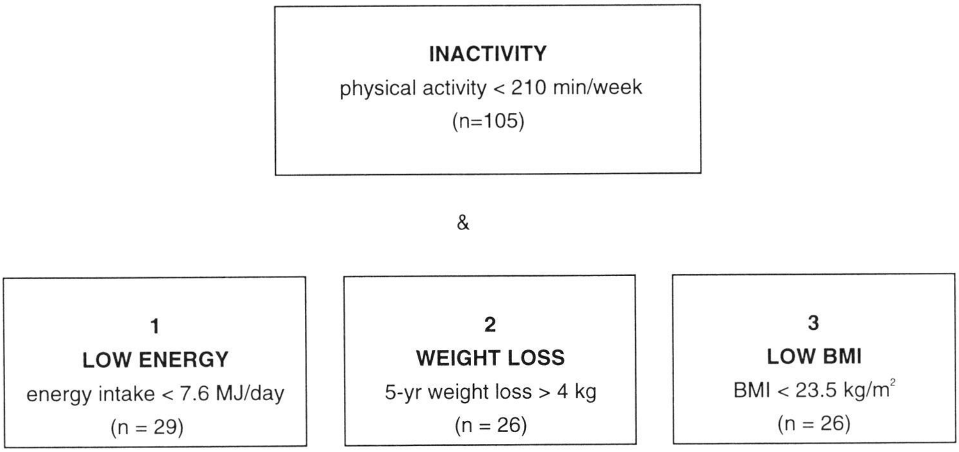


Figure 2.1.1 Working definitions of frailty

Statistical Analysis

Unadjusted means and percentages were calculated. Differences between frail and nonfrail according to all three working definitions (dependent variable) were tested using logistic regression, adjusting for age. Independent variables included health-related characteristics, functional status, diet (cross-sectional) and 3-year functional decline and mortality. P values of the coefficients of the independent variables were used for testing in univariate models, adjusting for age. The number of participants available for analysis varied due to missing values for some variables. Data were analyzed using SAS statistical software, version 6.11 (SAS Inc., Cary, NC).

Results

Table 2.1.1 shows mean values of the selection criteria. The inactivity/low energy intake criterion resulted in 29 frail (6%) and 421 nonfrail men. The inactivity/weight loss and inactivity/BMI criteria both resulted in 26 frail (6%) and 424 nonfrail men. Seven men were defined as frail according to both inactivity/weight loss and inactivity/low energy, 9 according to both inactivity/weight loss and inactivity/low BMI, and 6 according to both inactivity/low energy and inactivity/low BMI. Only two men were frail according to all three working definitions. The mean age of the men was 75 in 1990, and most men were married. Based on inactivity/low energy intake, frail men were older (78 years, $p = 0.0003$).

Health-related characteristics

Both inactivity/weight loss and inactivity/low BMI were associated with a significantly lower self-rated and physician-rated health (Table 2.1.2). Inactivity/low energy intake and inactivity/weight loss were associated with a higher number of diseases. Inactive weight-losing men had a higher prevalence of cardiovascular disease (62% in frail vs. 28% in nonfrail), chronic obstructive pulmonary disease (42% vs. 22%) and diabetes mellitus (23% vs. 8%). Inactivity/low energy intake and inactivity/low BMI were both associated with a higher prevalence of heart failure (21 and 23% vs. 7%) and diabetes mellitus (21 and 23% vs. 8%). Inactivity/low energy intake was associated with a higher sum of skinfolds, inactivity/low BMI with a lower sum of skinfolds.

Functional capacity

Table 2.1.3 shows the difference in functional status between frail and nonfrail men. According to all working definitions, frailty was associated with low performance on walking speed and more self-reported disabilities. Frail men were more often disabled in mobility and BADL. Further, inactivity/low energy was associated with lower performance on chair stands, inactivity/weight loss with lower performance on standing balance, chair stands and lower grip strength, and inactivity/low BMI with lower grip strength.

Table 2.1.1 Mean values (± SD) of the selection criteria in frail and nonfrail elderly men (Zutphen Elderly Study, 1990)

	Inactivity + low energy		**Inactivity + weight loss**		**Inactivity + low BMI**	
	frail(n = 29)	nonfrail (n = 421)	frail(n = 26)	nonfrail (n = 424)	frail (n = 26)	nonfrail (n = 424)
Physical activity (min/wk)	101 ± 66	639 ± 550	74 ± 57	635 ± 551	106 ± 65	605 ± 549
Energy intake (MJ/day)	6.6 ± 0.7	9.0 ± 1.9	8.4 ± 1.6	8.9 ± 2.0	8.9 ± 1.7	8.9 ± 2.0
Weight loss (kg/yr)	1.2 ± 4.8	1.0 ± 4.5	7.5 ± 4.2	0.9 ± 4.7	2.2 ± 3.0	1.0 ± 4.6
BMI (kg/m^2)	26.2 ± 3.5	25.5 ± 3.0	24.3 ± 2.4	25.8 ± 2.9	21.7 ± 1.5	25.6 ± 3.0

Table 2.1.2 Health characteristics (means ± SD or percentages) of frail and nonfrail men in 1990*

	Inactivity + low energy		**Inactivity + weight loss**		**Inactivity + low BMI**	
	frail(n = 29)	nonfrail (n = 421)	frail(n = 26)	nonfrail (n = 424)	frail (n = 26)	nonfrail (n = 424)
Physician-rated health (1-5) †	3.3 ± 0.9	3.7 ± 0.9	3.0 ± 0.9	3.7 ± 0.9 ‡	3.2 ± 1.0	3.7 ± 0.9 ‡
Self-rated health (1-4) †	3.2 ± 0.8	3.4 ± 0.7	3.0 ± 0.8	3.4 ± 0.7 ‡	3.1 ± 0.8	3.4 ± 0.7 ‡
Number of diseases	2.4 ± 1.5	1.7 ± 1.3 ‡	2.7 ± 1.4	1.7 ± 1.3**	2.2 ± 1.6	1.7 ± 1.3
Systolic blood pressure (mm Hg)	156 ± 26	150 ± 21	147 ± 19	150 ± 22	150 ± 21	150 ± 22
Diastolic blood pressure (mm Hg)	84 ± 10	82 ± 12	82 ± 12	82 ± 12	78 ± 12	82 ± 12
Serum cholesterol (mmol/L)	6.21 ± 1.35	6.07 ± 1.10	6.12 ± 1.53	6.08 ± 1.09	5.87 ± 1.39	6.09 ± 1.10
Serum albumin (g/L)	43.7 ± 2.8	43.2 ± 2.4	42.8 ± 2.46	43.3 ± 2.4	42.2 ± 2.2	43.3 ± 2.5
Sum of 2 skinfolds (mm)	33.3 ± 10.8	29.8 ± 9.5 $	27.2 ± 8.38	30.2 ± 9.7	22.2 ± 6.4	30.5 ± 9.6**
Percent smoking	21	18	27	17	23	17

* the number of observations is variable due to missing values.

† a higher score indicates better health

‡ $p \leq .05$, \$ $p \leq .01$, ** $p \leq .001$ using logistic regression, adjusting for age (see methods)

Table 2.1.3. Functional status (means ± SD or percentages) of frail and nonfrail men in 1990*

	Inactivity + low energy		Inactivity + weight loss		Inactivity + low BMI	
	frail (n = 29)	nonfrail (n = 421)	frail (n = 26)	nonfrail (n = 424)	frail (n = 26)	nonfrail (n = 424)
Number of disabilities (%)	3.0 ± 3.5	0.9 ± 1.6 $	2.5 ± 2.9	0.9 ± 1.7 ‡	2.5 ± 3.8	0.9 ±1.6 ‡
disabled in IADL	62	44	67	40	56	41
disabled in mobility	39	11 $	44	11 ‡	29	12 †
disabled in BADL	14	2 †	15	2 ‡	19	2 ‡
Low performance (%)						
walking speed	55	21 ‡	50	22 ‡	54	22 ‡
standing balance	24	15	35	14 †	12	15
shoulder rotation	7	12	23	11	23	11
five chair stands	57	25 ‡	50	26 †	48	26
Grip strength (kPa)	68 ± 18	77 ± 20	66 ± 18	77 ± 19 †	68 ± 20	77 ± 19 †
MMSE (0-30)	26 ± 3	26 ± 3	26 ± 2	26 ± 3	26 ± 3	26 ± 3

* The number of observations is variable due to missing values.

IADL = Instrumental Activities of Daily Living, BADL = Basic Activities of Daily Living, MMSE = Mini-Mental State Examination

† p ≤ .05, ‡ p ≤ .01, $ p ≤ .001 using logistic regression, adjusting for age (see methods)

Table 2.1.4. Dietary characteristics (mean ± SD or percentages) of frail and nonfrail men in 1990*

	Inactivity + low energy		Inactivity + weight loss		Inactivity + low BMI	
	frail (n = 29)	nonfrail (n = 421)	frail (n = 26)	nonfrail (n = 424)	frail (n = 26)	nonfrail (n = 424)
En% total protein	16 ± 3	14 ± 3 $	16 ± 3	14 ± 3 ‡	14 ± 2	15 ± 3
En% total fat	38 ± 7	38 ± 6	39 ± 7	38 ± 6	40 ± 6	38 ± 6
En% total carbohydrates	43 ± 8	44 ± 7	42 ± 7	44 ± 7	43 ± 5	44 ± 7
En% alcohol	3 ± 5	3 ± 5	3 ± 4	4 ± 5	4 ± 5	3 ± 5
Cholesterol (mg/MJ)	31 ± 10	30 ± 8	34 ± 10	30 ± 8 †	33 ± 10	30 ± 8
Fiber (g/MJ)	3.4 ± 0.9	3.0 ± 0.9 †	3.0 ± 0.7	3.0 ± 0.9	2.9 ± 0.7	3.0 ± 0.9
Drinking alcohol (%)	55	75	65	75	62	75
Following a prescribed diet (%)	31	21	23	21	19	21

* The number of observations is variable due to missing values.

En% = energy percentage

† $p \leq .05$, ‡ $p \leq .01$, \$ $p \leq .001$ using logistic regression (intake variables were not adjusted for age)

Diet

Table 2.1.4 shows the difference in a number of dietary characteristics between frail and nonfrail men.

Macronutrient intake. Both inactivity/low energy and inactivity/weight loss were associated with a higher energy percentage of protein. The inactivity/weight loss group had a higher intake of dietary cholesterol; the inactivity/low energy group had a higher fiber intake.

Micronutrient intake. Prevalence of intake below the Dutch recommended allowances for calcium, magnesium, phosphorus and vitamins B1, B2, B6, C, and E were studied (data not shown). Prevalence of suboptimal micronutrient intake was especially high for vitamin E (72%), magnesium (64%), and vitamin B1 (50%) in all the men. Prevalence of suboptimal intakes was higher in the inactivity/low energy group for almost all micronutrients, except for vitamins B2 and C. Adjustment for energy intake made these differences disappear. Intake of vitamin supplements was low (ranging from 2% taking vitamin A+D to 6% taking multivitamins), and there was no difference between frail and nonfrail men.

Functional decline and mortality

In 1993, 20% (n = 90) of the men had died, 40% (n = 120) of the remaining participants reported more disabilities, and 35% (n = 92) had declined in performance tests. Due to death and non-response, the number of frail men became small: 13 inactive/low energy, 9 inactive/weight-losing, and 10 inactive/low BMI frail men. Age-adjusted odds ratios (ORs) and 95% confidence intervals (CI) of decline in self-reported disabilities, performance tests, and mortality are presented in Table 2.1.5. Inactive/weight losing men reported more often an increase in disabilities (79% frail vs. 36% of nonfrail men, OR: 5.2), a decline in performance tests (38% vs. 14%, OR: 3.7) and higher mortality (50% vs. 18%, OR: 4.1). Decline in performance tests was most prevalent in inactive/low BMI men (45% in frail vs. 14% in nonfrail men, OR: 5.7).

Table 2.1.5. Functional decline and mortality of frail and nonfrail men between 1990 and 1993: Odds ratios (95% confidence interval) adjusted for age.

Characteristic	N*	Inactivity & low energy vs. Nonfrail	Inactivity & weight loss vs. nonfrail	Inactivity & low BMI vs. nonfrail
Reporting more disabilities	298	1.6 (0.5-5.1)	5.2 (1.04-25.8)	2.3 (0.6-8.3)
Declined performance	268	0.5 (0.1-4.5)	3.7 (0.8-16.2)	5.6 (1.6-19.5)
Mortality	450	1.1 (0.5-2.8)	4.1 (1.8-9.4)	2.0 (0.8-4.7)

* N = number of participants with information available.

Discussion

The results of our study indicate that inactivity in combination with weight loss seems to be a suitable working definition for selecting a frail elderly population among community-dwelling elderly men. Participants who were inactive and had lost more than 4 kg in 5 years had an adverse health profile (lower self-rated and physician-rated health, more diseases) and functional capacity (more disabilities, lower grip strength, walking speed, standing balance and chair stand performance) compared with more active and weight stable/gaining men. The inactivity/weight loss combination was also predictive for mortality and functional decline 3 years later. Inactivity in combination with either an energy intake below 7.6 MJ per day or BMI below 23.5 kg/m^2 also selected a group with a worse health and functional profile, but differences between frail and nonfrail elderly subjects according to these working definitions were less pronounced. None of the working definitions selected frail men with adverse dietary characteristics. Nevertheless, weight loss does indicate a negative energy balance. Furthermore, suboptimal micronutrient intakes were prevalent in all men.

The term *frailty* is often used in the literature to denote impaired or institutionalized elderly. Frail elderly who are at a high risk of becoming disabled but still live in the community are excluded then. Little research has been done to define criteria for selecting frail elderly people. Winograd et al[57] and Owens et al[58] studied screening criteria to identify frail hospitalized elderly individuals who are at risk of an increased length of hospital stay, mortality or nursing home placement. Early preventive intervention demands ways of identifying frailty before irreversible health consequences have occurred. We therefore investigated how a frail population can be identified among non-institutionalized elderly persons. Strawbridge et al[59] studied a measure of frailty among non-institutionalized elderly. They defined frailty as having problems or difficulties in two or more of four domains (physical functioning, nutrition, cognitive functioning and sensory) assessed through 16 variables. To improve applicability we have chosen three working definitions based on only two variables.

A major problem in studies among the elderly is high non-response. Elderly subjects participating in research are a selective group who are likely to have a higher educational and socioeconomic background and fewer health problems. Frail elderly people are thus less likely to participate, making it harder to study frailty prevalence, risk factors and possible interventions. The use of data from an ongoing follow-up study may alleviate this problem because recruitment already took place at a younger age. In our study the response rate was 74% in 1985, 78% in 1990, and 72% in 1993. Still, the level of functioning was quite high. Even those men defined as frail reported few disabilities. Men who still participated in the follow-up in 1993 reported fewer disabilities and better performance in 1990 than men who no longer participated. Men who died during the follow-up time had an even worse functional status.[22] To be able to study the predictive value of the working definitions, extra efforts should be made to minimize this selective dropout process.

Another point of consideration is the occurrence of misclassification with regard to physical activity, dietary intake and weight loss. The physical activity questionnaire we used is considered to be reliable and was validated in a subsample of Zutphen Study participants.[50] The validity and reproducibility of the cross-check dietary history method are also well established.[60] However, it has been reported that participants with a high BMI tend to underestimate their energy intake and that those with a low BMI tend to overestimate it[61] The higher sum of skinfolds and BMI in the inactivity/low energy group may partly result from lifestyle during earlier periods, but it is likely to reflect some underestimation of dietary intake. The minimal reported energy intake of 3 MJ per day also suggests underestimation. Energy intake therefore seems to be a less reliable selection criterion. Weight loss could only be calculated over a 5-year period. Recent weight loss over the last year may be a more sensitive indicator for a declining health status.

Finally, we examined only men. It would be interesting to study the appropriateness of inactivity/weight loss in identifying a frail population of both men and women, especially because physical activity and energy intake are usually lower in women.

Significant weight loss over time is seen as the most important indicator for determining poor nutritional status (Nutritional Screening Initiative) and is associated with an increase in mortality in nursing home residents.[62] Our results show that, in combination with inactivity, weight loss also predicts mortality in non-institutionalized men. On the basis of our results we recommend physicians, home care workers and elderly individuals to document a weight history.

Our results suggest that a combined intervention of exercise and nutrition might be effective in preventing or postponing a further decline in health.

Further research into the sensitivity and specificity of this criterion is needed. In the provision of care services a sensitive criterion is preferable (minimizing the number of false negatives) to prevent withholding care from people who need it. Recruitment of a frail population for preventive trials requires more specific criteria (minimizing the number of false positives).

For screening purposes a simple and rapid evaluation would be preferred. Measurement of dietary intake is time-consuming and expensive, and therefore less applicable. By contrast, body weight is a simple, widely accepted and routinely collected anthropometric measurement. There are validated and easy to administer questionnaires for measuring physical activity in the elderly. Inactivity in combination with weight loss therefore looks like a simple, inexpensive and effective criterion for selecting a frail population among community-living elderly men. Future intervention studies will have to show whether this selection criterion will also identify a population that benefits from preventive actions.

2.2

Inactivity and weight loss: effective criteria to identify frailty?

JMM Chin A Paw, CPGM de Groot, SV van Gend, HC Schoterman, EG Schouten, M Schroll, WA van Staveren. Submitted.

Abstract

The aim of this study was to examine the effectiveness of inactivity and weight loss as criteria to identify a population of frail, independently-living elderly persons. We used data from the SENECA study, a longitudinal study on nutrition, lifestyle and health of elderly Europeans.
The study population (N = 849, aged 75 to 80) was classified in four subgroups: (1) inactive elderly (lowest tertile activity score; N = 204); (2) weight losing elderly (lowest quintile: ≥ 6.3% weight loss over 4-5 years; N = 108); (3) both inactive and weight losing (N=54); (4) neither inactive nor weight losing: reference (N = 483). Differences in health, physical functioning and nutritional characteristics between groups 1, 2 and 3 respectively and the reference group were calculated.
Both inactive, weight losing (group 3) and inactive subjects (group 1) reported significantly more chronic diseases (2.2 and 1.8 vs. 1.1), use of medications (both 2.3 vs. 1.1), self-rated health (2.8 and 3.1 vs. 3.8) and relative health (1.9 and 2.1 vs. 2.6), more frequently reported disabilities (81 and 80 vs. 43%), use of care services (26 and 21 vs. 6%), and had a lower physical performance score (17 and 18 vs. 22) compared to the weight-stable, active reference group. In addition, few social contacts, inadequate micronutrient intake and biochemical deficiencies were more prevalent in both groups. Weight-losing elderly were not significantly different from the reference group with respect to these characteristics.
Physical inactivity alone or in combination with weight loss seems to be a practical and inexpensive screening criterion for identifying functionally vulnerable persons among non-institutionalized elderly. Standardized criteria that identify frail populations will facilitate the development and implementation of strategies that aim at favoring older persons' independence.

Introduction

Prevention of disability is a major theme in gerontologic research.[5;11;12;23] Frail elderly people are especially susceptible to disability due to their reduced physiologic reserves.[5] The evaluation of preventive interventions requires identifying this functionally vulnerable group, preferably before disability and institutionalization have occurred. Little research has been done to define criteria that identify frail elderly. The term *frailty* is often used for disabled or institutionalized elderly.[3] Winograd et al[57] and Owens et al[58] developed a list of criteria which appeared to be effective in identifying elderly hospitalized patients at risk for mortality and nursing home utilization. In both studies, patients who met one of a list of criteria were classified as frail. Examples of these criteria are: dependence in Activities of Daily Living (ADLs), impaired mobility, prolonged bed rest, malnutrition, polypharmacy or chronic and disabling illness,[57] poor cognition, recent weight loss, older than 85, needing assistance to get to the bathroom, taking more than 4 medicines.[58] Nevertheless, individuals may exhibit susceptibility to functional decline and disability while still living independently. In a population of independently-living elderly men, the combination of physical inactivity and weight loss appeared to be effective in selecting a group of men with an increased risk of three-year functional decline and mortality.[63] Unfortunately, although women tend to make up a large segment of the frail elderly population, this study was restricted to men. Physical activity and energy intake are typically lower in women, making them possibly even more vulnerable.[12;64] Both inactivity and weight loss are related to a loss of muscle mass and muscle strength, which is a major threat to functional independence.[5;7] Inactivity and weight loss may thus be relatively simple and inexpensively measured indicators of frailty. We were interested in the appropriateness of these criteria in identifying a population of both men and women with an adverse health status associated with an increased susceptibility to disability.

The aim of this study was to examine the effectiveness of inactivity and weight loss as criteria for identifying a population of frail, independently living elderly persons. To examine this, differences in health, functioning and nutritional characteristics were studied between elderly who are physically inactive, losing weight or both, versus relatively active and weight-stable or weight-gaining older persons. This was studied using data for both men and women from the SENECA follow-up study (Survey in Europe on Nutrition and the Elderly, a Concerted Action).

Methods

Study population

The SENECA Study is a mixed longitudinal study on nutrition, lifestyle and health of elderly Europeans[65] in birth cohorts 1913-1918. Baseline measurements (N = 2586) were collected in 1988/1989 and repeated in 1993 (1221 reexamined + 210 newly invited participants). For the present analyses 849 participants were selected who were living independently and for whom weight change between 1988/1989 and 1993 and physical activity score in 1993 could be calculated. Participants were living in Hamme (Belgium), Roskilde (Denmark), Haguenau (France), Padua (Italy), Culemborg (the Netherlands), Vila Franca de Xira (Portugal), Betanzos (Spain), Yverdon (Switzerland), and Marki (Poland).

Data collection

Data were collected according to a standardized protocol which has been described in detail elsewhere.[66;67]

General questionnaire. Data on the presence of chronic diseases, use of medication (presently or in the past year), fractures, self-rated health and health relative to peers, smoking, self-rated activity, dietary habits, social contacts and living situation were obtained from a standardized questionnaire.[68]

Physical activity. Habitual physical activity was assessed with the validated Voorrips' activity questionnaire on housework, leisure-time activity and sports.[69] The questionnaire asked questions about household activities (e.g. cleaning, cooking, walking stairs, shopping), sports and leisure time activities in the past year. Intensity as well as duration in terms of hours spent a week (sports) or minutes spent a day (leisure time), and months spent a year were taken into account. A total activity score was calculated from the household, sports and leisure time scores.

Anthropometry. Body weight, height, skinfold thicknesses, and circumferences were measured by trained personnel. Weight was measured to the nearest 0.5 kg on a calibrated scale in the morning, after breakfast, and after emptying the bladder. The percentage of weight change between 1988/1989 and 1993 was calculated. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2), and the waist-hip ratio by dividing waist circumference (cm) by hip circumference (cm). Mid-upper arm muscle circumference (cm) was calculated as mid-upper arm circumference (cm) - 0.3142 x triceps skinfold thickness (mm).[70]

Functional status. Functional limitations were evaluated through observed performance of seven different tasks that simulate activities of daily living (US Physical Performance Test, PPT) and which have been described in detail elsewhere.[68] The sum scores of all seven items could range from 0 (worst performance) to 28 (best performance). Two performance tests were added: standing balance and chair stands. In the test for standing balance the participant was asked to hold a tandem position for 10 seconds. Low performance was defined as not being able to hold this position for 10 seconds. In the chair-stand test the time required to stand up from a chair (with arms folded across the chest) as quickly as possible five times was measured. Low performance was defined by the inability to complete the test within 17 seconds (slowest quartile). Disabilities were assessed as self-reported disabilities in 16 daily activities. The total ADL score, calculated as the sum of the 16 questions, reflects the number of activities that could not be performed independently. A mobility score (MI) out of four questions (e.g. use stairs, move outdoors), and a self-care score (SI) out of seven questions (e.g. dress, feed yourself, cut toenails) were also calculated.

Dietary intake. Information about dietary intake was obtained by trained interviewers using a modified version of the dietary history method. This method consisted of a 3-day estimated record and a frequency checklist of foods (past month as the reference period) based on each country's meal patterns.[64] The interviewer checked portion sizes by weighing them or by using standardized household measures. Nutrient composition was calculated with local nutrient databases. The dietary nutrient intakes were compared with the lowest European RDIs by town and gender.[71] For vitamin B6, 50% of the US recommended dietary allowance[72] was used as the reference, since several European countries do not have recommended intakes for this vitamin.

Biochemical characteristics. Blood samples were collected by venepuncture after an overnight fast with the subject in sitting position. Biochemical assessment included determination of vitamins A, E, B_6, B_{12}, folic acid, hemoglobin, haematocrit and albumin concentrations.

Statistical analysis

Four groups were defined by the presence or absence of inactivity and weight loss (Table 2.2.1). Inactivity was defined as Voorrips' activity score in the lowest sex-specific tertile (3.2 for men, 2.4 for women). Weight loss was defined as percent weight change over 4-5 years in the lowest quintile (6.3% weight loss or more). Differences in health, functioning and nutritional characteristics between groups 1, 2 and 3 respectively versus group 4 were evaluated using a t-test for normally distributed variables, the Wilcoxon test for variables with a skewed distribution, and a Chi-square test for categorical variables. Data analysis was carried out using a SAS statistical software package (version 6.11).

Table 2.2.1 Subgroups according to activity score and weight change

Group	N	Inactivity	Weight loss
1.	204	+	-
2.	108	-	+
3.	54	+	+
4.	483	-	-

Results

Table 2.2.2 shows mean activity scores and weight changes in the 4 subgroups. The largest differences occurred in the leisure time scores. Mean weight loss was 6.9 kg (10%) in the weight loss group and 8.0 kg (11%) in the inactivity/weight loss group. Mean weight change was negligible (≤1.3%) in the inactive and reference group. The percentage of men and women (about 50%) was not significantly different between the four subgroups. The mean age was 77 years (range: 75-80).

Table 2.2.2 Activity scores and weight change (mean ± SD) per subgroup (SENECA'S Follow-up Study, 1993)

	Inactivity **group 1** **(N = 204)**	**Weight loss** **group 2** **(N = 108)**	**Inactivity & weight loss** **group 3** **(N = 54)**	**Reference** **group 4** **(N = 483)**
Activity score	1.3 ± 0.8	11.0 ± 7.8	1.3 ± 0.8	9.3 ± 6.0
[range]	[0 to 3.2]	[2.6 to 43.0]	[0.0 to 3.0]	[2.4 to 44.2]
Household score	1.1 ± 0.7	2.0 ± 0.8	1.1 ± 0.7	1.9 ± 0.8
Sport score	0.02 ± 0.2	0.5 ± 1.2	0.02 ± 0.2	0.8 ± 1.6
Leisure time score	0.2 ± 0.5	8.5 ± 7.7	0.2 ± 0.5	6.7 ± 6.0
Weight change				
Percentage	1.3 ± 5.3	-10.3 ± 3.9	-11.0 ± 4.6	0.6 ± 4.9
[range]	[-6.2 to 26.9]	[-24.0 to -6.3]	[-27.1 to -6.5]	[-6.3 to 35.9]
Kilogram	0.8 ± 3.7	-6.9 ± 3.0	-8.0 ± 4.0	0.3 ± 3.2
[range]	[-5.3 to 22.5]	[-5.3 to -22.5]	[-22.1 to -3.3]	[-5.5 to 25.1]

Health and anthropometric characteristics

Table 2.2.3 presents health and anthropometric characteristics per subgroup. Inactive and inactive weight-losing elderly subjects reported a higher number of chronic diseases (1.8 and 2.2 vs. 1.1) and medicines (both 2.3 vs. 1.5), lower self-rated health (3.1 and 2.8 vs. 3.8) and relative health (2.1 and 1.9 vs. 2.6) in comparison to the reference group ($p \leq 0.001$ for all variables). BMI and waist-hip ratio were significantly lower in weight-losing elderly (23.4 vs. 26.5 and 0.88 vs. 0.92, respectively, $p \leq 0.001$) and higher in inactive elderly (27.9 vs. 26.5, $p \leq 0.001$ and 0.94 vs. 0.92, respectively, $p = 0.05$). Weight-losing and inactive weight-losing persons were more often smokers (21 and 26 vs. 13 % $p \leq 0.05$), and prevalence of fractures (19 vs. 9 %, $p = 0.02$) was higher in the inactive weight-losing group.

Table 2.2.3 Health and anthropometric characteristics (mean ± SD) of the study population per subgroup (SENECA'S Follow-up Study, 1993)*

	Inactivity group 1 (N = 204)	Weight loss group 2 (N = 108)	Inactivity & weight loss group 3 (N = 54)	Reference group 4 (N = 483)
Health				
Number of chronic diseases	1.8 ± 1.4**	1.1 ± 1.0	2.2 ± 1.7**	1.1 ± 1.1
Number of medicines	2.3 ± 1.6**	1.6 ± 1.4	2.3 ± 1.8**	1.5 ± 1.5
Percent (n) fractures in last 4 yr	12 (24)	12 (13)	19 (10) ‡	9 (42)
Self-rated health (1-5)	3.1 ± 0.9**	3.8 ± 0.9	2.8 ± 1.0**	3.8 ± 0.7
Relative subjective health (1-5)	2.1 ± 0.6**	2.5 ± 0.6	1.9 ± 0.8**	2.6 ± 0.6
Percent (n) presently smoking	12 (24)	21 (23) †	26 ± 14 $	13 (63)
Anthropometry				
BMI (kg/m^2)	27.9 ± 4.6**	23.4 ± 3.9**	25.5 ± 4.9	26.5 ± 3.7
Arm muscle circumference (cm)	24.5 ± 2.8	22.2 ± 3.0**	23.5 ± 2.9	24.3 ± 2.8
Waist-hip ratio	0.94 ± 0.09 ‡	0.88 ± 0.07**	0.91 ± 0.07	0.92 ± 0.08

* The number of observations is variable due to missing values.

†1 = not healthy, 5 = healthy

‡p ≤ .05, $p ≤ .01, ** ≤ .001 compared with the reference group.

Functional status

Functional characteristics are presented in Table 2.2.4. Both the inactive and inactive weight-losing groups had an inferior functional status when compared to the reference group: median PPT-score (18 and 17 vs. 22) and relative self-rated activity were lower and prevalence of poor standing balance (42 and 54 vs. 19%), disabilities in activities of daily living (80 and 81 vs. 43%) both in mobility and self-care activities, and use of care services (home care: 21 and 26 vs. 6%, Meals-on-Wheels: 11 and 17 vs. 2%) were higher ($p \leq 0.001$ for all variables). Remarkably, standing balance was superior in the weight-losing group (37 vs. 70% with low performance). Because the cooperation of participants varied between different towns, performance test scores were available for only 613 participants.

Table 2.2.4 Functional characteristics (percentages and number of subjects) of the study population per subgroup (SENECA'S Follow-up Study, 1993)*

	Inactivity group 1 (N = 204)	Weight loss group 2 (N = 108)	Inactivity & weight loss group 3 (N = 54)	Reference group 4 (N = 483)
Physical Performance				
PPT score (0-28) (median, P10-P90)	18 (9-23) ‡	22 (15-25)	17 (0-23) ‡	22 (15-26)
% (n) poor standing balance	42 (58) ‡	20 (17)	54 (15) †	19 (69)
% (n) poor chair stand performance	58 (80)	50 (43)	68 (19)	61 (221)
Disabilities				
% (n) disabled in ADL	80 (161) ‡	44 (47)	81 (43) ‡	43 (205)
% (n) disabled in mobility	51 (104) ‡	24 (26)	65 (35) ‡	18 (85)
% (n) disabled in self-care	45 (92) ‡	14 (15)	53 (28) ‡	18 (88)
Use of care services				
% (n) home care for medical reasons	21 (43) ‡	7 (8)	26 (14) ‡	6 (31)
% (n) Meals-on-Wheels	11 (22) ‡	3 (3)	17 (9) ‡	2 (11)
Self-rated activity				
% (n) feeling less active than peers	33 (63) ‡	11 (11)	42 (21) ‡	6 (27)
% (n) feeling less active than 4 yr ago	79 (161) ‡	51 (55)	87 (47) ‡	56 (269)

* The number of observations is variable due to missing values.

† $p \leq .05$, ‡ $p \leq .001$ compared with the reference group.

Dietary habits and social contacts

Table 2.2.5 presents dietary habits and social contacts. Following a diet (36 and 34% vs. 17%, $p \leq 0.01$) and chewing difficulties (35 and 28 vs. 15%, $p \leq 0.02$) were more prevalent in inactive and inactive weight-losing elderly. Subjects in this group had also changed their eating habits more often in the last year. Weight-losing elderly also used vitamin and mineral supplements more often. Low fat (59%), low salt (48%) and diabetic (26%) were the predominant diet modifications recommended. The type of diet modification did not differ significantly between individuals who were inactive, losing weight, or both and the reference group (data not shown).

The inactive weight-losing group reported a lower number of close friends (mean 1.3 vs. 2.4, p = 0.01). Both inactive and inactive weight-losing participants had fewer social contacts compared to the reference group (49 and 48 vs. 26% contacted friends less than once a week, $p \leq 0.001$). Few social contacts occurred less often in weight-losing participants (6 vs. 17% p = 0.006).

Table 2.2.5 Dietary habits and social contacts (% and n) of the study population (SENECA'S Follow-up Study, 1993)*

	Inactivity	**Weight loss**	**Inactivity & weight loss**	**Reference**
	group 1 (N = 204)	**group 2 (N = 108)**	**group 3 (N = 54)**	**group 4 (N = 483)**
Dietary habits				
On specific diet	36 (72) $	20 (22)	34 (18) ‡	17 (83)
With changed eating habits	33 (65)	32 (34)	52 (28) $	25 (122)
With chewing difficulties	35 (70) $	13 (14)	28 (39) †	15 (74)
Taking vitamin supplements	19 (38)	44 (47) $	30 (16)	23 (113)
Social contacts				
Mean (± SD) number close friends	2.0 ± 2.3	3.1± 3.1	1.3 ± 1.6 †	2.4 ± 2.6
< Weekly contacting friends	49 (99) $	20 (22)	48 (25) $	26 (123)
< Weekly being contacted	37 (75) $	6 (7) †	23 (12)	17 (82)
Living alone	73 (149)	62 (67)	61 (33)	69 (333)

* The number of observations is variable due to missing values.

† p≤.05, ‡ p≤.01, $ p≤.001 compared with the reference group.

Dietary intake and biochemical characteristics

Table 2.2.6 shows prevalence of intakes below the Recommended Daily Allowances (RDA) and low biochemical values. Low energy (<6.3 MJ per day) and micronutrient (vitamins A, B_1, B_2, C, iron and calcium) intakes were more prevalent among inactive elderly. Inadequate intakes of vitamins A, B_2, B_6, iron and calcium were more prevalent among inactive, weight-losing elderly subjects.

Table 2.2.6 Percentage (n) of the study population with nutrient intakes below the lowest European Recommended Daily Allowances(RDA)[71] and low biochemical values* (SENECA'S Follow-up Study, 1993)†

	Inactivity group 1 (N = 204)	Weight loss group 2 (N = 108)	Inactivity & weight loss group 3 (N = 54)	Reference group 4 (N = 483)
Intakes below RDA				
energy < 6.3 MJ/d	32 (63) $	22 (24)	28 (15)	20 (97)
vitamin A	50 (99)**	23 (25)	63 (34)**	32 (152)
vitamin B_1	33 (66) $	23 (25)	28 (15)	23 (111)
vitamin B_2	34 (67)**	17 (18)	41 (22)**	20 (98)
vitamin B_6	14 (26)	11 (11)	19 (9) ‡	10 (38)
vitamin C	10 (19) $	8 (9)	6 (3)	4 (20)
iron	29 (58)**	20 (22)	30 (16)**	13 (63)
calcium	29 (57)**	14 (15)	37 (20)**	12 (55)
Biochemical characteristics				
vitamin E	1 (2)	0 (0)	2 (1)	1 (3)
vitamin B_6	4 (2)	5 (1)	6 (1)	2 (2)
vitamin B_{12}	9 (16) $	7 (7)	15 (7)**	4 (17)
hemoglobin	5 (10)	6 (6)	13 (6) $	5 (22)
haematocrit	27 (50)	31 (31)	32 (15)	22 (102)
serum albumin	4 (8) $	2 (2)	2 (1)	1 (5)

* Plasma a-tocopherol < 4.74 mg/l, plasma pyridoxal-5'phos < 20 nmol/l, plasma vit B_{12} < 150 ng/l, hemoglobin for men < 130g/l, for women < 120 g/l (WHO 1968), haematocrit for men < 43 %, for women < 39 %, serum albumin < 35 g/l [66].

† The number of observations is variable due to missing values.

‡ p≤.05, $ p≤.01, ** p≤.001 compared with the reference group.

Vitamin A, E and folate status were adequate (0, 0.3 and 0.4% below the reference, respectively [data not shown]). Inactive subjects showed more frequent low vitamin B_{12} (9 vs. 4%, p = 0.01) and serum albumin concentrations (4 vs. 1%, p = 0.08). Inactive weight-losing elderly had more frequent low vitamin B_{12} (15 vs. 4%, p = 0.001) and low hemoglobin concentrations (13 vs. 5%, p = 0.02).

Discussion

The results of our study indicate that inactive elderly have less favorable health and nutritional characteristics and poorer physical functioning. In inactive, weight-losing elderly the situation was even worse. Inactivity in combination with weight loss therefore seems to be a suitable criterion for identifying a frail elderly population among community-dwelling elderly persons. These findings are in concordance with earlier studies which found inactivity and weight loss alone or combined to be associated with a less favorable health status.[47;63;73-75]

Several factors may have influenced the results. One point of consideration is the definition of physical inactivity and weight loss. We used the gender-specific lowest tertile of the total activity score to define participants as inactive. The Voorrips questionnaire has been shown to be valid for classifying elderly subjects into categories of high, medium and low physical activity. This questionnaire has demonstrated a test-retest correlation (r = 0.89) and has been validated against repeated 24-hour activity recalls and pedometer measurements (r = 0.78 and 0.72, respectively).[69] Seventy-one and sixty-seven percent of the subjects respectively were classified in the same activity tertile for both methods. Subjects in the lowest quintile of weight change (6.3% weight loss or more over 4-5 years) were defined as weight-losing. The literature mentions several values of weight loss over different periods (from more than 5% in 1 month to more than 10% between age 50 and old age) to be associated with morbidity and mortality.[47;74] Involuntary weight loss is particularly associated with poor health.[47;74;76] We did not separate voluntary and involuntary weight loss. Weight loss could have been the result of positive changes in lifestyle such as dietary changes or increased physical activity, or poor health such as preexisting disease or medication side effects. In our study the number of chronic diseases was higher in the inactive, weight-losing group, but not in the weight loss only group. The percentage of participants following an energy/fat-restricted diet did not differ significantly between the groups, but activity level was indeed highest in the weight-losing group. It appears that weight loss is associated with poor health, especially when combined with inactivity.

Secondly, elderly subjects participating in research are a selective group who are likely to have a higher educational and socioeconomic background and fewer health problems. Frail elderly are less likely to participate. Non-responders at baseline (49%) were in a worse health and nutritional status than participating elderly.[65] Moreover, participating subjects in 1993 (58%) were the healthier segment of the original population, since dropout due to death and health changes had occurred.[77] Nevertheless, inactivity and weight loss identify a relatively frail sub-population, even among such a health-selected group. A longer follow-up would be needed to find out whether inactivity in combination with weight loss is also predictive of a further decline in health, functioning and nutritional status. Controlled trials should provide information about the effectiveness of physical exercise and dietary modifications in improving health and preventing disability.

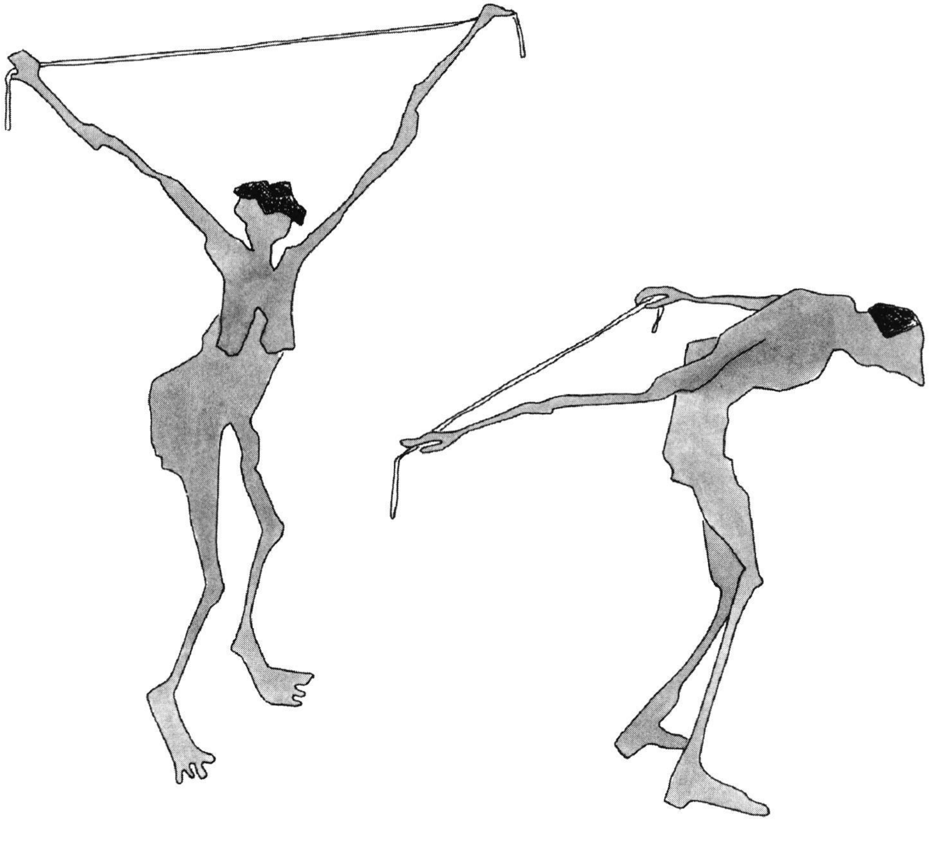
A third point of consideration is that we have only rough indicators of health, functional ability and nutritional status. The number of diseases, medicines, disabilities and the perceived health are all assessed with a questionnaire and a rather subjective indication of health status. However, self-ratings of health do appear to be strongly related with changes in functioning.[31;78]

Adequacy of intakes below the RDI and biochemical values below the reference as indicators of poor nutritional status can be discussed. RDIs differ between countries and reference values of blood levels vary even within a country. Additionally, reference factors such as chronic disease, inflammation, bioavailability, absorption and metabolism may have a greater influence than nutritional factors. Underestimation of energy intake and consequently micronutrient intake may have occurred. Overweight people tend to underreport their food intake more than normal weight people do.[74] This may be an explanation for the higher prevalence of inadequate energy intakes in combination with a higher BMI in inactive persons. Still, prevalence of low micronutrient intake and blood values can give an indication of which individuals are at risk of developing nutritional deficiencies.

In conclusion, our results suggest that inactivity with or without weight loss seems to be a practical screening criterion for identifying functionally vulnerable persons among a non-institutionalized elderly population. Both are inexpensive and simple to measure. Having standardized criteria that identify frail populations will facilitate the development and implementation of strategies that aim at favoring older persons' independence.

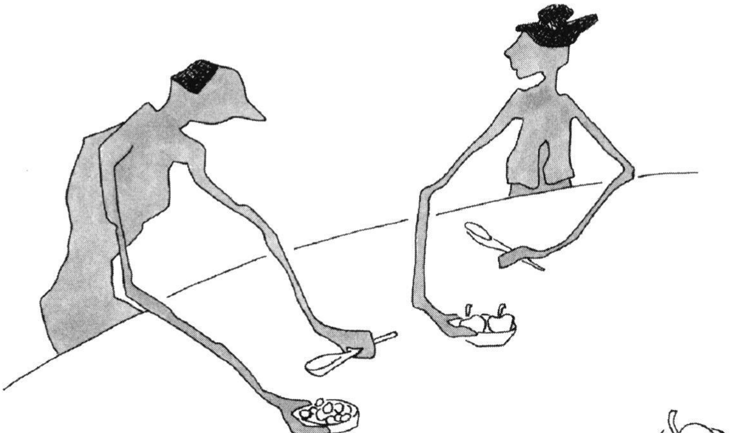
3

The effectiveness of physical exercise and nutrient dense foods in frail elderly: a randomized controlled trial



3.1

Effects of exercise and micronutrient enriched foods in the functional improvement of frail elderly persons



JMM Chin A Paw, N de Jong, EG Schouten, GJ Hiddink, FJ Kok. Submitted.

Abstract

This randomized, placebo-controlled trial examined the effects of an exercise program and micronutrient enriched foods, both developed for widespread applicability, on functional performance, fitness and disabilities in frail elderly.
Independently-living frail elderly people (n = 157) aged 67-96 were randomly assigned to: a) a twice weekly, progressive group exercise of moderate intensity designed to improve daily functioning (n = 39); b) food products enriched with vitamins (100% RDA) and minerals (25-100% RDA) (n = 39); c) both (n = 42) or d) neither: control (n = 37). Non-trained groups followed a social program, non-supplement groups received identical regular products. A performance score was constructed based on 6 performance tests, a fitness score based on 7 fitness tests, and an ADL score based on the ability to perform 16 daily activities (ADLs).
Performance (+8%) and fitness scores (+3%) were significantly increased in trained compared to non-trained subjects (-8% and -2%, respectively) (difference in change: 1.9 points, p <0.001 for performance and 0.9 points, p = 0.05 for fitness, adjusted for baseline scores). This beneficial effect of exercise was even stronger in a more frail subgroup (n = 62) and in a more compliant subgroup (n = 143). No exercise effects on ADL score were observed. Consumption of nutrient dense products did not affect performance, fitness or ADL scores.
Our widespread applicable and convenient exercise program improved physical performance and fitness in a population of frail elderly. Daily consumption of micronutrient enriched foods at 25-100% of the RDA showed no functional benefits within 17 weeks.

Introduction

Aging is associated with a decline in physical performance affecting an individual's ability to perform activities of daily living and quality of life. Research into the prevention, management and rehabilitation of functional disability in older persons is of great importance. Frail elderly are at a high risk of functional decline. Major determinants of this vulnerable state are biological aging, chronic diseases, malnutrition and physical inactivity.[3;5;7] Lower energy expenditure, due to lower activity levels, may result in lower food consumption, increasing the risk of sub-optimal nutrient intakes. Both an inadequate dietary intake and inactivity have been associated with a loss of muscle mass and function, resulting in functional limitations[7] and an even further decline in activity levels. Appropriate exercise or multi-vitamin/mineral supplementation may prevent and/or reverse the functional decline, immobility, and suboptimal nutritional status. The combination of both may be even more effective.

The research of the past decade has demonstrated the benefit of exercise for the frail and very old.[14-16;26;79;80] However, many exercise programs studied are not feasible for widespread implementation and long term adherence (expensive equipment, high intensities and frequencies, repetitive movements and individual supervision). In the development of our all-round exercise program, designed for improvement of daily functioning, we emphasized applicability, convenience and enjoyment.

The effects of micronutrient supplementation on physical functioning have not been rigorously studied.[15;27;81] Several trials have shown positive effects of macro and micronutrient supplementation on body weight but not on muscle strength. However, cross-sectional correlations between dietary intakes of vitamin B6, magnesium, potassium, and muscle capacity have been reported.[26] Because lower levels of activity result in lower energy requirements, we chose not to supplement with extra energy, carbohydrates, fats or proteins, but only with vitamins and minerals. We provided several food products suitable for daily use enriched with vitamins (100% the recommended daily allowances ([RDA]) and minerals (25-100% RDA) of which low intake has been reported in elderly people.
The aim of the present study was to examine the effects of our exercise program and enriched foods on physical functioning of frail community-dwelling elderly people. Performance-based tests, several fitness components and self-rated ability to perform daily activities were selected as outcome measures. Because exercise may have differential effects depending on the underlying nutritional state, the interaction between both interventions was also studied.

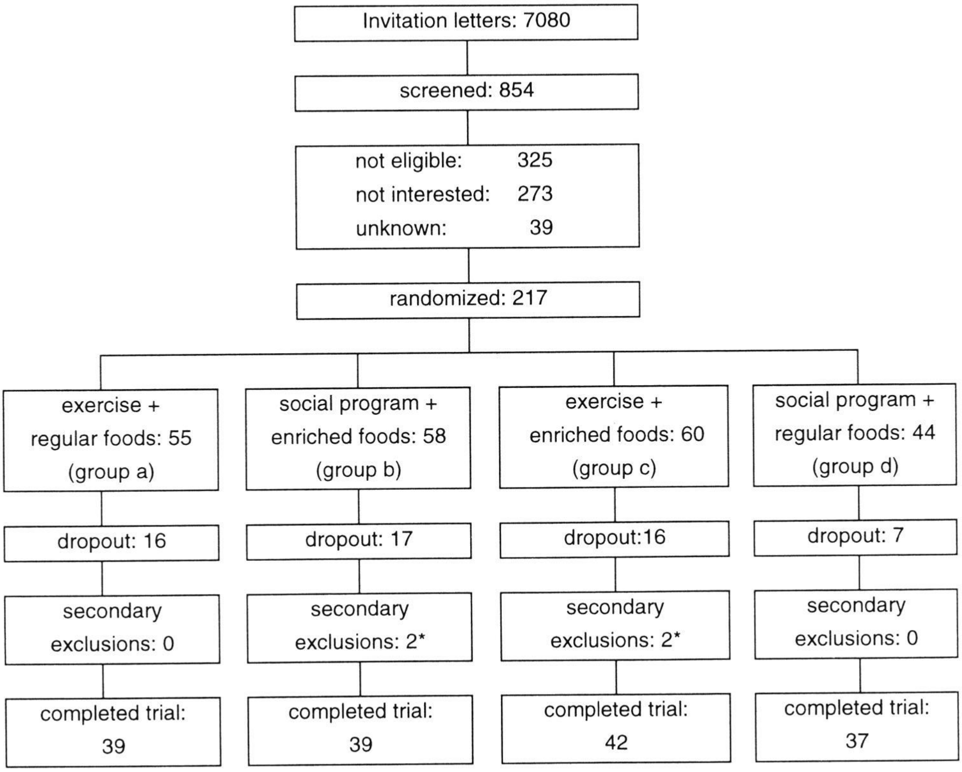
Methods

Design

The study was a randomized, placebo-controlled intervention trial based on a two-by-two factorial design that permitted an assessment of the effects of the exercise and nutritional intervention independently as well as a possible interaction effect.

Study population

Subjects were recruited by mail from senior housing complexes, Meals-on-Wheels programs, home care organizations and general practitioners (see Figure 3.1.1). Subsequent telephone screening selected those fulfilling the following inclusion criteria: age 70 or older, a need for care services (e.g. home care, Meals-on-Wheels), no regular exercise, self-reported body mass index (BMI) below 25 kg/m^2 or involuntary weight loss, non-institutionalized, not taking multivitamins for the last month, no terminal disease or rapidly deteriorating health status, and the ability to comprehend the procedures of the study. A total of 217 eligible and interested subjects were enrolled in the study from January through July 1997 and randomly assigned to: (a) supervised group exercise (n = 55), (b) nutrient dense foods (n = 58), (c) both (n = 60) or (d) control group (n = 44) by sealed envelopes. Fifty-six subjects dropped out. The main reasons for dropout were health problems (41%) including disease, hospital stay and recent falls or fractures. Four subjects were excluded from analysis because of missing or invalid measurements (sprained ankle, foot operation), resulting in a study population of 157 subjects. The study protocol was approved by the medical ethics committee of the Division of Human Nutrition and Epidemiology of Wageningen Agricultural University and a written informed consent was obtained from each subject.



* The asterisk indicates subjects excluded because of invalid or missing performance or fitness scores.

Figure 3.1.1. Study profile

Exercise intervention

Subjects assigned to exercise participated for 17 weeks twice a week in 45 minutes of supervised, progressive group exercise of moderate intensity. All exercises were described in a manual, shown on an instruction video and rehearsed with all 5 teachers. The classes included 5-10 minutes of warm-up activities (walking and exercise-to-music routines), 20-25 minutes of training functional abilities (chair rises, stooping, catching, toe raises) focused on improving muscle strength, coordination, flexibility and endurance, as well as a cool-down period with stretching exercises. The intensity was gradually increased with more standing exercises and repetitions, stimulating the use of wrist and ankle weights (450 gram each) and the use of different materials (e.g. foam tubes, elastic bands, wrist/ankle weights). Participants and teachers were instructed to train at an intensity between 6 and 8 on a 10-point perceived exertion scale (1 = very, very light and 10 = very, very heavy). A fixed value on a perceived exertion scale can be used for exercise prescription instead of more expensive methodologies (e.g. heart rate, ventilatory threshold).[82] To adjust for the effect of socializing and attention, subjects not randomized to exercise participated in a social program (lectures, games, crafts) once every two weeks for 90 minutes under the supervision of a creative therapist. Subjects were asked not to engage in other exercise programs. Transport to and from all sessions was arranged.

Nutritional intervention

Subjects were supposed to eat one fruit product (juice, compote) and one dairy product (vanilla custard, fruit yogurt, vanilla fruit soft curd cheese) daily for 17 weeks. A sufficient stock of fresh products was delivered at home once a week. The nutrient dense foods were enriched with several vitamins and minerals. Two products delivered on average 0.48 MJ and 100% of the Dutch Recommended Daily Allowances (RDA) of vitamin D, E, B1, B2, B6, folic acid, B12 and C and 25-100% of the Dutch RDA of calcium, magnesium, zinc, iron and iodine. The exercise and control group received identical but non-enriched products (similar energy content). Compliance was assessed by measuring the serum vitamin levels.

Measurements

Measurements were performed at baseline and after 17 weeks of intervention.

Functional capacity

Functional capacity was evaluated by six performance tests; 1) the ability to balance 10 seconds in tandem stand; 2) average usual gait speed and step length over a distance of 6 m without or 3) with a handbag (5 kg); the time required for: 4) standing up from a chair five times (chair-stand test); 5) touching the left foot with the right hand and vice versa (in sitting position); and 6) putting on and buttoning up a coat.

Physical fitness

Physical fitness was assessed using seven components of the validated Groningen Fitness test for Elderly (GFE).[83] 1) a block-transfer test for measuring manual dexterity (eye-hand coordination); 2) a reaction time test: reacting to the onset of a light by pushing a button as fast as possible; 3) keeping a balance board in equilibrium during 30 seconds; 4) flexibility of the hip and spine using a standard 'sit-and-reach' box; 5) shoulder flexibility test: bring a rope, with a fixed and a moveable handle, symmetrically over the head and behind the body, while keeping the arms stretched and the hands as close together as possible; 6) isometric hand grip strength of the dominant hand measured with a hand grip dynamometer (best of three trials); 7) maximum isometric strength of the right musculus quadriceps femoris measured sitting on a quadrisometer with lower legs hanging down. A detailed description of the test components can be found elsewhere.[83] All performance and fitness tests were carried out under standard conditions by the same researcher. For each test (except for the tandem stands: 1 if able, 0 if unable) a 0 to 4 score was given based on gender-specific quintiles. A score of 2 corresponds with an average ability to perform the test; 0 means far below and 4 far above average. If a subject was unable to perform the test he or she was given a 0 score. A performance and fitness sum score was computed by summing up the scores of the individual tests.

Self-rated disabilities

The capacity to perform activities of daily living (ADLs) was assessed as self-rated disabilities in 16 daily activities.[84] For each item the level of competence was asked on a 4-point scale (can do without difficulty, with difficulty but without help, only with help, unable to perform). A combined ADL score was calculated as a sum score of all 16 items, a mobility score (MI) as the sum of four of these items (move outdoors, use stairs, walk at least 400m, carry a heavy object), and a self-care ability score (SI) as the sum of seven items (walk between rooms, use the toilet, get dressed, get in and out of bed, cut toenails, feed yourself).

Other measures
Physical activity was assessed using a validated questionnaire based on the Physical Activity Scale for the Elderly (PASE), slightly adjusted for use in Dutch older subjects.[85;86] Weight and height were measured (wearing underclothes) and used to calculate body mass index (BMI: kg/m^2). Information on age, diseases, medication and falls was collected in a personal interview.

Statistical analysis
Data were analyzed using SAS statistical software, version 6.11 (Statistical Analysis System; SAS Institute Inc. Cary, USA). Analyses focused on estimating the overall effect of the two interventions on changes in performance, fitness and ADL scores. Means (± standard deviations [SD]), medians (10th-90th percentiles) or percentages of baseline characteristics were calculated for each intervention group. An interaction between the effects of exercise and nutrient dense foods was tested by means of regression analyses with the changes in performance, fitness or ADL as dependent variable, and both interventions and an interaction term as independent variables. Because there was no evidence of an interaction between both interventions ($p = 0.57$ for fitness, $p = 0.55$ for performance and $p = 0.26$ for ADL score), the effects of each intervention were analyzed separately. Student's t-tests or Wilcoxon's rank sum tests were performed to study the difference in changes in the individual performance and fitness tests between trained (groups a+c) and non-trained subjects (groups b+d) with nutrient dense (groups b+c) and regular foods (groups a+d) respectively. To further assess the significance of the interventions as modified or confounded by age and baseline performance, fitness or ADL scores, a regression analysis was done with these variables as covariates. A subgroup analysis was performed excluding subjects not meeting the inclusion criteria (younger than 70, a measured BMI >25 kg/m^2) and the most active subjects (PASE score in the highest quartile). Another subgroup analysis was performed excluding subjects who attended less than 75% of program sessions. A p-value ≤ 0.05 was considered statistically significant.

Results

Characteristics of the participants

Table 3.1.1 presents baseline characteristics of subjects per intervention group. About 70% were women. At baseline the subjects averaged an age of 78.7 (range: 67-96), had a mean BMI of 24.5 kg/m², rated their health a 7, and reported a mean, respectively median number of diseases and medicines of two. The most frequently reported diseases were cardiovascular (38%) and musculoskeletal (33%). Almost a third of the subjects had experienced at least one fall in the year preceding the trial.

Table 3.1.1 Baseline characteristics (mean ± SD) of the study population per intervention group (N = 157).

	Exercise (group a) n = 39	**Nutrient dense foods (group b) n = 39**	**Both (group c) n = 42**	**Control (group d) n = 37**
Age (yr)	76.2 ± 4.5	79.2 ± 4.8	78.9 ± 6.0	78.6 ± 6.6
Percent male	28	28	26	32
Percent living alone	67	69	69	70
BMI (kg/m²)	24.4 ± 2.9	24.5 ± 2.4	25.0 ± 2.5	24.1 ± 3.1
PASE-score (0-400)*	62 (27-100)	59 (34-103)	60 (30-111)	59 (27-117)
Perceived health (0-10)†	7.0 ± 1.2	6.9 ± 1.7	6.9 ± 1.3	7.0 ± 1.4
Number of medications*	2 (0-6)	2 (0-6)	3 (0-5)	3 (0-7)
Number of self-reported diseases	1.7 ± 1.0	1.9 ± 1.2	1.9 ± 1.2	1.9 ± 1.4
cardio-vascular (%)	28	51	36	35
musculoskeletal (%)	31	33	38	30
pulmonary (%)	8	10	19	5
Percent smoking	10	13	7	16
Percent with falls (past year)	38	26	36	27

*median (10^{th}-90^{th} percentile)

† a higher score indicates better health

Compliance

Attendance at the exercise sessions was high (median: 90% of all sessions, range: 47-100%). Compliance with the nutritional intervention, estimated on the basis of the changes in blood vitamin concentrations, was also high. The percentage of subjects with biochemical values below the reference decreased significantly by more than 50% (from 62% to 27%) among subjects consuming enriched foods compared to a small increase (from 67 to 71%) in subjects consuming regular foods ($p<0.001$).

Functional performance, physical fitness and activities of daily living

Tables 3.1.2 and 3.1.3 show the baseline mean or median scores for the individual performance and fitness tests, the sum score and the 17 weeks changes according to the type of intervention: exercise (groups a+c) versus no exercise (groups b+d), and nutrient dense (groups b+c) versus regular foods (groups a+d). After 17 weeks the performance sum score in trained subjects had increased by 8% (0.9 points) compared to a decline of 8% (-0.8 points) in non-trained subjects (difference: $p<0.001$). Improvement occurred especially in the tests for chair stands, touching toes and walking speed. The beneficial effects of exercise on fitness sum score was smaller ($p = 0.14$). Exercise improved balance significantly. Further, small improvements were observed in quadriceps strength, manual dexterity and reaction time. The changes in performance and fitness scores in subjects receiving nutrient dense foods were similar compared to subjects receiving regular products.

Table 3.1.2 Mean (± SD) or median (10th-90th percentile) baseline performance scores and 17-week changes according to type of intervention (N = 157).

	Exercise (groups a + c) n=81	**No exercise** (groups b + d) n=76	**Nutrient dense foods** (groups b + c) n=81	**Regular foods** (groups a + d) n=76
buttoning up a coat (s)	30.3 (19.8-52.0)	34.2 (21.7-59.3)	31.4 (20.9-63.0)	31.8 (20.3-52.0)
*change**	*-1.2 (-10.0-8.5)*	*-1.9 (-14.5-9.9)*	*-2.3 (-14.5-9.9)*	*-1.1 (-9.3-8.5)*
touching toes (s)†	5.2 (4.0-9.5)	5.4 (4.1-10.0)-	5.2 (4.0-9.3)	5.4 (4.1-10.3)
*change**	*-0.7 (-2.7-0.6)*	*0.1 (-2.5-1.8)‡*	*-0.5 (-2.5-0.6)*	*-0.3 (-2.8-1.4)*
chair stands (s)†	18.6 (14.4-33.2)	18.9 (15.0-31.3)	18.9 (14.2-33.6)	18.5 (15.0-31.6)
*change**	*-2.3 (-7.7-1.4)*	*-1.0 (-6.4-3.8) $*	*-1.8 (-7.8-2.2)*	*-1.9 (-6.0-2.5)*
walking speed (m/s)	0.89 ± 0.2	0.86 ± 0.2	0.89 ± 0.2	0.87 ± 0.2
change	*0.06 ± 0.1*	*0.0 ± 0.04 ‡*	*0.0 ± 0.1*	*0.01 ± 0.1*
step length (m)	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1
change	*0.01 ± 0.04*	*0.0 ± 0.04*	*0.0 ± 0.04*	*0.0 ± 0.04*
walking speed + 5 kg (m/s) †	0.1 (-0.1-0.2)	0.84 ± 0.2	0.84 ± 0.2	0.85 ± 0.2
change	*0.1 (-0.1-0.2)*	*0.0 (-0.1-0.1)‡*	*0.05 (- 0.1-0.2)*	*0.02 (-0.1-0.2)*
tandem stands (% able)				
pre-intervention	72	65	68	68
post-intervention	78	67	75	70
sum score (0-21)	10.9 ± 6.3	9.6 ± 5.7	10.0 ± 6.1	10.5 ± 6.1
change	*0.9 ± 2.8*	*-0.8 ± 3.4***	*0.3 ± 3.3*	*-0.1 ± 3.1*

* negative change indicates improvement

† calculated for subjects who succeeded in performing the test

‡ p ≤0.004, $ p = 0.03 difference between exercise and no exercise according to the Wilcoxon signed rank test

** p< 0.001 difference between exercise and no exercise according to students t-test

Table 3.1.3 Median (10^{th}-90^{th} percentile) baseline fitness scores, mean (± SD) fitness sum score and 17-week changes according to type of intervention (N = 157).

	Exercise (groups a+c) n = 81	**No exercise (groups b+d) n = 76**	**Nutrient-dense foods (groups b+c) n = 81**	**Regular foods (groups a+d) n = 76**
grip strength (kgf)	23 (15-38)	22 (16-34)	23 (16-36)	22 (16-36)
change	*0 (-3-5)*	*1 (-3-4)*	*1 (-3-5)*	*0 (-3-4)*
quadriceps strength (kgf)	28 (9-48)	24 (13-42)	27 (13-45)	25 (11-47)
change	*1.5 (-4.9-8.7)*	*0.3 (-4.6-6.0)*	*1.3 (-3.8-7.8)*	*0.9 (-5.4-6.8)*
shoulder flexibility (°)*	49.7 (43.7-55.5)	47.6 (42.3-53.3)	48.2 (42.0-55.8)	49.3 (43.3-55.5)
change	*-1.1 (-6.1-2.4)*	*-0.6 (-4.5-1.6)*	*-1.0 (-4.5-2.8)*	*-0.6 (-4.5-1.6)*
hip/spine flexibility (cm)	21 (6-37)	22 (0-34)	23 (0-36)	20 (0-37)
change	*0 (-3-6)*	*0 (-5-3)*	*0 (-3-6)*	*0 (-5-3)*
balance (0-100)	74 (37-86)	73 (41-85)	73 (43-86)	73 (31-85)
change	*4 (-7-17)*	*2 (-12-13)* ‡	*2 (-7-15)*	*2 (-10-17)*
block transfer test (s)	54.2 (45.8-67.4)	56.3 (48.4-72.6)	55.9 (46.0-71.2)	54.6 (47.9-68.4)
change †	*-2.0 (-7.8-4.9)*	*-0.2 (-10.4-9.6)*	*0.8 (7.4-7.0)*	*-1.6 (-10.4-6.6)*
reaction time (ms)	237 (189-325)	245 (194-358)	225 (180-364)	252 (196-330)
change †	*-1.0 (-60-58)*	*1.5 (-84-55)*	*6.0 (-74-69)*	*-7.5 (-71-51)*
sum score (0-28)	14.9 ± 6.4	12.8 ± 5.6	14.1 ± 6.4	13.7 ± 5.9
change	*0.5 ± 2.5*	*-0.2 ± 3.2*	*0.1 ± 2.7*	*0.1 ± 3.1*

* calculated for subjects who succeeded in performing the test.

† negative change indicates improvement.

‡ $p = 0.05$ difference between exercise versus no exercise according to Wilcoxon's rank sum test.

Table 3.1.4 shows the self-rated disabilities at baseline and the change after 17 weeks of intervention according to the type of intervention. Baseline ADL, mobility and self-care scores were almost maximal. Still, only 18% were able to perform all ADL activities without difficulties or help. A small overall decline in ADL scores of -0.5 (0.01%), which was similar between treatments, was found.

Table 3.1.5 shows the crude and adjusted mean difference in changes in performance, fitness and ADL sum scores between exercise (groups a+c) and no exercise (groups b+d) respectively and nutrient dense (groups b+c) and regular foods (groups a+d). After adjustment for the baseline scores the beneficial effects of exercise on performance and fitness became stronger (difference between trained and non-trained from 1.75 to 1.93 points for performance, p<0.001, and from 0.68 points, p = 0.14, to 0.91 points, p = 0.05 for fitness). After adjustment for baseline scores the nutritional intervention remained ineffective in improving performance, fitness or ADL scores.

Table 3.1.4 Median baseline ADL, mobility and self-care scores* (10^{th}-90^{th} percentile) and mean (± SD) 17-week changes according to type of intervention (N = 153 †).

	Exercise (groups a+c) n = 80	**No exercise (groups b+d) n = 74**	**Nutrient dense foods (groups b+c) n = 79**	**Regular foods (groups a+d) n = 75**
ADL score (0-48)	45 (34-48)	43 (35-48)	44 (34-48)	44 (34-48)
change	*-0.6 ± 3.4*	*-0.4 ± 3.3*	*-0.9 ± 3.6*	*-0.1 ± 3.0*
mobility score (0-12)	11 (5.5-12)	11 (6-12)	11 (6-12)	11 (5-12)
change	*-0.4 ± 1.7*	*-0.1 ± 1.4*	*-0.4 ± 1.6*	*-0.1 ± 1.5*
self-care score (0-21)	20 (17-21)	20 (17-21)	20 (17-21)	20 (17-21)
change	*-0.1 ± 1.6*	*-0.2 ± 1.5*	*-0.2 ± 1.6*	*-0.1 ± 1.5*

* higher scores indicate better performance.

† numbers vary slightly due to missing data.

Table 3.1.5 Mean difference (95% confidence interval) in change in performance, fitness and ADL scores between subjects receiving exercise versus no exercise and subjects receiving nutrient dense versus regular products.

	Exercise versus no exercise	Nutrient dense versus regular products
Performance score (N = 157)		
crude	1.75 (0.79-2.71)*	0.40 (-0.60-1.40)
adjusted for baseline performance	1.93 (0.85-2.85)*	0.45 (-0.53-1.43)
Fitness score (N = 156)		
crude	0.68 (-0.22-1.58)	-0.04 (-0.88-0.96)
adjusted for baseline fitness	0.91 (0.01-1.81)†	-0.36 (-0.54-1.26)
ADL score (N = 153)		
crude	-0.11 (-1.17-0.95)	-0.75 (-1.81-0.31)
adjusted for baseline ADL and age	-0.25 (-1.23-0.73)	-0.40 (-1.38-0.58)

* $p < 0.001$, † $p = 0.05$ according to regression analysis

Subgroup analysis

Since not all subjects fitted the inclusion criteria, a subgroup analysis was performed in subjects older than 70 with a BMI below 25 kg/m^2. Additionally, the most active subjects (highest quartile of PASE score) were excluded, resulting in 62 subjects. The beneficial effects of exercise increased to 2.5 points (p = 0.002) for performance and 1.8 (p = 0.02) for fitness sum scores (adjusted for baseline scores). Again, no effects on ADL score were found. The nutritional intervention remained ineffective in improving performance (0.35 points, p = 0.66), fitness (0.12 points, p = 0.88) or ADL scores (-0.72 points, p = 0.49). The exercise effects were also increased in a subgroup with higher attendance (>75% of exercise/social sessions, n = 143): 2.0 points (p<0.001) and 1.2 (p = 0.02) for performance and fitness scores respectively (adjusted for baseline scores).

Discussion

Our specifically-designed exercise program significantly improved functional performance in a group of frail Dutch elderly people. We also found a small effect on fitness but no effects on self-rated disabilities. We observed no effects of the nutrient dense foods. The stronger effect on performance emphasizes the specificity of training: strength training is expected to improve muscle strength, while an all-round functional program is necessary for an improvement of functional tasks.

Most studies on frail elderly have focused on institutionalized elderly people.[15;16;25;26;80] Frail yet independently-living elderly subjects are a high-risk group for functional decline. Improving their functional status may prevent or postpone the need for expensive institutionalization and home health care. The observed beneficial effects of exercise on frailty are in concordance with earlier trials.[15;16;80] Fiaterone et al[15] demonstrated the efficacy of high-intensity, high-frequency progressive resistance training under individual supervision in improving muscle mass and strength in institutionalized frail elderly subjects. Long-term adherence to and widespread applicability of these types of programs (individually performed, repetitive exercises using expensive, unfamiliar equipment) is not to be expected, though. We have therefore tried to develop an exercise program that can be more easily adopted in the habitual lifestyle of this vulnerable population group.

The effects of nutritional supplementation on the functional capacity of frail elderly people has not been studied rigorously. Gray-Donald et al[27] reported an increase in body weight without significant changes in muscle mass or strength after 12 weeks of supplementation with macro and micronutrients. Only a few studies have focused on the effects of both exercise and nutritional supplementation.[15;81] Both studies found significant effects of strength training on muscle strength but no effects for nutritional supplementation. In addition to extra vitamins and minerals (one third and 25-75% of the RDA respectively), the nutritional supplements in these studies also included carbohydrates, protein and fat.

Study population

Our study focused on frail elderly people. Criteria to select frail elderly subjects are lacking.[4] We used a need for care services (e.g. home care, Meals-on-Wheels) and physical inactivity (no regular exercise) as the main selection criteria. Furthermore, subjects' body weight had to be below average or they had to suffer from involuntary weight loss. For both body weight and weight loss we had to rely on the subjects' own report. Because recruitment tends to favor enrollment of healthier, better nourished and more active subjects, recruitment of a frail study population group appeared very intensive and time-consuming. We finally succeeded in recruiting a substantial group of elderly individuals who were on average less healthy and active compared to Dutch healthy elderly persons; self-rated health (7.0 versus 7.7),[87] activity level (68 versus 72 for men, 65 versus 98 for women),[85] and fitness, performance and ADL scores were all below average.[22;88;89]

The somewhat higher pre-intervention fitness score of subjects randomized to exercise compared to the non-exercise subjects may suggest a limited comparability. Since greater improvements are usually found for subjects with lower initial values, it is unlikely that the observed effects of exercise were due to these higher initial fitness scores. Furthermore, performance and ADL scores were similar at baseline.

Measurements

For the measurement of functional status we used performance-based as well as self-reported measures. Performance-based measures are considered to be less influenced by poor cognitive function, culture, language and education, and therefore more valid and objective than self-reported measures. The Groningen Fitness test for Elderly is a reliable and valid test for the evaluation of physical fitness in the elderly.[83] The performance and fitness tests used proved to be safe and practical in a frail population. The simple tests are good predictors of independence and mobility in the elderly.[24]

No effects on ADL scores, the self-reported measure of functional status, were found. A possible explanation is that baseline scores were already high, leaving little room for improvement. With increasing age people may adapt to experienced functional limitations, resulting in little change in their perceived ability to perform certain activities despite an actual decline. Indeed, some subjects did not report any difficulties with activities, despite clear disabilities. Another explanation is that subjects became more critical and aware of their abilities and disabilities. We also believe that the ADL questionnaire might not be specific enough to measure improvement. Only information on general activities was asked, while exercising subjects spontaneously mentioned improvement in more specific activities like putting on a bra, opening sugar bags and tabs or closing the curtains.

Interventions

During the development of the specific training program, improvement in performance of daily activities and feasibility for widespread implementation by frail elderly persons were emphasized rather than a mere increase in muscle strength or endurance. This was done by focusing on skills and activities (walking, stooping, chair rises), using different materials, music, game-like activities and group sessions. Whenever necessary, exercises were adjusted to less mobile persons to ensure the program was suitable for all levels. Furthermore, transportation to and from the sessions was arranged. In general, the program was judged acceptable and enjoyable, which is evident by the high compliance and low dropout rate. Participants were very enthusiastic and no incidents occurred.

We chose to enrich food products with vitamins and minerals (at 25-100% of the Dutch RDAs) for which the intake is frequently low in elderly people. Because of the lower energy requirements due to low levels of activity, we chose not to supplement with extra energy, carbohydrates, fats or proteins. There are several possible explanations as to why consumption of the nutrient dense products did not improve physical performance, fitness or ADL. First, the amount of micronutrients or duration of the study may have been insufficient to find an effect on functional performance despite an increase in blood concentrations.[2] Another explanation is that micronutrient supplementation is not effective in improving performance, fitness or ADL. The effects of micronutrient supplementation on physical performance have not been reported before, but earlier trials with energy supplements suggest no effects of nutritional supplementation on muscle strength and mobility.[15;27;81] Finally, the baseline nutritional status may not have been sufficiently compromised to find any effects. We selected elderly persons with a BMI below average to increase prevalence of a sub-optimal nutritional status. This BMI was calculated on the basis of self-reported body height and weight. Height was often overestimated and weight underestimated, resulting in a higher actual BMI. Furthermore, the interpretation of BMI in the elderly is also questionable, considering the difficulties with measurement of stature (kyphosis) and the varying body proportions. The value of micronutrient supplementation in an extremely malnourished population requires further exploration.

To summarize, it appears that our exercise program is an effective practical intervention toward reversing or slowing down the age-related decline in performance and physical fitness in a population of frail older persons. Daily micronutrient supplementation at 25-100% of the RDA showed no additional functional benefits within 17 weeks.

3.2

Effects of physical exercise and micronutrient supplementation on the psychological well-being of frail elderly

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Submitted.

Abstract

The effects of 17 weeks of physical exercise and micronutrient supplementation on the psychological well-being of 139 independently-living, frail elderly (inactive, body mass index ≤ 25 or experiencing weight loss) was examined.
Participants, aged 67-96, were randomly assigned to a) all-round, moderate intensity, group exercise; b) daily micronutrient enriched foods (25-100% RDA); c) both; d) neither. A social program and identical regular foods were offered as attentional control and placebo .
At baseline, general well-being score was significantly correlated with physical fitness ($r = 0.28$, $p<0.001$) and serum pyridoxine and 25(OH)D concentration (correlation coefficient of $r = 0.20$ and 0.23 respectively, $p<0.05$), but not with physical activity level and other blood vitamin concentrations. General well-being and self-rated health had not changed after 17 weeks of either intervention. Social involvement increased in all groups.
Perceived psychological well-being in frail elderly seems to be a rather stable concept which is not responsive to 17 weeks of exercise or nutritional intervention. The significant correlations between well-being and physical fitness and several blood vitamin concentrations at baseline suggest that long-term interventions may be effective.

Introduction

Declines in health, mobility, autonomy and social contacts may place frail elderly at a risk of deterioration of their psychological well-being. It is generally accepted that dementia and depression have a genetic background: however, environmental factors such as physical activity and nutritional intake may also have an important effect.

Proposed psychological benefits of exercise include a reduction of anxiety and depression, an increase in self-esteem, positive mood and general well-being and an improved reactivity to stress.[90-92] Hypothetical mechanisms by which exercise may mediate psychological well-being include physiological explanations such as changes in body temperature, muscular tension, modified brainwave activity, hormonal (e.g. catecholamines) or metabolic adaptations, or alterations in the brain monoamines or opioid peptides. Psychosocial explanations include the opportunity of socializing, enhanced feelings of competency and self-mastery associated with physical improvements, and distraction of day-to-day stressors.[28;92]

Nutritional supplementation may represent another possible approach toward improving feelings of well-being. Severe vitamin deficiencies result in dramatic disturbances of behavior, cognitive functions, emotional state and personality, but subjects with subclinical vitamin deficiencies also showed behavioral changes such as an increased tendency toward depression, irritability, lassitude and impairment of short term memory.[93] Improved well-being has been observed after thiamin supplementation in elderly women with a marginal thiamin deficiency.[35] Because dietary intake is often inadequate in frail elderly, they are specifically at a risk of marginal nutritional status, which may negatively effect their well-being.

There is little experimental evidence of the beneficial effects of physical activity or micronutrient supplementation on psychological well-being, especially in the elderly.[28;35;94] Findings have been equivocal and well-controlled studies are scarce. The present study was therefore designed to examine the effects of a 17-week all-round progressive exercise program, consumption of enriched foods, and both combined, on the psychological well-being of frail elderly. We have focused on subjective health, self-respect, morale, optimism and social contacts as aspects of general well-being. We hypothesized that an improved fitness and nutritional status improves psychological well-being. The association between physical fitness and biochemical status and well-being will also be addressed.

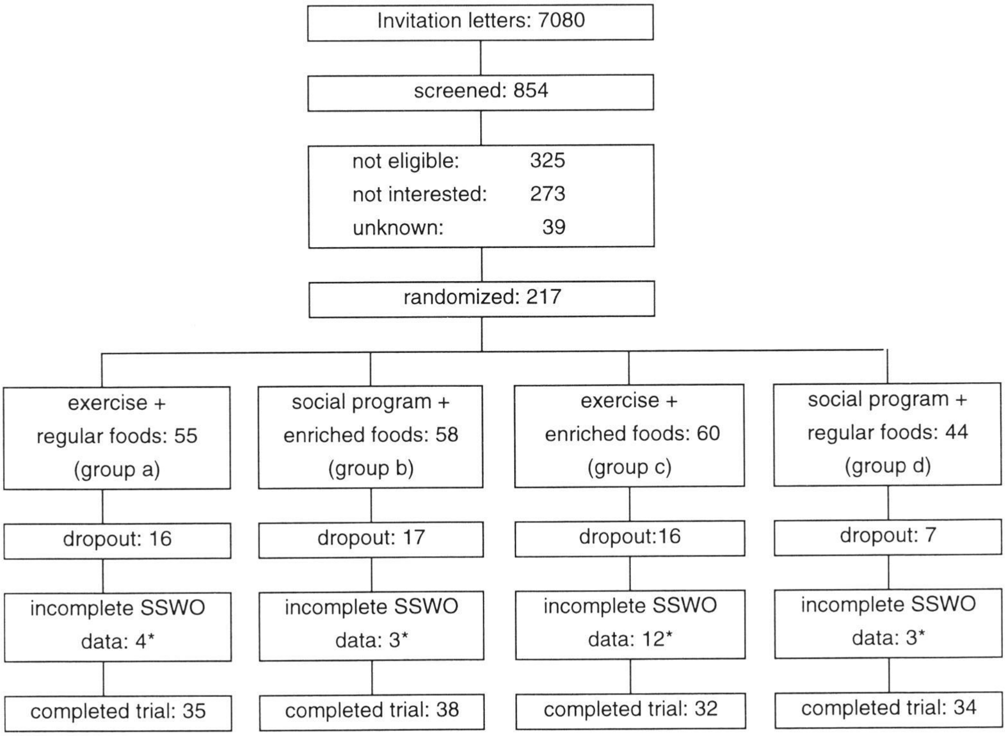
Methods

Design

The study was a randomized, placebo-controlled intervention trial with all-round progressive exercise and micronutrient enriched food products based on a two-by-two factorial design that permitted an assessment of the effects of both interventions independently, as well as a possible interaction effect on the health and nutritional status of frail elderly subjects. In this report we describe the effects on psychological well-being. The study protocol has been approved by the medical ethics committee of the Division of Human Nutrition and Epidemiology of Wageningen Agricultural University, and written informed consent has been obtained from each participant.

Study population

Volunteers were recruited by personal mail (> 7000 letters) from senior housing facilities, Meals-on-Wheels, home care organizations and general practitioners, flyers posted in senior housing facilities and advertising in regional/facility newsletters (see Figure 3.2.1). Initial efforts were aimed at inviting possible participants to attend an informational meeting. Subsequently, 854 interested elderly were screened by telephone on the following inclusion criteria: age 70 or older, use of care services (e.g. home care, Meals-on-Wheels), not participating regularly in physical activities of moderate to high intensity, self-reported BMI ≤ 25 kg/m^2 or involuntary weight loss, non-institutionalized, no terminal disease or rapidly deteriorating health status, not taking multivitamins for the last month, and the ability to comprehend the procedures of the study. The 217 eligible subjects were randomly assigned to (a) supervised group exercise (n = 55), (b) enriched food products (n = 58), (c) both (n = 60) or (d) neither: control group (n = 44). Group assignment took place before baseline measurements by sealed envelopes. Couples were randomized together. Participants were enrolled in the study from January through July 1997.



* The changes in SSWO scores for these participants could not be calculated due to missing data.

Figure 3.2.1. Study profile

Exercise intervention

Subjects assigned to exercise participated twice a week for 45 minutes in a standardized, supervised group exercise program of moderate, gradually increasing intensity. The main objective of the program was maintenance/ improvement of mobility and performance of daily activities that are essential to independent functioning. The emphasis was placed on skills training: strength, coordination, flexibility, speed and endurance were trained in the context of motor actions (walking, scooping, chair stands) and motor behavior (activities of daily living, games). To enhance enjoyment and accessibility, game-like activities were included and exercises were adjustable to individual mobility levels. A detailed description of the program can be found in *Chapter 4*. To adjust for the effect of socializing and attention, those not randomized to exercise participated in a social program (lectures, games, crafts) once every two weeks for 90 minutes under the supervision of a creative therapist. The other week they were visited at home while being brought a stock of fresh food products. Participants were asked not to engage in other exercise programs. Transport to and from all sessions was arranged.

Nutritional intervention

Participants were instructed to eat daily one fruit product, available in 2 types of juice and compote, and one dairy product, available in vanilla custard, 2 types of fruit yogurt and vanilla fruit soft curd cheese. Every week a stock of fresh products (100 gram portions, except the cheese: 75 gram) was delivered at home or at the exercise/social program. Two enriched products provided on average 0.5 MJ and ~100% of the Dutch RDA of vitamins D, E, B1, B2, B6, folic acid, B12 and C and ~25 to 100% of the Dutch RDA of calcium, magnesium, zinc, iron and iodine. The exercise and control group received identical but non-enriched foods (of similar energy content). Compliance was assessed by measuring the serum vitamin levels.

Measurements

Subjective well-being was assessed by the Dutch Scale of Subjective Well-being for Older persons (SSWO).[29] This scale consists of 30 items divided in 5 subscales: health (5 items), self-respect (7 items), morale (6 items), optimism (7 items) and contacts (5 items). The total SSWO score indicates general well-being. The test-retest reliability coefficient was 0.85.[29] Participants were asked to fill out the questionnaire at home and return it. All items were recoded to 0-2. For each sub-scale a mean item-score was calculated and multiplied by 10, resulting in a range of 0-20 for the total score and on all sub-scales. A higher score indicates a higher well-being.

Information on age, marital status, educational level, social contacts, number of friends, diseases, medication, smoking habits, use of care services and self-rated health was collected in a personal interview. Subjective health was measured as general self-rated health (1 = very poor health, 10 = excellent health) and relative health compared to other persons the same age (worse, the same or better). A question about relative health compared to pre-intervention was included in the post-intervention questionnaire. Social involvement was measured as frequency of being contacted and frequency of contacting (visits, phone calls, letters). Physical activity was assessed using a validated questionnaire based on the Physical Activity Scale for the Elderly (PASE), slightly adjusted for the Dutch elderly.[85;86]

Weight and height were measured (wearing underclothes) and used to calculate body mass index (BMI; kg/m^2).

A Fitness score (0-35) was calculated on the basis of the scores on seven components of the validated Groningen Fitness test for Elderly (GFE):[83] manual dexterity (eye-hand coordination), reaction time, standing balance, flexibility of the hip and spine, shoulder flexibility, hand grip strength, and strength of the right musculus quadriceps femoris. Higher scores indicate higher fitness. A detailed description of the test components can be found elsewhere.[83]

Fasting blood samples were collected between 7:00 and 9:00 a.m. at the participants' homes and stored at -80°C until analysis. For practical reasons, non-fasting blood samples collected at our research center were used for determination of ascorbic acid. Serum pyridoxine and ascorbic acid were determined by high-performance liquid chromatography (HPLC) fluorimetric detection, serum 25(OH)D by competitive protein-binding assay, erythrocyte thiamin on the basis of transketolase reactivation (ETK), and erythrocyte riboflavin on the basis of glutathione reductase reactivation test (EGR). Before and after intervention samples were analyzed in the same run.

Statistical Analysis

Data were analyzed using SAS statistical software, version 6.11 (Statistical Analysis System; SAS Institute Inc. Cary, USA). Means (± standard deviations [SD]), medians (10^{th}-90^{th} percentiles) or percentages of baseline characteristics were calculated for all four intervention groups. Spearman correlation coefficients were calculated between SSWO sum score and variables of interest at baseline, and between the 17-week changes in physical fitness score and blood vitamin concentrations and the 17-week changes in SSWO sum score. Differences in SSWO sum score between the different categories of gender, marital status and level of education were tested for significance with the Wilcoxon or Kruskall-Wallis test.

An interaction between the effects of exercise and enriched foods was tested by means of regression analyses with the change in SSWO sum score as a dependent variable, and both interventions and an interaction term as independent variables. Because there was no evidence of an interaction between the two interventions ($p = 0.14$), the subsequent analysis was performed according to factor (exercise and enriched foods). The average changes for exercise (groups a+c) versus no exercise (groups b+d) and for enriched foods (groups b+c) versus regular foods (groups a+d) were tested with Student t-tests and Wilcoxon rank sum tests. A p-value ≤ 0.05 was considered statistically significant.

Results

Baseline characteristics of the participants

Table 3.2.1 presents baseline characteristics of the study participants. About 30% of the participants were men. In the total population, mean age was 78.1 years (range: 67-96), mean BMI 24.5 kg/m^2, median activity score 61, and mean and median reported number of diseases and medicines 2, respectively. About half of the population was widowed, three quarters had a low or intermediate education level and the median number of friends was 3. Almost half of all participants received help with household activities for health reasons, 36% received prepared meals, and 16% received medical assistance. The exercise group (group a) was slightly younger and more active.

Table 3.2.1. Baseline characteristics (mean ± SD) of the study population according to intervention group (N = 139).

	Exercise (group a) n = 35	**Enriched foods (group b) n = 38**	**Both (group c) n = 32**	**Control (group d) n = 34**
Age (years)	76.1 ± 4.3	79.6 ± 4.9	79.1 ± 6.1	78.7 ± 6.6
Male (%)	26	29	25	32
Marital status (%)				
Married	37	32	38	32
Widowed	54	53	50	56
Divorced	9	5	3	6
Never married	-	11	9	6
Education (%)*				
Low	40	25	37	41
Intermediate	40	56	47	47
High	20	19	16	12
Number of real friends	3 (0-6)	2 (0-6)	3 (0-6)	2 (0-5)
BMI (kg/m^2)	24.4 ± 3.0	24.4 ± 2.5	25.2 ± 2.3	24.2 ± 3.2
PASE score (0-400) †	63 (27-100)	59 (34-103)	58 (34-93)	59 (27-117)
Fitness score (0-28)	15.3 ± 5.5	13.2 ± 5.5	16.7 ± 5.9	14.4 ± 4.3
Number of medications †	2 (0-6)	2.5 (0-5)	3 (0-5)	3 (0-7)
Number of self-reported diseases	1.7 ± 0.9	1.9 ± 1.2	1.8 ± 1.0	1.9 ± 1.4
Use of care services for health reasons (%)				
Meals-on-Wheels	29	39	47	32
Household assistance	40	50	47	35
Medical care	14	21	16	15

* low = primary or lower vocational training, intermediate = intermediate vocational or higher general training, high = higher vocational or university training.

† median (10th-90th percentile)

Dropout and compliance

Of the 217 randomized subjects, 56 (26%) dropped out. Dropout was lower in the control group (16%) than in the intervention groups (26-29%). Almost half (n = 25) of dropouts occurred during or immediately after the baseline measurements. Reasons were mentioned such as: too much distress and program too long or at an inconvenient time. The main reasons for dropout during the intervention period were health problems (41%), including hospitalization (e.g. hip operation, kidney stones, n = 14) and disease (e.g. cancer, rheumatoid arthritis, n = 9). The remaining 161 participants' attendance at the exercise sessions was high (median: 90%, range: 47-100%). No adverse events occurred during the sessions. Attendance at the social program was slightly lower: 80% (range: 50-100%). Compliance with the nutritional intervention, estimated on the basis of changes in blood vitamin concentrations, was also high. The percentage of participants with one or more concentrations below the reference significantly decreased among participants consuming enriched foods (from 59% to 10%) compared to hardly any changes (from 62 to 58%) in participants consuming regular foods ($p = 0.0001$).

Non-response

A pre and post-intervention SSWO score was available for 139 participants of the total 161 who successfully completed the intervention trial. The main reasons for not returning the SSWO were difficulties with questions and forgetfulness. Other reasons were illness/hospitalization (n = 3) and refusal (n = 2). Comparing those who returned the questionnaire and those who did not revealed that non-responders were on average slightly older (81.2 ± 4.8), reported a slightly higher number of diseases (2.2 ± 1.5) and had a lower education level (50% in the lowest level). Percentage of men, mean BMI, median number of medicines and use of care services were similar.

Psychological well-being

Table 3.2.2 shows the median SSWO scores and the mean 17-week changes according to type of intervention: exercise (groups a+c) versus no exercise (groups b+d) and nutrient dense (groups b+c) versus regular foods (groups a+d). Baseline median SSWO sum score was 13 out of a 20-point maximum, and 30% scored below the norm (13 for men and 11 for women).[29] The median SSWO sum score was higher in men than in women (15 and 13 respectively, p = 0.003), and higher in married than in widowed subjects (15 and 12 respectively, p = 0.01). Divorced and single subjects scored in between (14). No significant differences in SSWO were observed according to level of education (low = 13, intermediate = 14 and high = 15, p = 0.33). However, participants reporting difficulties with their income scored significantly lower than participants experiencing infrequent or no difficulties with their income (14 vs. 11, p = 0.04). The median SSWO score was also lower among dropouts (12 vs. 13, p = 0.02) (data not shown).

Table 3.2.2. Subjective well-being at baseline (median, P10-P90) and 17-week changes (mean ± SD) according to type of intervention (N = 139).*

	Exercise (groups a+c) n = 67	**No exercise (groups b+d) n = 72**	**Enriched foods (groups b+c) n = 70**	**Regular foods (groups a+d) n = 69**
SSWO scores (0-20) †				
- Health	16 (2-20)	16 (2-20)	16 (2-20)	16 (2-20)
change	*0.0 ± 4.3*	*-1.0 ± 5.3*	*-0.3 ± 5.1*	*-0.6 ± 4.6*
- Self-respect	16 (7-19)	16 (9-20)	16 (7-19)	16 (9-20)
change	*-0.2 ± 2.8*	*-0.1 ± 2.7*	*-0.5 ± 2.9*	*0.2 ± 2.6*
- Morale	15 (7-20)	17 (8-20)	17 (8-20)	17 (7-20)
change	*0.6 ± 3.0*	*0.1 ± 3.0*	*0.2 ± 3.1*	*0.5 ± 2.9*
- Optimism	13 (4-17)	10 (4-17)	10 (4-17)	13 (6-17)
change	*-0.6 ± 3.3*	*-0.5 ± 2.8*	*-0.6 ± 2.8*	*-0.5 ± 3.4*
- Contacts	12 (4-18)	12 (4-20)	11 (4-17)	12 (4-20)
change	*0.1 ± 4.0*	*0.4 ± 4.3*	*0.4 ± 3.8*	*0.1 ± 4.4*
- Total	13 (7-17)	13 (8-17)	13 (7-17)	14 (8-18)
change	*0.0 ± 2.0*	*-0.1 ± 1.9*	*-0.1 ± 2.0*	*0.0 ± 1.9*
- % low SSWO	37	32	37	32
change	*-6*	*7*	-	*1*

* numbers vary slightly due to missing data.

† higher scores indicate higher well-being.

Table 3.2.3 shows the correlation coefficients between SSWO score and indicators of health and nutritional status at baseline. Baseline SSWO scores were positively correlated with self-rated health (r = 0.39, p = 0.0001), fitness scores (r = 0.28, p = 0.001) and serum pyridoxine (r = 0.20, p = 0.03) and 25(OH)D (r = 0.23, p = 0.01) concentrations. No significant correlation was observed between SSWO and age, number of friends, activity scores, number of diseases or medications, BMI and concentrations of thiamin, riboflavin and ascorbic acid.

Table 3.2.3 Correlation between SSWO score and indicators of nutritional and health status at baseline (n = 139).*

	SSWO score	
	r	**p**
General		
Age	-0.11	0.19
Number of friends	0.11	0.21
Health indicators		
Self-rated health	0.40	0.0001
Number of diseases	-0.05	0.58
Number of medicines	-0.07	0.43
Physical activity score	0.11	0.23
Fitness score	0.28	0.001
Nutritional indicators		
BMI	0.03	0.71
ETK activity	0.20	0.03
Blood vitamin D concentration (nmol/L)	0.23	0.01

* numbers vary slightly due to missing data

Median SSWO score had not changed significantly after 17 weeks of intervention (Table 3.2.2). The number of participants scoring below the norm declined by 6% in exercising participants and increased by 7% in non-exercising participants (no significant difference). Prevalence of low SSWO scores remained the same in both in the enriched and regular foods group. Changes in SSWO score were not correlated to change in fitness score (r = -0.05, p = 0.56) or blood vitamin concentrations (ranging from r = -0.13, p = 0.17 for pyridoxine to 0.02, p = 0.87 for riboflavin).

Subjective health and social involvement

Table 3.2.4 shows information on subjective health and social involvement of the study population. Self-rated health was 7 on a 10-point scale and had not changed in 17 weeks. The percentage of participants feeling healthier than people of similar age increased in all groups. The percentage of participants feeling healthier than before intervention was higher among exercisers (28%) than among non-exercisers (13%) (p = 0.06), and lower among the enriched foods group (14%) than the regular foods group (26%) (p = 0.21). Overall, the number of participants with few social contacts (twice a week or less) declined. This was not significantly different between the intervention groups.

Table 3.2.4. Subjective health and social contacts of the study population at baseline and after 17 weeks of intervention according to type of intervention (N = 139)*.

	Exercise (groups a+c) n = 67	**No exercise (groups b+d) n = 72**	**Enriched foods (groups b+c) n = 70**	**Regular foods (groups a+d) n = 69**
Subjective health				
Mean (± SD) self-rated health†	6.9 ± 1.2	6.9 ± 1.5	6.9 ± 1.5	6.9 ± 1.3
change	*-0.2 ± 1.0*	*0.1 ± 1.2*	*-0.2 ± 1.0*	*0.2 ± 1.3*
Feeling healthier than same-aged (%)	57	60	60	57
change	*6*	*1*	*3*	*4*
Feeling healthier than pre-intervention (%)	28	13	14	26
Social involvement				
Being contacted ≤ 2 wk (%)	21	24	20	25
change	*-5*	*-3*	*6*	*-9*
Contacting others ≤ 2 wk (%)	33	42	39	37
change	*-9*	*-15*	*-12*	*13*

* numbers vary slightly due to missing data

† 1 = very bad, 10 = excellent

Discussion

This study showed that SSWO score as a measure of psychological well-being was not responsive to 17-week interventions with exercise or enriched foods in a group of frail older people. Well-controlled studies on the effects of exercise and micronutrient supplements on psychological well-being are scarce and the available data are equivocal.[28;35;94] Our findings are in concordance with those of Blumenthal et al[95] and Swoap et al,[96] who found no significant improvement in the psychological well-being of men and women older than 60 years of age following 16 weeks of aerobic activity or yoga/flexibility exercises (N = 97) and 26 weeks of high or moderate intensity aerobic exercise (N = 49) respectively. Both studies examined healthy elderly subjects. Frail elderly are likely to experience lower psychological well-being due to declines in health, mobility, autonomy, social contacts and nutritional status. They may therefore experience greater gains in well-being following improved physical fitness and nutritional status. Indeed, SSWO scores at baseline were significantly correlated with physical fitness and serum pyridoxine and 25(OH)D concentrations, but not with physical activity level and other blood vitamin levels. No relation between changes in physical fitness and biochemical status on the one hand and changes in SSWO score on the other hand was observed.

This is, to our knowledge, the first controlled trial examining the effects of the consumption of foods enriched with a physiological dose of several micronutrients on the well-being of frail elderly. Bunker et al[94] observed a significant improvement in well-being in 12 weeks in both a multi-nutrient supplemented (a high-protein dairy drink containing vitamins and macronutrients and a capsule containing a mixture of trace elements) and placebo (starch-containing capsule) group of frail, housebound elderly people, with an even greater improvement in the control group. This suggests that the improvement was presumably not due to the supplement but to the effects of socializing and attention. Moreover, the importance of an appropriate control group is emphasized. Smidt et al[35] observed a significantly increased well-being after 6 weeks of thiamin supplementation in healthy elderly women with a marginal thiamin deficiency compared to baseline and placebo supplemented values. In our study the supplementation dose (1 mg versus 10 mg thiamin daily) and prevalence of thiamin deficiency (14% versus 48%) were much lower, but the amount and duration of supplementation we used was effective in increasing blood vitamin levels. The difference in measures of psychological well-being complicates comparison between studies.

Psychological well-being

One explanation for the lack of effects may be that the outcome measure chosen to assess subjective well-being is not sensitive enough to detect subtle changes, despite significant changes in objective measures such as physical fitness score, functional abilities (Chapter 3.1) and biochemical values.[2] Indeed, many participants reported that they enjoyed program participation and the contacts with the researchers and other participants very much, suggesting an improved well-being.

There is no standardized operationalization of psychological well-being. We used the score on the validated 'Scale of Subjective Well-being for Older persons' as an index of general well-being. The scale covers questions about health, self-respect, morale, optimism and contacts. Validity of the SSWO was assessed by investigating the relationship between SSWO scores and several objective indices for objective well-being:[29] elderly persons scoring relatively high on the SSWO exhibited a higher level of activity, mobility, performance of daily activities, had a few more facilities in their dwellings and less complaints about their dwelling situation, made less use of care services, and also had social contacts more frequently. In our study population a lower SSWO score was observed among widowers and among those with lower fitness scores, blood vitamin levels, self-rated health, educational levels, and having problems with their income. The SSWO score can thus be used to classify the elderly in categories of well-being but may be less suitable as an effect measure in intervention studies.

Another possibility is that subjective well-being may be a fairly stable concept which is rather insensitive to change, particularly at an older age. Studies on subjective health (one aspect of well-being) suggest that older people adapt to deterioration in health and functional status by changing their expectations and norms, resulting in a decreasing association between functional status and self-rated health with increasing age.[97;98] Health appraisals at an older age may be more based on attitudes and health habits instead of on medical and functional factors.[99] A similar finding was reported in a study by Ardelt,[100] who suggested that wisdom, a person's degree of psychosocial development, has a stronger influence on life satisfaction than objective life conditions such as improved fitness and nutritional status. Another possible mechanism explaining the stability in subjective well-being are social comparisons. In a study of Heidrich and Ryff[98] the effects of social comparisons appeared to be strongest for women in the poorest health, resulting in psychological outcomes similar to women in good health.

Study population

Our study focused on frail but still independently-living elderly people. Frail elderly are often underrepresented in gerontologic research because recruitment tends to favor enrollment of healthier, better nourished and more active participants. Nonetheless, physical frailty represents a major threat to successful aging. Consequently, the frail may particularly benefit from interventions aiming at reducing disability. Standardized criteria to select frail elderly are lacking.[4] We used a need for care services (e.g. home care, Meals-on-Wheels), physical inactivity (no regular exercise) and involuntary weight loss or a body mass index below average as the main selection criteria. Recruitment of the target population appeared very difficult and time-consuming. Full participants were probably less frail than non-responders and dropouts. Nevertheless, our study population was on average less healthy and active compared to healthy Dutch elderly; self-rated health (7.0 versus 7.7), activity level (67.6 versus 71.9 for men, 64.6 versus 97.9 for women)[85] and physical fitness were all below average. The percentage of participants scoring below the norm for SSWO was higher than in the norm population (30 versus 11%).[29]

Interventions

The exercise program was enjoyed and well tolerated, as suggested by the high compliance and lack of adverse events. For people with inactive lifestyles it may be necessary to develop initial exercise efficacy before adopting an exercise program. Confidence in abilities was stimulated by training a range of daily routine activities. We chose for exercise of moderate, gradually increasing intensity because exercise at an intensity, for a duration and at a frequency that is subjectively perceived as pleasant is presumably more effective in improving subjective well-being.[101] Further, enjoyment in and accessibility to the program were emphasized.

The nutritional intervention was positively evaluated, well tolerated and effective in reversing micronutrient deficiencies. Instead of vitamin pills, enriched food products in various tastes have been developed because the consumption of tasty food products is more attractive than taking yet another tablet. Despite the lack in improvement in well-being scores, many subjects - both in the enriched and in the regular foods group - mentioned that they felt much better and asked when the products would be available for sale and what micronutrients were added. Further study is needed to determine whether a longer duration of the exercise program and supplementation with enriched foods (at these dosages) is effective in improving well-being.

In conclusion, psychological well-being in frail elderly people seems to be a rather stable concept which is not responsive to 17 weeks of intervention with exercise and/or micronutrient enriched foods. The significant correlations between well-being and physical fitness and several blood vitamin concentrations at baseline suggest that changes in well-being may occur after long-term interventions.

3.3

Immune response in frail elderly: effects of exercise and micronutrient enriched foods

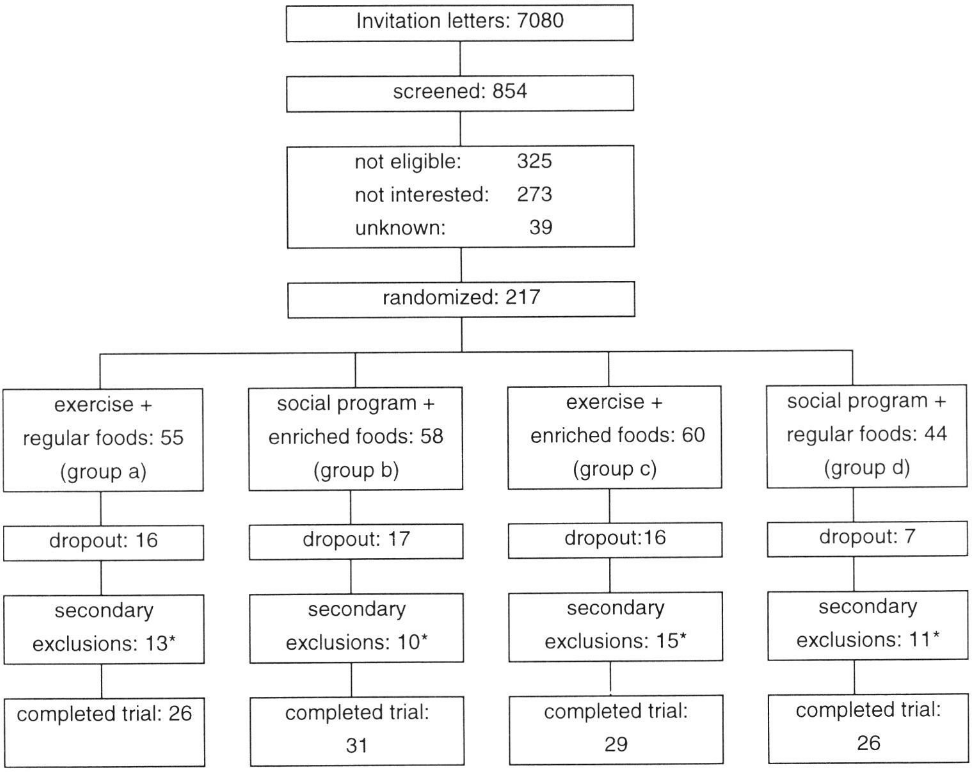
JMM Chin A Paw, N de Jong, EGM Pallast, GC Kloek, EG Schouten, FJ Kok. Submitted.

Abstract

The purpose of the study was to examine the effects of 17 weeks of physical exercise, micronutrient enriched foods, or both combined, on cellular immune response in frail elderly.
Independently living, frail elderly (N = 112) aged 67-96 were randomly assigned to a) twice weekly all-round, moderate intensity, progressive group exercise (n = 26); b) daily micronutrient enriched foods (25-100% RDA) (n = 31); c) both (n = 29) or d) neither: control (n = 26) for 17 weeks. A social program and identical regular foods were offered as control. Cellular immune response was measured by delayed-type hypersensitivity skin test response (DTH) against 7 recall antigens expressed as total number of positive reactions and sum of diameters of all positive responses.
Non-exercising subjects showed on average a decline of 0.5 responses (-26%) compared to an unchanged responsiveness among exercising subjects (difference in change = 0.5, 95% CI: 0.04-0.89 adjusted for baseline DTH, activity level and micronutrient status). The difference between non-exercising and exercising subjects in change in the sum of diameters of all positive responses was smaller (adjusted difference in change = 2.1 mm, 95% CI:-1.0-4.8). No significant difference was observed between enriched versus regular foods.
Our findings suggest that exercise may prevent or slow down the age-related decline in immune response. Micronutrient enriched foods (at 25-100% the RDA) for 17 weeks did not affect immune response. As infectious diseases can have debilitating or even fatal consequences for the elderly, prevention of the age-related decline in cellular immune response could significantly improve their quality of life.

Introduction

Part of the age-related decline in immunocompetence[37;38] may be caused by nutritional deficiencies and/or decreased physical activity. Previous studies in healthy elderly have suggested that supplementation with multiple micronutrients[41;42] or pharmacological doses of single nutrients (e.g. vitamin E)[102;103] improve cellular immune response as measured by delayed-type hypersensitivity skin tests. Data on the effects of regular low-to-moderate intensity exercise on immunity suggest a possible beneficial effect on immune function as well.[38;104;105] Cross-sectional studies



* The asterisk indicates subjects excluded because of the use of anti-inflammatory medication or systemic corticosteroids, suffering from rheumatoid arthritis or cancer in the past 5 years, invalid (> 60 hours between application and measurement of reactions) or missing DTH measurements.

Figure 3.3.1 Study profile

found significantly increased natural killer cell activity and T-cell function in highly conditioned elderly compared to age-matched untrained controls.[39]
Two controlled intervention studies,[39;40] however, failed to find effects of 12 weeks of resistance and cardiovascular training respectively on immune function in healthy elderly subjects. Because both physical activity and nutritional intake are often marginal in frail elderly, we hypothesized that intervening with an adequate exercise and nutritional program may beneficially effect immune response in this vulnerable

population group. We therefore developed an exercise program and micronutrient enriched food products appropriate for frail older adults and studied the effects of either intervention or both combined on cellular immune response in a frail Dutch elderly population.

Methods

Design

The study was a randomized, controlled intervention trial based on a two-by-two factorial design that permitted assessing the effects of the exercise and nutritional intervention independently, as well as a possible interaction effect on various indicators of health and nutritional status in frail elderly. In this report we describe the effects on cellular immune response. The study protocol was approved by the medical ethics committee of the Division of Human Nutrition and Epidemiology of Wageningen Agricultural University.

Study population

Subjects were recruited by mail from senior housing complexes, Meals-on-Wheels programs, home care organizations and general practitioners (see Figure 3.3.1). Telephone screening selected those fulfilling the following inclusion criteria: age 70 or older, a need for care services (e.g. home care, Meals-on-Wheels), not participating regularly in physical activities of moderate to high intensity, self-reported BMI $\leq$ 25 kg/m^2 or involuntary weight loss, non-institutionalized, not taking multivitamins for the last month, no terminal disease or rapidly deteriorating health status, and the ability to comprehend the procedures of the study. Each participants' general practitioner approved study participation. A total of 217 eligible subjects were enrolled in the study from January through July 1997 and randomly assigned to: (a) supervised group exercise (n = 44), (b) nutrient dense food products (n = 55), (c) both (n = 60) or (d) control group (n = 58). Group assignment took place before baseline measurements with sealed envelopes. Couples were randomized together. We assigned a few more subjects to the intervention groups because we expected a higher dropout in these groups. Fifty-six subjects dropped out. Almost half (n = 25) of the dropouts occurred during or immediately after the baseline measurements. Reasons mentioned were, for instance: too much trouble, duration of program too long or at an inconvenient time. The main reasons for dropout during the intervention period were health problems including hospitalization (e.g. hip operation, kidney stones, n = 14) and disease (e.g. cancer, rheumatoid arthritis, n = 9). Additional exclusion criteria for the present analysis on cellular immune response were the use of anti-inflammatory medication or systemic corticosteroids, suffering from rheumatoid arthritis or cancer in the past 5 years, and invalid (> 60 hours between application and reading of skin reactions) or missing DTH measurements, resulting in a study population of 112 subjects (see Figure 3.3.1). Written informed consent was obtained from each participant.

Exercise intervention

Subjects assigned to exercise participated for 17 weeks twice a week in 45 minutes of supervised, progressive group exercise of moderate, gradually increasing intensity. The main objective of the program was maintenance/ improvement of mobility and performance of daily activities essential for independent functioning. An emphasis was placed on skills training: strength, coordination, flexibility, speed and endurance were trained in the context of motor actions (walking, scooping, chair stands) and motor behavior (activities of daily living, games). A detailed description of the program can be found in *Chapter 4*. To adjust for the effects of socializing and attention, subjects not randomized to exercise participated in a social program (lectures, games, crafts) once every two weeks for 90 minutes under the supervision of a creative therapist. The other week they were visited at home while being brought a stock of fresh food products. Subjects were asked not to engage in other exercise programs. Transport to and from all sessions was arranged.

Nutritional intervention

The main objective of the nutritional intervention was to improve micronutrient intake and status. Subjects were supposed to eat one fruit product (100 gram portions juice and compote) and one dairy product (100 gram portions vanilla custard and fruit yogurt, 75 gram portions vanilla fruit soft curd cheese) daily for 17 weeks. Fresh products were delivered at home or at the exercise/social program once a week. The nutrient dense foods were enriched with several vitamins and minerals whose intake or status is known to be low in elderly people. Two products provided on average 0.48 MJ and 100% of the Dutch RDA of vitamin D (7.5 μg), E (8.9 mg α-tocopherol equivalents), B1 (1 mg), B2 (1.4 mg), B6 (1.6 mg), folic acid (0.26 mg), B12 (2.5 μg) and C (70 mg) and 25-100% of the Dutch RDA of calcium (225 mg), magnesium (75 mg), zinc (4.75 mg), iron (4.25 mg) and iodine (0.24 mg). The exercise and control group (groups a and d) received identical but non-supplemented foods (amounts of vitamins and minerals in regular products at the highest 15% of the concentration in enriched products). Energy content of the nutrient dense and regular foods was similar. The products were coded. This code was broken after the intervention period. Compliance was assessed by measurement of serum vitamin levels.

Immunological assessment

Cell-mediated immunity was assessed with the Multitest CMI skin test antigen applicator (Pasteur-Merieux, Lyon, France). Seven antigens: tetanus toxoid, diphtheria toxoid, streptococcus (group C), tuberculin, *Candida (albicans), Proteus mirabilis* and *Trichophyton mentagrophytus* and a glycerin control were applied on the inner forearm. Indurations were measured 48 hours (range: 41-54 hours) after application. The size of each induration was measured in two perpendicular diameters, both measured in duplicate. The mean of the four readings was used. An induration with a diameter of 2 mm was considered a positive response. Two scores were calculated: 1) the number of positive responses, 2) the sum of the diameter of all positive responses (sum diameter). The skin tests were applied by the same researcher (MCAP) and read by 5 observers unaware of group assignment.

Other measurements

Physical activity was assessed using a validated questionnaire[85;86] performed in a personal interview. Weight and height were measured to calculate body mass index (BMI). Fasting blood samples were collected between 7:00 and 9:00 a.m. at the participants' homes and stored at -80°C until analysis. For practical reasons, non-fasting blood samples collected at our research center were used for determination of ascorbic acid. Serum pyridoxine and ascorbic acid were determined by high-performance liquid chromatography (HPLC) fluorimetric detection, serum 25(OH)D by competitive protein-binding assay, erythrocyte thiamin on the basis of transketolase reactivation (ETK), and erythrocyte riboflavin on the basis of glutathione reductase reactivation tests (EGR). Before and after intervention-samples were analyzed in the same run. Biochemical deficiency was defined as one or more blood vitamin concentrations (vitamin D, B1, B2, B6, C) below the Dutch reference values.

Statistical analysis

Statistical analysis was performed with SAS 6.11 (Statistical Analyses System; SAS Institute Inc. Cary, USA). With a sample size of 26 subjects in each intervention group we were able to detect a change of 0.5 responses or 4 mm in sum diameter with $\beta = .80$ and $\alpha = .05$. An interaction between the effects of exercise and nutrient dense foods on cellular immune response (CIR) was tested by means of regression analyses with the change in delayed-type hypersensitivity (DTH) responsiveness as the dependent variable, and both interventions and an interaction term as independent variables. Because there was no evidence of interaction ($p = 0.64$ for number of responses, $p = 0.63$ for sum diameter), the analysis was performed according to factor (exercise and nutrient dense foods). Means ($\pm$ SD), medians (10^{th}-90^{th} percentiles) or percentages of baseline characteristics were calculated. Differences in changes in the number of positive responses or sum diameter between exercise (groups a + c) versus no exercise (groups b + d) and nutrient dense (groups b + c) versus regular foods (group a + d) were tested by using Student's t-tests. To evaluate the significance of the interventions as modified or confounded by baseline DTH responsiveness, activity level and prevalence of biochemical deficiency, regression analysis was performed with these variables as covariates.

Results

Attendance at the exercise sessions was high (median: 90%, range: 47-100%). Compliance with the nutritional intervention, estimated on the basis of changes in blood vitamin concentrations, was also high. Biochemical deficiency declined significantly in the enriched foods groups (from 57% to 14%) compared to hardly any change (from 58 to 52%) in participants consuming regular foods (p = 0.001). At baseline the exercise group was slightly younger, more active and biochemical deficiency was less prevalent compared to the 'social' group. Mean age was slightly lower in the enriched compared to the regular foods group (Table 3.2.1).

Table 3.3.1 Baseline characteristics of the study population (N = 112) according to type of intervention (exercise versus no exercise and nutrient dense versus regular products).

	Exercise n = 55	**No exercise** n = 57	**Enriched foods** n = 60	**Regular foods** n = 52
Percent male	29	33	32	31
Mean (± SD) age (years)	78.6 ± 5.9	79.7 ± 5.9	80.2 ± 5.7	77.9 ± 5.9
Mean (± SD) BMI (kg/m^2)	24.7 ± 2.7	24.2 ± 2.7	24.7 ± 2.4	24.2 ± 3.1
Median (P10-P90) activity score	62 (30-111)	59 (34-95)	59 (34-108)	58 (30-100)
Percent with biochemical vitamin deficiency *†	56	59	57	58

* one or more from a total of 5 concentrations below the reference (vitamin D (25OHD) <30 nmol/L B1 (ETK-ac) >1.25, B2(EGT-ac) >1.25, B6 (PLP) <20 nmol/L, C <23 µmol/L).

† N = 108, due to missing values

Table 3.2.2 shows baseline values of DTH responsiveness and the 17-week change. At baseline, mean number of positive responses in the total study population was 2.0 ± 1.3, mean sum diameter 12.8 ± 10.6 mm. After 17 weeks of intervention these numbers declined with -26% and -22% respectively in non-trained subjects but were practically unchanged in the exercise group (0% and -9% respectively). The change in number of responses was significantly different between exercise and no exercise when adjusted for baseline DTH responsiveness, activity score and prevalence of biochemical deficiency (adjusted difference = 0.5, 95% CI: 0.04-0.89, p = 0.04). This was not the case for sum diameter (adjusted difference = 1.9 mm, 95% CI:-1.02-4.75).

No significant difference between nutrient dense and regular products was observed (change in number of responses = -20% and -5% respectively, change in sum diameter = -16% in both groups).

Prevalence of anergy remained the same in exercising subjects versus an increase from 16 to 25% in non-trained subjects. In the enriched foods group, prevalence of anergy increased from 12 to 20% versus no change in the regular foods group.

Table 3.2.2 Mean (± SD) baseline delayed-type hypersensitivity and 17-week changes according to type of intervention (exercise versus no exercise and nutrient dense versus regular products, N = 112).

	Exercise (groups a+c) n = 55	**No exercise (groups b+d) n = 57**	**Enriched foods (groups b+c) n = 60**	**Regular foods (groups a+d) n = 52**
Number of responses (0-7)				
- baseline	2.0 ± 1.3	1.9 ± 1.4	2.0 ± 1.4	1.9 ± 1.2
change	*-0.0 ± 1.4*	*-0.5 ± 1.2**	*-0.4 ± 1.3*	*-0.1 ± 1.3*
Sum diameter (mm) †				
- baseline	13.4 ± 10.0	12.1 ± 11.3	13.4 ± 11.6	12.1 ± 9.4
change	*-1.2 ± 9.5*	*-2.7 ± 8.2*	*-2.1 ± 9.3*	*-1.9 ± 8.4*
Percent anergic ‡				
- baseline	13	16	12	17
change	*0*	*9*	*8*	*0*

* p = 0.03, significantly different between exercise and no exercise when adjusted for baseline DTH responsiveness, physical activity score and prevalence of biochemical deficiency.

† N = 108 due to missing values

‡ anergic = no positive responses

Discussion

Our exercise program beneficially affected in vivo measures of cellular immune response in 17 weeks: DTH responsiveness declined in non-trained subjects compared with no change in exercising subjects. This beneficial effect was small, though, and only significant for the number of positive responses. A clear effect of micronutrient enriched foods at 25-100% the RDA was not observed. Variability in changes in DTH responsiveness was large.

Mean DTH responsiveness in our frail population group was similar to a population of healthy Dutch older adults (2 responses and 13 mm).[106] The reason for the decline in DTH among non-exercising subjects is not clear and cannot be ascribed to seasonal effects because enrollment took place from January until July. One explanation may be the declining health status and loss of physiologic reserves which are characteristic of frailty.[5] A different explanation may be that different observers performed pre and post-intervention readings of the DTH responses. Reproducibility of the Multitest between 4 of the 5 observers was assessed in 10 healthy adults (age 22-49): the largest difference between mean scores of observers was 0.8 for the number of observations and 2.4 mm for sum diameter. Intervention groups were randomly distributed among observers; it is therefore unlikely that the differences between intervention and control are due to variability between observers.

To our knowledge, this is the first controlled trial studying the effects of all-round exercise training and nutrient dense foods on cellular immune response in frail elderly. Our results suggest that an adequate exercise program may prevent or slow down the age-related decline in cellular immune response. Two earlier studies[39;40] failed to find effects of resistance or endurance training on DTH responsiveness or natural killer cell activity and T cell function in healthy elderly subjects. Exercise may be specifically beneficial in frail, inactive elderly persons.

Our observations with regard to the micronutrient enriched foods are in line with those of Bunker et al,[107] who also failed to find an effect of 12-week micronutrient supplementation on DTH responses in housebound elderly (DTH tended to improve in both the experimental and control group). Other studies did observe favorable effects on immunity in the elderly,[41;42] but with slightly higher doses and a longer intervention period (12 months). The level or duration of supplementation in our study may have been insufficient for any effects to become apparent. Indeed, Bogden[41] reported an improvement of DTH responses after 12 months but not after 6 months of daily micronutrient supplements at higher doses (20-450% RDA) in healthy elderly subjects. However, the supplements we used were effective in increasing blood vitamin values.[2]

Study population

Our study focused on frail but still independently living elderly people. Criteria to select frail elderly are lacking.[4] We used a need for care, no regular exercise and self-reported body weight below average or involuntary weight loss as the main selection criteria. On average, our study population was less healthy and active compared to healthy Dutch elderly persons:[64;85] self-rated health, physical functioning, energy intake (data not shown) and activity levels were inferior. Because subjects often overestimated height and underestimated weight, actual BMI was often higher than 25. Still, the majority showed biochemical evidence of vitamin deficiency.[2]

The main reasons for dropout were health related. There is a possibility of bias if the health reasons for dropout were unevenly distributed between groups. Dropout due to health reasons was indeed higher in the exercise groups, but most of these reasons seemed unrelated to exercise: e.g. recurrence of cancer and hospitalization due to cardiac infarction, kidney stones or hip fracture. At baseline small differences in activity level, micronutrient status and DTH responsiveness occurred in favor of exercisers compared to the social group, while age was slightly higher in the nutrient dense compared to the regular food group. We controlled for these differences by including these variables as covariates in multivariate analysis.

Measurement of DTH

Multitest CMI system appears to be a good test for measuring delayed-type hypersensitivity (DTH) in the assessment of cell-mediated immunity and may be used to evaluate and follow immunocompetence.[108-110] An association has been shown between depressed DTH and mortality in older subjects.[111] Repeated application of this test had minimal booster effects on DTH responses.[109] In our study, application of the test was done by one researcher. Unfortunately, for logistic reasons pre and post-intervention readings were performed by 5 different observers and not exactly 48 hours after application (range 41-54 hours). This may explain why we found a large variability in changes and only a significant effect on changes in number of responses and not in sum diameter, which is the measure that is more subjective and sensitive to time. Large clinical trials of longer duration are needed to determine the effect of changes in DTH on incidence of infectious diseases in the elderly.

An important strength of this study is its emphasis on feasibility. The exercise program was especially designed for frail elderly and adaptable to different mobility levels. Long-term adherence to varied, all-round programs that emphasize enjoyment, versatility in movement and movement behavior including daily activities and games seems more realistic than adherence to individually performed, repetitive exercises using expensive, unfamiliar equipment. Supplements consisted of enriched food products instead of vitamin pills. Consumption of tasty food products is more attractive than taking yet another tablet. Enriched foods also contain other important nutrients.

In conclusion, our data suggest that exercise may prevent or slow down the age-related decline in cellular immune response in frail elderly. The beneficial effects were nonetheless small and further research is warranted. Seventeen weeks of consuming micronutrient enriched foods at physiological doses (25-100% the RDA) did not affect cellular immune response despite an improvement in blood vitamin concentrations. As infectious diseases can have debilitating or even fatal consequences for the elderly, prevention of the age-related decline in cellular immune response may be one of the reasons to promote exercise.

4

Design and feasibility of an exercise program for frail elderly

JMM Chin A Paw, N de Jong, M Stevens, P Bult, E.G. Schouten. Submitted

Abstract

The present report describes the design and feasibility of a 17-week, twice-weekly, all-round, progressive exercise program for frail elderly which was designed for widespread implementation and long-term adherence. The main objective of the program was maintenance/improvement of mobility and performance of daily activities essential for independent functioning.
An emphasis was placed on skills training, meaning that the specific activities required for independence in daily activities were practiced. Exercises focused on an efficient use of all motor qualities: strength, speed, endurance, flexibility and coordination, which were trained by performing motor actions such as walking, kneeling and chair stands. These activities were performed in the context of motor behavior such as games and daily activities. Feasibility of the exercise program was examined in a population of 115 community-dwelling, frail older adults (age: 67-94).
Seventy-two percent (83 of 115) completed the 17-week program. Program appreciation and attendance were high. Seventy-three percent reported wanting to continue participating if possible - the majority only once a week, though. At follow-up (1 to 1½ years after program termination) 30% were still participating in an exercise program.
Our exercise program was enjoyed and accepted by a population of frail, previously sedentary elderly persons. Widespread implementation of this program could increase physical activity among frail older adults. Initiation and maintenance of physical activity remain important topics for future research.

Introduction

Physical frailty can be defined as a state of reduced physiologic reserve associated with an increased susceptibility to disability[5] and represents a large threat to older people's functioning and quality of life. Physical inactivity is one of the primary contributors to physical frailty. Recent research[14;15;16;25;26;80;112] has shown the trainability of the frail and oldest old. The next stage would be the development and evaluation of programs that are effective as well as feasible in 'real life' circumstances. Once the efficacy of a program has been shown, the emphasis should shift from evaluation of the outcome to evaluation of the process.[113] Literature on the design and feasibility of exercise protocols adequate for this vulnerable population remains scarce.

Participation must be maintained in order to obtain health effects associated with physical activity. This notwithstanding, approximately 50% of individuals who start an exercise program will stop within the first 6 months.[114] Exercise adherence is affected by many factors. In older adults the enjoyment of the exercise activity, access to a facility, social support and exercise leadership have been identified as important determinants.[114-116] Consequently, widespread participation in physical exercise by frail older persons requires programs that are safe and effective as well as enjoyable and accessible. Up to now, many studies have emphasized effect evaluation and involved training programs on expensive equipment at high intensities and frequencies.[14;25;26;112] Widespread and long-term adherence to these types of programs seems unlikely. Our primary goal was therefore to develop an exercise program suitable for widespread implementation and long-term adherence.

The uniqueness of our program is its focus on skills training, meaning that the specific activities required for independence in daily activities were practiced. Because there is such specificity in training effects, the specific activities necessary for independence must be practiced. Through skills training people can acquire versatility in movement.[117] In a randomized controlled trial this 17-week comprehensive, progressive exercise program was evaluated. Effects of the program on health and nutritional status have been described in *Chapter 3* and the complementary thesis of Nynke de Jong.[2] The present report describes the design of the program and its feasibility for implementation among community-dwelling frail elderly.

Design of the exercise program

Objective

The main objective of the program was maintenance/improvement of mobility and performance of daily activities essential for independent functioning by maintaining versatility in movement. In addition to sufficient muscle strength to carry, lift, stand

and walk, the performance of daily activities also requires abilities such as reaching, bending and grasping. A comprehensive program was thus developed consisting of exercises that focus on an efficient use of all motor qualities: strength, speed, endurance, flexibility and coordination. These qualities were trained by performing motor actions such as walking, kneeling, reaching, chair stands, catching, and kicking, performed in the context of motor behavior such as games and daily activities.[117]

Secondary goals were to increase enjoyment of spontaneous physical activity, improve general well-being, and increase energy intake through higher energy expenditure and improved appetite.

Frequency and duration

The program consisted of 34 sessions of 45 minutes each, at a frequency of twice a week. The program length was 17 weeks. This period was chosen based on the results of earlier studies which found effects of exercise on muscle strength, walking speed and effects of micronutrient supplementation on blood vitamin concentrations within 12 weeks.[15;43] A longer intervention period (e.g. 1 year or longer) would have been preferable for the study of long-term feasibility. This was not possible for practical and financial reasons.

Type of exercise

The contents of the sessions were designed by human movement scientists (JMMCAP, MS, PB) in cooperation with experienced exercise trainers, in conformity with the current recommendations for the frail and very old.[13;118-120] All sessions are described in a manual for exercise teachers, including instructional video and music cassettes.

All classes started with 5-10 minutes of warm-up activities: walking whenever possible, exercise-to-music routines, becoming familiarized with the equipment. This was followed by 20-25 minutes of skills training. First, training focused on learning to apply motor qualities (strength, speed, flexibility, coordination and endurance) to perform and sustain motor actions (reaching, throwing, catching, kicking, chair stands, bending down, toe and heel raises). It subsequently aimed at learning to apply these motor actions in the context of motor behavior as in game-like and cooperative activities such as throwing and catching a ball while standing up and sitting down on a chair, musical chairs and team pursuit races. The cool-down period consisted of stretching and relaxation activities (e.g. finger and wrist rolls, shoulder rolls, reaching, leg stretches). Movements through a full range of motion were included to improve total body flexibility. All exercises were adjustable to the individual mobility level. Illustrative examples of two lessons are included as an appendix.

Training was done in group sessions of 8 to 15 participants under the supervision of a trained and experienced teacher. The first two sessions focused on the proper techniques of stretching and routine activities such as stooping, sitting down and standing up from a chair, and familiarization subjects with exercising, the teacher and each other. Two 8-week cycles followed. A different type of equipment was used every week. Each 8-week cycle ended with circuit training using different types of equipment from the preceding 8 weeks. Table 4.1 presents an overview of the structure of the program. Music was used to standardize rhythm, increase enjoyment and reduce the perception of effort[121] of exercises.

Table 4.1. Schedule of an exercise program designed for frail older people.

Week*	Equipment	Examples of exercises
1	Introduction	Teaching the adequate way of standing, sitting, standing up from and sitting down on a chair, stooping and stretching the main muscle groups.
2 and 10	(Cherry) pip-bags	Throwing, catching, squeezing, kicking/throwing it away and returning it, standing and walking on toes and heels with pip-bag on head, reaching around the body, team pursuit race
3 and 11	Foam tubes	Squeezing, throwing and catching, turning it in hands or with feet, walking along it, stepping over it, playing tennis (tube = racket and balloon = ball), team pursuit race
4 and 12	Clubs	Rotating it in the hands, throwing and catching, arm swings, touching feet (raising one foot), raise legs over/around, scratching the back, slalom
5 and 13	Ropes	Around the arm/wrist/hand, moving the rope with the feet in certain positions, walking along it, stepping over it, throwing and catching, swinging, team pursuit race
6 and 14	Balls	Moving it around the body with hand(s), squeezing, throwing and catching, kicking, rolling and bouncing (see appendix)
7 and 15	Elastic bands	Rolling it in one hand then squeeze it, stretching the band in different positions (arm and leg muscles), walking along it, stepping over it, moving it with the feet in certain positions
8 and 16	Wrist and ankle weights	Working from toes to head: flexion, extension, abduction, adduction, rotation (e.g. arm curls, hip rotations, leg swings, foot circles)
9 and 17	Circuit training	A variation of exercises using equipment of the preceding weeks (see appendix)

* 2 sessions per week

Intensity

The intensity was gradually increased by using different materials such as foam tubes, ropes, balls, clubs, elastic bands and weights. During the second 8-week cycle the number of repetitions increased, exercises were performed more often standing up straight, and the use of wrist and ankle weights (450 gram each) was stimulated. Participants and teachers were instructed to use a perceived exertion scale to maintain moderate to high intensity (6-8 on a 10 point scale, 1 = very, very light, 10 = very, very heavy; see Figure 4.1). Instructions on using the scale were illustrated in an exercise brochure and verbally explained by one of the project leaders (JMMCAP). It was clarified that at this intensity participants should feel their muscles work and their body temperature and breathing frequency rise. A fixed value of the perceived exertion scale can be used for exercise prescription instead of more expensive methodologies (e.g. heart rate, ventilatory threshold).[82]

	1	very, very light
	2	
	3	very light
	4	
	5	fairly light
Exercise	**6**	
at this	**7**	**somewhat hard**
level	**8**	
	9	very hard
	10	very, very hard

Figure 4.1 Exercise intensity scale based on a Rated Perceived Exertion scale (RPE)

Feasibility

Feasibility of the exercise program was examined in a population of 115 Dutch community-dwelling frail elderly. Feasibility was assessed using information on participant evaluation, dropout, attendance, occurrence of adverse events and the implementation process. The program was conducted in senior citizen centers and elderly housing complexes. To improve accessibility, free transport to and from the exercise sessions was arranged. Participation in the program was also free of charge. To improve exercise maintenance after the intervention period, participants were given a brochure with available exercise programs in their living neighborhood.

Methods

Study population

The study population consisted of subjects randomized to the exercise program in a randomized controlled trial examining the effects of the exercise program alone or in combination with micronutrient enriched food products on the health and nutritional status of frail elderly. More than 7000 invitation letters were sent to senior housing complexes and clientele of general practitioners, Meals-on-Wheels and home care organizations. The main screening criteria for frailty were inactivity (not participating regularly in physical activities of moderate to high intensity) and self-reported BMI ≤ 25 kg/m^2 or involuntary weight loss. Physical inactivity in combination with weight loss appeared to be an effective screening criterion for the identification of frailty among non-institutionalized elderly.[63] Because most people were unaware of whether they were losing weight, a BMI below average was also included. Additional inclusion criteria were: age 70 or older, requirement of care services (e.g. home care, Meals-on-Wheels), non-institutionalized, no terminal disease or rapidly deteriorating health status, not taking multivitamins for the last month, and the ability to comprehend the procedures of the study. Screening was done by telephone. Initially 854 persons were interested in attending an informative meeting. Eventually 217 eligible and interested subjects were enrolled in the study. Three subjects younger than 70 were allowed to participate because their partners fulfilled the inclusion criteria.

A total of 115 subjects were randomized to exercise, and 83 (72%) successfully completed the 17-week program. Almost half (n = 13) of all dropouts withdrew during or just after the baseline measurements. Among the reasons mentioned were too much distress and program too long or at an inconvenient time. The main reasons for dropout during the intervention period were health problems, including hospital admittance (e.g. hip operation, kidney stones) and disease (e.g. cancer, rheumatoid arthritis). Two subjects, both suffering from rheumatoid arthritis, dropped out because of pain during exercising (Table 4.2).

Table 4.2 Reasons for dropout (n) from a 17-week exercise program for frail elderly people.

Reason	Exercise group (n = 32)	Non-exercise group (n = 24)
1. During or immediately after the baseline measurements (the long waiting time for taxis, too much trouble)	13	12
2. Hospitalization (cardiac infarction, pacemaker, kidney stones or hip operation)	11	3
3. Health problems (recurrence of cancer, eye cataract, exacerbation of rheumatoid arthritis)	7	2
4. Other (holidays, too much distress)	1	7

Measurements

Pre-intervention: information on age, perceived health, disease, medication, smoking habits, use of care services and falls was collected by questionnaire. Weight and height were measured (with subjects wearing underclothes only) and used to calculate body mass index (BMI). Physical activity was assessed using a validated questionnaire based on the Physical Activity Scale for the Elderly (PASE), slightly adjusted for Dutch elderly.[85;86]

During the intervention: attendance, perceived intensity, difficulties with the exercises and adverse events were recorded in program diaries by participants and exercise teachers. The project leaders (JMMCAP, NdJ) obtained reasons for dropout.

Post-intervention: participants were asked to fill out and return an evaluation questionnaire. Information was obtained on general program evaluation (10-point scale), duration and frequency of the exercise sessions, perceived difficulties with the exercises/activities, clearness of instructions, perceived improvement in program and daily activities, and planned continuation of an exercise program.

Follow-up (1 to 1½ years after the intervention): follow-up exercise status and reasons for exercising or not exercising were determined by telephone questionnaire.

Results

Population characteristics

Table 4.3 presents baseline characteristics of exercise participants and dropouts. About 30% of participants were men. At baseline the subjects averaged 78 years of age (range: 67-94), had a mean BMI of 24.7 kg/m^2 and a median activity score of 62. Self-rated health was 6.9 (on a 10-point scale) and the mean and median number of diseases and medicines was two. Most frequently reported were cardio-vascular (33%) and musculoskeletal diseases (35%). About a third of the subjects had experienced at least one fall in the year preceding the trial. Forty percent received household assistance for health reasons, 36% received prepared meals, and 16% medical assistance. Age, number of medications, prevalence of musculoskeletal problems and use of care services were slightly higher among dropouts, level of activity and self-rated health slightly lower (Table 4.3).

Table 4.3. Baseline characteristics (mean ± SD) of exercise participants and dropouts.

	Exercise Participants n = 83	**Dropouts n = 25***
Age (years)	77.6 ± 5.4	80.5 ± 5.2
Percent male	27	16
Percent living alone	68	80
BMI (kg/m^2)	24.7 ± 2.7	24.5 ± 2.4
Median physical activity score (10th-90th percentile) †‡	62 (30-105)	49 (30-86)
Self-rated health (1-10) †	6.9 ± 1.2	6.2 ± 1.8
Median number of medications (10th-90th percentile)	2 (0-5)	4.5 (0-8)
Number of self-reported diseases	1.8 ± 1.1	1.9 ± 1.3
Percent with cardiovascular disease	33	22
Percent with musculoskeletal disease	35	57
Percent with pulmonary disease	13	13
Percent smoking	8	8
Percent with falls (in the past year)	36	40
Percent using care services for health reasons (%)		
Meals-on-Wheels	36	40
Household assistance	41	64
Medical assistance	16	40

* information was available on 25 of all 32 dropouts

† 1 = very bad, 10 = excellent

‡ a higher score indicates higher activity

Attendance and exercise intensity

Attendance at the exercise sessions was high (median: 90% of all sessions, range: 47-100%). The median intensity of all exercise sessions for all participants as rated by the exercise trainers was seven. Self-rated intensity could not be calculated due to incomplete and invalid data for the majority of participants. No adverse events occurred during the classes.

Program evaluation

Table 4.4 shows the results of the post-intervention evaluation questionnaire on the exercise program. A program evaluation questionnaire was returned by 75 of 83 subjects (92%). The exercise program was rated an 8.7 (± 1.1) on a 10-point scale (1 = very bad, 10 = excellent). The most frequently mentioned reasons for positive program appraisal were the supporting and skilled leadership in addition to a pleasant atmosphere. Duration and frequency of exercise sessions were convenient, according to the majority of the group (92% and 81% respectively). More than half of the subjects reported problems with exercises during the program, but experienced improvement during the 17 weeks. The majority (58%) also experienced improvement in performing daily activities (e.g. walking, household activities). Seventy-three percent stated that they wanted to continue the exercise program, although two thirds of them only once a week. A telephone follow-up questionnaire 1 to 1½ years later revealed that only 20 (29%) of the 70 responders had actually continued exercising. Reasons for not participating in an exercise program at time of follow-up were: not able to (16%), not interested (7%), other hobbies (7%), or inconvenient location of exercise accommodation (7%).

Table 4.4 Evaluation of the exercise program by frail elderly people (n = 75)

Mean (SD) overall judgment (1-10)*	8.7 ± 1.0
Duration of program (%)	
too short	3
good	92
too long	4
Program frequency (%)	
too low	1
good	81
too high	12
Percentage that experienced difficulties with exercises	65
Percentage that experienced improvement in daily activities	58
Percentage interested in continuation of program	73
twice a week	33
once a week or less	65

* 1 = very bad, 10 = excellent

Discussion

The present report describes a comprehensive exercise program developed for widespread implementation among frail elderly. Our exercise program proved to be enjoyable and well tolerated by frail elderly, which is evident by the high appreciation and attendance and lack of adverse events. Further, dropout during the program was low (13 of the 96 who actually started) and mainly due to reasons unrelated to the program. Participants were very enthusiastic and spontaneously mentioned improvements in daily activities such as dressing and household tasks.

Recruitment of the target population appeared very difficult and time-consuming. Our study focused on frail but still independently-living elderly people. Standardized criteria to select frail elderly subjects are lacking.[4] The results presented in *Chapter 2* suggest that inactivity in combination with weight loss is an effective criterion for identifying frailty among non-institutionalized elderly people. Besides physical inactivity (no regular exercise) and involuntary weight loss we used requirement of care services (e.g. home care, Meals-on-Wheels) as the main inclusion criteria. Because individuals were usually not aware as to whether they were losing weight, a below-average body weight was also included. Chronic diseases (such as cardiovascular disease, diabetes, stroke, osteoporosis, depression, chronic pulmonary disease, or arthritis) were no reason for exclusion. For many of these conditions exercise will offer benefits and inactivity appears more dangerous. Still, participating subjects were probably the healthier segment of the target population. Indeed, dropouts had an inferior health profile. Our study population was nonetheless less healthy and active on average compared to average Dutch healthy elderly persons; self-rated health (7.0 versus 7.7),[87] activity level (67.6 versus 71.9 for men, 64.6 versus 97.9 for women)[85] and physical functioning (*Chapter 3.1*) were below average. To stimulate initiation of the program we emphasized that the program was accessible for all mobility levels and that subjects were always free to withdraw. In an attempt to improve the response rate, the cooperation of physicians and personnel from home care and Meals-on-Wheels-organizations was requested with recruitment of the target population. Home care organizations were initially very interested in cooperating but withdrew due to internal reorganizations. Only a few physicians were willing to screen their patients for potentially eligible individuals. Active counseling by health care workers may be an efficient means of contacting this risk group on condition that financial compensation for the time spent in exercise promotion is provided.

An important limitation of the feasibility study is that evaluation of the program is based on the judgment of participants who successfully completed the program. Participants remaining at the end of 17 weeks and returning the evaluation questionnaire were on average more active, rated their health slightly higher, used a lower number of medications and required assistance for health reasons less often than dropouts. Furthermore, because participation was free, people may have been reluctant to mention negative experiences. Another interesting source of information would have been the evaluation by the exercise teachers. We did not acquire standardized information from the exercise teachers but their informal reactions were very positive. In addition, they used the program outside the study setting, and educational sessions on our exercise program were requested for their colleagues.

The moderate, gradually increasing intensity of the program may have been of specific importance. Starting at a low, individually-adapted level and gradual progression may promote initial confidence in a range of specific activities. Developing self-efficacy in exercise may be essential before inactive people with physical limitations are willing to initiate an exercise program. Self-efficacy has been associated with both adoption and maintenance of physical activity.[115] The low exercise capacity in frail elderly individuals requires for a mild progression in exercise intensity. This is underlined by the fact that most dropouts took place during or immediately after the baseline measurements.

Rating of perceived exertion (RPE) was used for prescribing and monitoring exercise intensity (a value of 6-8 on a 10-point RPE scale). All teachers and a subgroup of participants were instructed to report the perceived exertion in a diary. Rating appeared to be difficult for both teachers and participants. Actually, the RPE scale is designed for rating by the exercising subject, not the teacher. Further, use of the RPE scale is mostly studied in healthy, active young to middle-aged subjects during treadmill running or cycling.[122] To our knowledge there is no information on the reliability and validity of this scale for the prescription and monitoring of exercise intensity in populations of frail older adults.

More than half (66%) of the subjects interested in continuing with exercise preferred a frequency of once a week. Expecting frail elderly individuals to participate twice a week in an exercise program is probably not realistic. A once-a-week structured exercise program combined with promoting a more active lifestyle during the other days may be a more realistic option for previously sedentary individuals. The efficacy of such an alternative should be determined in future studies.

An important determinant of exercise adherence is the enjoyment of the exercise activity.[114-116] Comprehensive programs, including a variety of activities such as daily activities and games, seem more enjoyable than individually performed repetitive exercises. Our program therefore focused on training skills rather than single motor qualities (e.g. strength training of specific muscle groups in specific postures). This is in concordance with the approach of Bult and Rispens,[117] who state that because of the close connection between motor qualities and actions, training strength, speed, flexibility, endurance and coordination should be incorporated as much as possible into motor actions (walking, kicking, throwing, etc.) and practicing movements should be integrated into motor behavior (activities of daily living, games, sports). Given the specificity of training effects, and because learning new activities becomes more difficult with increasing age, practice and maintenance of existing motor actions seem more appropriate for older adults than exercising on unfamiliar fitness equipment. The variety of activities also prevents boredom.

Another important determinant of exercise adherence is exercise leadership.[114-116] Our program was coordinated by well-trained, enthusiastic exercise teachers who provided motivation, individual assistance, feedback regarding performance, and social support. Because of the stimulating effect of the social contacts, and for cost-efficiency reasons, we chose for exercising in group sessions.

Although 73% stated that they wanted to continue the program, 1-1½ years after termination of the intervention study only a third was still exercising. This is in concordance with adherence rates observed by others in the general population of less than 50% in the first 6 months to a year and significantly less thereafter.[114;115] Long-term adherence might have been higher had participants been able to continue with our specific exercise program with the same teacher and group members. Besides the difference in program contents, in a real-life situation participants have to arrange and pay for transportation. This may be an important barrier for exercise participation, particularly for frail elderly persons. Indeed, 7% mentioned an inconvenient location of accommodations as a reason for non-participation. To improve accessibility we arranged free transportation to and from the sessions, and program participation was free of charge. Provision of accessible, convenient exercise facilities and inexpensive transport should be arranged to retain the immobile frail population. Programs should be available near or inside senior apartment complexes and nursing homes and costs should be low.

In summary, our exercise program proved to be acceptable and feasible in a population of frail, previously sedentary elderly individuals. Convincing this vulnerable group to initiate and sustain an exercise program remains a difficult but crucial task. We recommend future research to focus on program designs feasible for widespread implementation and long-term adherence. Our data suggests that a frequency of twice weekly may be unrealistic in the long term. A structured exercise program once a week combined with a more active lifestyle during the other days may be a more realistic option for previously sedentary individuals. The efficacy of such an alternative should be determined in future studies.

Acknowledgments

We wish to acknowledge the cooperation of the volunteers in this study; the fieldwork team; all exercise teachers: Isabella Borburgh, Anne Bout, Joke van de Kaa, Karin Samson, Joke Seinen, Rita Wubbels and Tineke Zwijnen for their dedication in coordinating the exercise sessions; and the Dutch Prevention Fund and the Dutch Dairy Foundation on Nutrition and Health, Maarssen, The Netherlands for their financial support.

Appendix

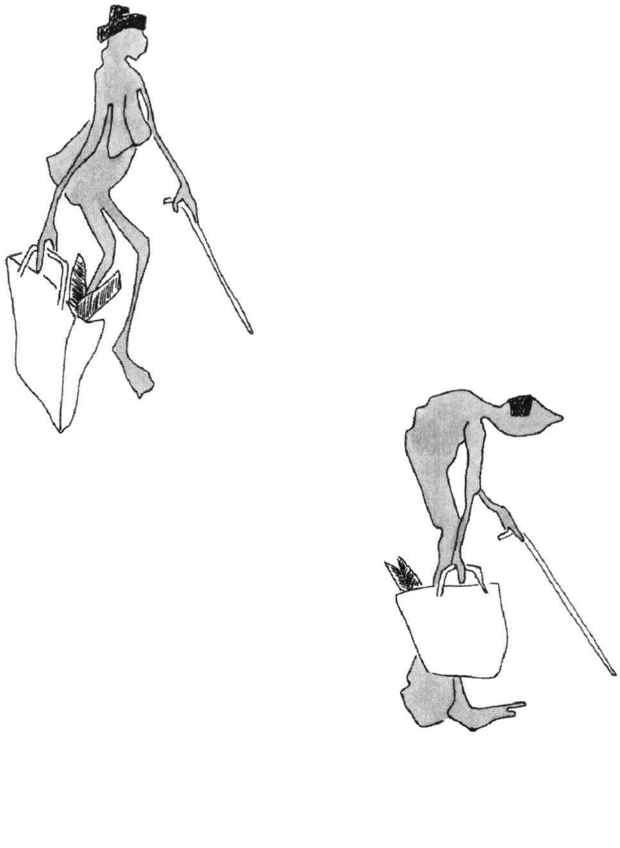
	Balls
Warming-up	Walking through the space (music: *'Polonaise'*): Moving the arms and shoulders fw and bw, knee lifts, walking on toes/heels, clap in front of/behind your body
Exercises	Sitting or standing (no music): • Roll the ball through the hands, wrists, fingers alternated with throwing upwards, bouncing, and squeezing the ball • throw the ball up and clap once, twice, three times, etc. before catching; same but standing up before catching • hold the ball with two hands and try to reach over your head to your shoulder • roll the ball successively behind your neck, back, knees, ankles, chair legs, with two hands, one hand, only the fingers Standing behind the chair (large movements, music: *'Maladie d'amour'*): • horizontal circles with the right arm twice fw (breaststroke), twice bw • repeat with left arm and both hands • circle fw with right leg, twice, the same circling bw • repeat with left leg • repeat with right arm and right leg twice fw, twice bw, same with left arm and left leg • both arms circle upward twice (breaststroke up) and twice reverse Walking through the space (music with increasing speed: *'Circus horses'*): • alternating: bounce the ball and throw from one hand to the other, both 8 counts • in 2 groups: group one is bouncing, group two is throwing Standing or sitting in two lines facing each other (in pairs, no music): • kick the ball in a controlled movement toward partner, alternating left and right leg • roll the ball across with your hands, alternating right and left • bounce the ball across, alternating right and left • alternating rolling and bouncing
Cooling-down	Standing behind a chair (music: *'Come back to Erin'*): • stretching the calves and psoas muscles Sitting on a chair: • hands reaching up to the ceiling, alternating left and right • hands in neck pushing the elbows bw and fw stretching chest and back muscles • bend your leg and pull towards you: gluteus muscles • straight legs in front of you, reaching forward: hamstrings • bend your leg, grab your heel and move the leg bw: quadriceps • rolling the shoulders, wrists and ankles

fw = forward, bw = backward

	Circuit
Warming-up	Walking through the space (music: *'River quartet'*): Passing on a ball, when the music stops the person holding the ball chooses and demonstrates an exercise, the others join in
Exercises	Walking through the space (alternating 2 min. fast and slow music: *'Dance with me'* and *'Lion King'*): Go to a station and read the assignment, make slow stretching movements until the faster music starts again Stations (in pairs): 1. Stand up from a chair (no hands if possible), walk around the pylon, return and sit down again. 2. Move the (cherry) pip-bag - giving it from hand to hand – successively around the neck, waist, one leg, both legs, and up again. 3. Facing each other: hold the foam tube horizontal: shooting and catching. 4. Facing each other: throwing and catching a foam frisbee. Walking through the space with arm movements followed by stretching movements (alternating 2 minutes fast and slow music): Stations (continued): 1. Tandem walk along a rope stepping over it at the end, repeat bw. 2. Playing tennis with a foam tube as racket and a balloon as ball, holding up the balloon as long as possible. 3. Sitting with the backs towards each other, handing the ball over the head, rolling it underneath the chair, reverse after a while. 4. Move the foam tube around the body of your partner from head to feet, the partner steps out of it, then change.
Cooling-down	(relaxation music) Stretching the main muscle groups

5

General Discussion



The main goal of health care for elderly people has extended from the prolongation of life to improving health-related quality of life. Essential components of optimal quality of life are independence and autonomy. Because of their decreased physiological reserves, frail elderly people are at an increased risk of dependency and disability and thus a decline in quality of life. For this reason they may particularly benefit from preventive interventions. Promising strategies to optimize and prolong quality of life are regular physical exercise and nutritional supplementation.

Widespread implementation of these strategies requires programs that are effective as well as enjoyable and accessible. We have developed an exercise and nutritional program tailored to the needs and capabilities of this vulnerable population. This thesis focuses on the effects of these intervention programs aiming at preventing or reversing frailty. Because standardized criteria that define physical frailty are lacking, we first examined efficacy of possible criteria in identifying a population of older people with a suboptimal health status associated with an increased susceptibility to disability.

In this chapter the main findings are summarized, followed by a discussion of general methodological considerations and the main conclusions of the thesis. The chapter ends with public health implications and recommendations for future research.

Main findings

Identification of frailty

Inactivity in combination with weight loss seems to be an effective screening criterion for identifying frailty. Based on the data of the Zutphen Elderly Study and the SENECA study (*Chapter 2*) we showed that elderly persons who were both inactive and losing weight had less favorable health and nutritional characteristics, poorer physical functioning, and were at an increased risk of functional decline and mortality. Both inactivity and weight loss are inexpensive and simple to measure. A pilot study, however, showed that older individuals are usually not aware of whether they are losing weight. For this reason we also used BMI below average as an inclusion criterion in the intervention study. Subjects with a BMI below average are more likely to have inadequate dietary intakes and a potentially compromised nutritional status.

Effects of physical exercise and nutrient dense foods

Physical exercise and micronutrient enriched foods
No effect modification was detected between physical exercise and micronutrient enriched foods. For this reason the analysis was performed according to factor: exercise was compared to no exercise and nutrient dense foods to regular foods.

Physical exercise
The effects of the exercise program are summarized in Figures 5.1 and 5.2. Figure 5.1 shows the difference in percentile change in physical functioning and well-being. Our exercise program proved effective in improving functional performance of frail Dutch elderly subjects in 17 weeks. We also found a small but significant effect on physical fitness but, surprisingly, no effect on self-rated disabilities (*Chapter 3.1*). The sum score on 7 functional tests and 7 fitness tests improved significantly in exercising subjects compared to a decline in non-exercising subjects. Improvements were largest in the tests for chair stands, touching toes, walking speed and balance - all activities of major importance for daily functioning.

No effects were observed on subjective well-being as measured by the SSWO questionnaire or on and self-rated health. The number of participants with few social contacts (twice a week or less) declined, but this was not significantly different between the exercise and social programs (*Chapter 3.2*).

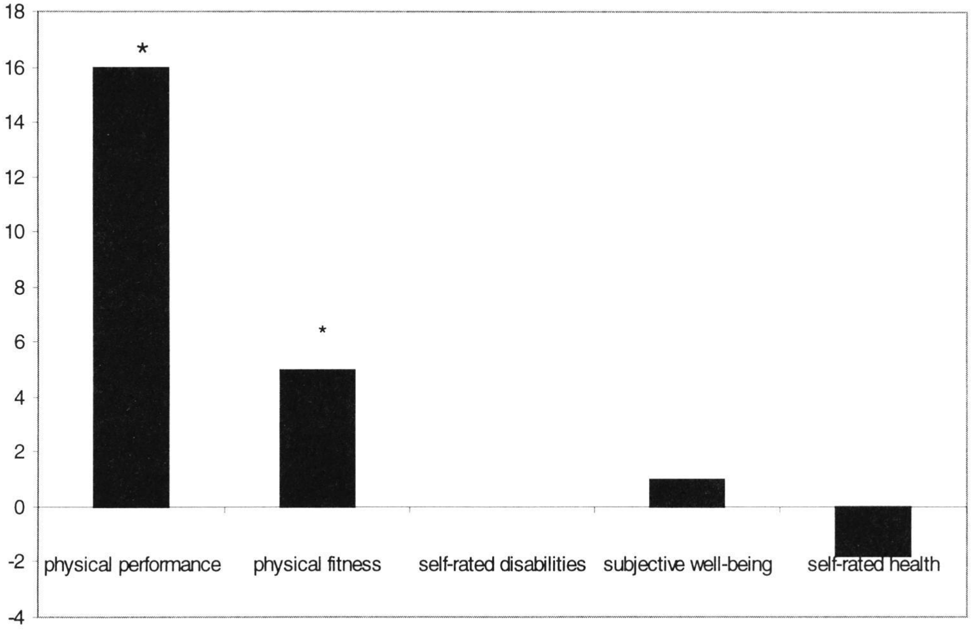


Figure 5.1 Difference in 17-week changes (%) in physical functioning and subjective well-being between subjects randomized to exercise and social program.

Cellular immune response was also beneficially affected by exercise (see Figure 5.2, *Chapter 3.3*). Delayed-type hypersensitivity skin test responsiveness declined in non-trained subjects compared with no change in exercising subjects. This beneficial effect was small, though, and only significant for the number of positive responses. The relevance of the observed effects on delayed-type hypersensitivity skin test responsiveness for incidence of diseases needs further attention.

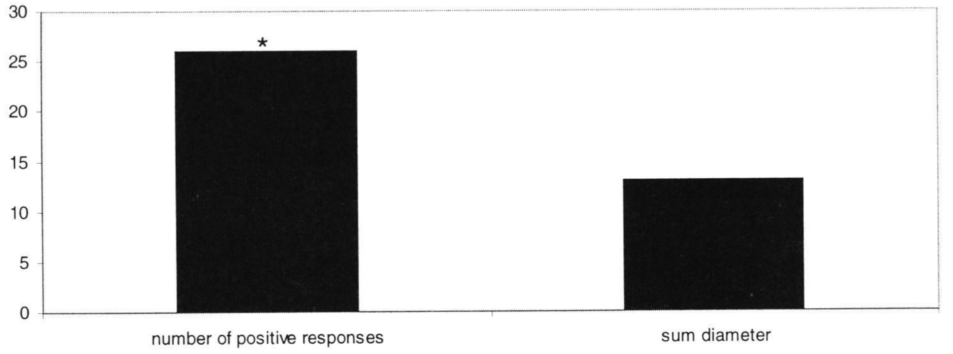


Figure 5.2 Difference in 17-week changes (%) in delayed-type hypersensitivity between subjects randomized to exercise and social program.

Micronutrient enriched foods

No effects of micronutrient enriched foods (supplementation at 100% of the Dutch RDA of vitamin D, E, B1, B2, B6, folic acid, B12 and C and 25-100% of the Dutch RDA of calcium, magnesium, zinc, iron and iodine) were observed on the chosen outcome measures despite a significant increase in biochemical status. A longer intervention period may be necessary before possible effects on physical functioning, well-being and immune response are perceivable.

Feasibility

Our exercise program proved to be acceptable and feasible in a population of frail, previously inactive elderly (*Chapter 4*). Program appreciation and attendance were high and no adverse events occurred. Further, dropout during the program was low (13 of the 96 who started) and mainly due to reasons unrelated to the program. Participants were very enthusiastic and spontaneously mentioned improvements in daily activities such as walking, dressing and household tasks. A high percentage - 73% - reported wanting to continue participating if possible, the majority only once a week. A frequency of twice a week does not seem realistic for long-term participation. Final conclusions about long-term feasibility in the 'real-life' situation require interventions of longer duration (at least one or two years). In a population of frail elderly this would require enormous effort and financial resources.

Methodological considerations

Many of the methodological strengths and limitations of the study have been discussed in the previous chapters. Some general methodological issues will be dealt with here: the intervention programs and measurement instruments, success of randomization, and external validity. We have concentrated mainly on the exercise intervention. For a more extensive discussion of the nutritional program we refer to the complementary thesis of Nynke de Jong.[2]

Intervention programs

An important strength of this study is its emphasis on feasibility. The exercise program focused on improvement of physical functioning, enjoyment and widespread applicability. The program included skills training, was performed in group sessions with inexpensive equipment and supervised by trained, enthusiastic and experienced teachers. Our program was accessible to all mobility levels, highly appreciated and effective in improving physical functioning.

A limitation of this type of program for research objectives is the difficulty in standardizing and measuring the intensity of training. The intention was a moderate and gradually increasing intensity at a frequency of twice a week. We tried to standardize and assess exercise intensity by using a perceived exertion scale. The scale was not validated for exercise prescription in a frail population or for having exercise trainers rate how they perceive the exertion levels of participants. Both participants and teachers experienced difficulties in assessing training intensity by this scale. Another option would have been continuous measurement of heart rate. This method has not been validated for this population or type of programs either. Further, the increased respondent burden and financial costs reduce its feasibility. A higher intensity and frequency might have resulted in greater effects, but most likely in a higher dropout rate and occurrence of injuries as well. In our opinion, expecting frail, previously sedentary elderly individuals to exercise at a higher frequency and intensity is unrealistic in 'real life' and for the long term. Results from the feasibility study show that a frequency of twice weekly may already be unrealistic in the long term. A structured once-a-week exercise program combined with a more active lifestyle during the other days may be a more feasible option for previously sedentary individuals. The effectiveness of such an alternative should be determined in future studies.

To secure safety, individual assistance, social support and proper performance of the exercises, the program was coordinated by trained exercise teachers. Because of the stimulating effect of the social contacts, and for cost-efficiency reasons, we chose for exercising in group sessions. A disadvantage of training in group sessions is that performance and intensity were not always optimal in all participants. The heterogeneity in mobility and fitness levels also complicated individual adjustment of intensity and capacity. A solution may be classification in categories of low, intermediate and advanced level. On the other hand, cooperation between participants of different mobility and fitness levels increased the intensity and variety of exercises for the more mobile individuals who provided assistance as well as for the less mobile individuals whose exercise possibilities increased.

Increased physical activity and metabolic rate may also increase energy intake. A higher energy intake can better secure an adequate intake of essential nutrients. Another approach toward preventing or reversing nutrient deficiencies is improving the nutrient density of the diet by supplementing it with nutrient dense foods. We chose to supplement with a physiological dose of micronutrients whose intake or status is known to be low in elderly people. This dose was sufficient for an improvement of biochemical status of the supplemented subjects in 17 weeks.[2] We prefer supplementation with enriched food products instead of vitamin pills because consumption of tasty food products is more attractive. Enriched foods also contain other important nutrients. Effects of enriched foods on the examined outcome measures could not be demonstrated. Few studies have examined the effects of improving micronutrient status on physical functioning or well-being.[27;94] Our findings suggest no short-term effects on these parameters.

Measurement instruments

Three criteria were important in the choice of measurement instruments: reliability, validity, and applicability. Reliability refers to the precision of a measurement. Validity is the extent to which the instrument measures the characteristic as intended. A superior measurable reference criterion or standard instrument for health-related quality of life is not available. We focused on indicators of quality of life for which valid and reliable measurement instruments were available: functional status, physical fitness, well-being and immune response.

An important issue is population specificity. Reliability and validity estimates are generally obtained in a healthy population and may not be generalized to a frail population with different characteristics. Another important aspect is responsiveness to change over time. The ability to discriminate between groups at one moment in time does not guarantee good responsiveness over time. The questionnaires assessing disabilities in activities of daily living and subjective well-being are both designed and validated for discrimination between groups, and may be less suitable for studying changes over time within individuals. This may explain why no changes were observed in the subjective measures of psychological well-being (SSWO scores), self-rated health and self-rated disabilities, while during the intervention many subjects reported that they felt much better. Subjects mentioned how much they enjoyed study participation, asked when the products would be available for sale, what micronutrients were added, and exercising subjects spontaneously mentioned improvement in several daily activities. These experiences were not reflected by the data on well-being and self-rated disabilities. Apparently, the questionnaires were not sensitive enough to recognize subtle changes. Frail individuals may improve in tasks not captured by the chosen questionnaire. For instance, the question 'are you able to dress yourself?' may not reveal if someone's ability to close her bra or close a shirt with small buttons improves. Zipping up or fastening clothes behind the back may be the only problem with dressing, as carrying the bag or deciding what to buy may be with shopping. Performance tests can differentiate function over a wide spectrum of ability and may be more sensitive to change. They may also be less subject to ceiling or floor effects seen in questionnaires.[123] Consequently, existing effects may have been underestimated or unnoticed.

Another possibility for the lack of effects on the subjective measures is a psychological mechanism called adaptation. It is striking that almost all participants reported chronic diseases, yet many had good self-perceived health and reported few disabilities. Adjustment to these diseases was apparently such that they were not perceived as a handicap and were therefore not reflected in the scores. With increasing age, people may adapt to deterioration in health and functional status by changing their expectations and norms, resulting in unchanged self-rated health and self-perceived ability to perform certain activities despite an actual decline.[97;98] People might also adapt to improvements, making subtle improvements indistinguishable. At an older age, health appraisals may be based more on attitudes and health habits than on medical and functional factors.[97;99]

With respect to applicability in frail populations, low 'respondent burden' is an essential characteristic of instruments. For this reason, and also for practical and financial reasons, standardization of the measurements was not always optimal. For example, pre and post-intervention readings of the skin test responses were performed at the subjects' homes by different observers and not exactly 48 hours after application. Because this was not different between intervention groups, it probably did not effect the difference in changes between intervention groups though increased variability. This may explain why we found large variability in changes and only a significant effect on changes in number of responses and not in sum diameter, the one measure that is more subjective and sensitive to time differences.

Observers could not be blinded to exercise or social group assignment, because they were often also involved in deliverance of the products and assistance at the exercise or social program. Observer bias can therefore not be ruled out. Potential of observer bias was minimized by performing all measurements according to a highly standardized protocol, using standardized questionnaires by trained observers who were unaware of the pre-intervention values.

Success of randomization

The purpose of randomization is to ensure comparability, particularly to eliminate any influence on the allocation of treatment by the researcher, either subconscious or deliberate. Premature withdrawal from the intervention study may destroy the unbiased comparison of treatments; an intention-to-treat analysis is therefore preferable. We were unable to obtain post-intervention data on all randomized subjects, and thus unable to perform an intention-to-treat analysis. This creates a possibility of selection bias if dropout is unevenly distributed between groups. This may especially be the case for dropout due to health reasons, which was indeed higher in the exercise groups. Most of the reasons for dropout seemed unrelated to exercise, for instance recurrence of cancer and hospitalization due to cardiac infarction, kidney stones or hip operation. Still, a few subjects in the exercise group dropped out because of exacerbation of rheumatoid arthritis. They might have continued had they been randomized to the social program.

The selective dropout may have resulted in a more healthy exercise group compared to the group following the social program. Indeed, small baseline differences in activity level, micronutrient status, physical fitness and DTH responsiveness were observed in favor of the exercise group. Age was slightly higher in the nutrient dense compared to the regular food group. We controlled these differences by including these variables as covariates in multivariate analysis. Because greater improvements are usually found for subjects with a lower initial health status, it is unlikely that the observed effects of exercise were due to this selective dropout. However, it underscores the issue of long-term adherence to exercise in frail people.

External validity of results

Because recruitment tends to favor enrollment of healthier, better nourished and more active subjects, recruitment of a frail study population appeared very intensive and time-consuming. Population characteristics can be partly controlled by the researcher by the choice of inclusion and exclusion criteria, but an important part is uncontrolled because some people do not respond, fail to give informed consent or withdraw from participation.

In an attempt to improve the response rate, the cooperation of physicians and personnel from home care and Meals-on-Wheels-organizations was requested with recruitment of the target population. Home care organizations were initially very interested in cooperating but had to withdraw due to internal reorganizations. Only a few physicians were interested in screening their patients for potentially eligible individuals. To further stimulate enrollment in the study we emphasized that the program was accessible for all mobility levels and that subjects were always free to withdraw. These efforts may have improved external validity, but because response rate was low and a substantial number of subjects dropped out as early as during the baseline measurements, our population probably still represented a selective group of frail elderly individuals in reasonably good condition. Effects might have been larger in a more frail population group, but such subjects are extremely difficult to recruit and retain in research.

We initially planned to recruit elderly clients from home care organizations who were still living independently. Main inclusion criteria were: not participating regularly in physical activities of moderate to high intensity and suffering from involuntary weight loss. Because recruitment through home care organizations was not available and subjects were often not aware as to whether they had lost weight, we included 'use of care services' and 'BMI below average (≤ 25 kg/m^2)' as inclusion criteria. An important point of consideration is the occurrence of misclassification with respect to the inclusion criteria: we had to rely on self-reported information obtained by telephone. It appeared that using care services did not always mean that one really needed care services for health reasons. Some subjects had domestic help just for convenience's sake, and some men ordered from Meals-on-Wheels because they had never learned to cook. Physical activity levels were assessed by asking respondents what activities they generally performed. Estimating the intensity of the mentioned activities was difficult. For instance, for some people gardening meant only watering the flowers, while others performed hard work, including mowing the lawn and growing and harvesting vegetables. Because subjects often overestimated height and underestimated weight, actual BMI was often above 25. As a result, not all participants were as frail as originally intended, but on average the study population was less healthy and active compared to average healthy Dutch elderly people. Self-rated health,[87] physical activity levels[85] and fitness, performance and ADL scores were all below average (*chapter 3.1*). The prevalence of low energy and micronutrient intakes were higher than in apparently healthy elderly subjects, and the majority had biochemical evidence of vitamin deficiency,[2] suggesting inadequate dietary intakes.

Most research on the elderly population has been done in healthy subjects or subjects with a particular disease, reducing external validity of the results since multi-morbidity is common in the general elderly population. Chronic diseases - such as cardiovascular disease, diabetes, stroke, osteoporosis, depression, chronic pulmonary disease, or arthritis - or multi-morbidity were no reason for exclusion from our intervention trial.

Conclusions

The main conclusion of this thesis is that exercise programs can be developed which are both effective and acceptable for frail, previously inactive elderly people. Our exercise program was highly appreciated and effective in reversing or slowing down the age-related decline in physical performance, physical fitness and cellular immune response.

Physical inactivity alone or in combination with weight loss seems to be an effective and inexpensive screening criterion for identifying these vulnerable persons among a non-institutionalized elderly population group. A prerequisite is that data on weight change be available because older adults are generally not aware of whether they are losing weight.

Seventeen weeks of consumption of micronutrient enriched foods at physiological doses (25-100% the RDA) did not affect functional status or cellular immune response, despite an improvement in blood vitamin concentrations.

Neither intervention established a measurable effect on psychological well-being, self-rated health or self-rated disabilities. However, further research using sensitive measurement instruments validated for this specific population is necessary before definite conclusions can be drawn.

Public health implications

Use of standardized criteria to identify frail populations, as proposed in this thesis, would facilitate development and implementation of effective preventive strategies. It would also facilitate a more effective allocation of limited health care resources. Since weight loss is such a criterion, we recommend physicians, home care workers and older people to document a weight history.

Our exercise program did not show measurable effects on all outcome measures. However, we did find a clear and significant effect on physical performance, which is extremely relevant for maintenance of independence. Based on these findings, and in addition to our informal experiences such as comments and remarks of participants about perceived improvement in functioning and well-being and findings from earlier studies, we urgently recommend older people to adopt an active lifestyle. It is not realistic to expect all frail individuals to exercise. However, a considerable proportion may not know the best way to stay active, may have the misconception that they are not capable of exercising, or are afraid that exercise will worsen their disability. Many may simply not know the available exercise possibilities, transportation options, etc. Frail individuals tend to experience a great initial resistance against participation in exercise programs due to their low capacity and low self-esteem, and convincing them to participate in exercise programs is an extremely difficult task. During recruitment many people mentioned they did not expect to be able to participate. After explaining that the program was accessible to all mobility levels and that withdrawal was always possible, many of these individuals successfully started and completed the intervention study. Once participating, appreciation and attendance were high while dropout remained low. A first step in promoting physical activity is thus education on the beneficial effects of appropriate exercise programs, the deleterious effects of inactivity, and the different available alternatives in exercise programs. General practitioners and home care workers could play an important role in education and promotion of preventive programs. Financial reimbursement for these activities needs to be considered.

An equally important strategy is the prevention of the age-related decline in activity at an earlier stage. More time and effort should be devoted to encouraging an active lifestyle from early childhood to advanced old age. A positive attitude toward physical activity attained during childhood is more likely to result in a lifelong physically active lifestyle.

Another important condition for widespread participation in preventive programs is the availability of appropriate programs. Educating exercise professionals in the implementation and coordination of appropriate programs should be a major point of attention. In planning these programs, problems such as lack of transportation and limited financial resources should also be considered. We recommend organization of exercise programs in or close to all senior homes.

Future research

Standardized criteria that identify frail populations are needed in order to improve comparability between studies. Inactivity in combination with weight loss may be such a criterion. Active counseling by home health care workers, general practitioners, family and friends may be an efficient means of contacting and motivating this risk group. Limitation of the number of measurements reduces the respondent burden and may also increase response rate and additionally decrease dropout during baseline measurements.

The assessment of the outcome measure is a critical aspect in the evaluation of efficacy of preventive programs. The development of measurement instruments that are valid and reliable for frail populations and sensitive for the distinction of subtle changes in time is a promising area for future research.

Until now, many studies have shown the physiologic and fitness benefits of exercise and physical activity for frail older adults. However, improvements in daily functioning and well-being for this age group are far more relevant than, for instance, decreased fat mass and cholesterol levels or increased maximal aerobic power. We recommend future research to focus more on quality-of-life-related outcomes. The emphasis on program designs that are effective as well as enjoyable and feasible for widespread implementation is very important. Programs should be tailored to the needs and capabilities of the frail and very old. Interesting topics are: the most appropriate training prescription, comparison of different types of exercise, the effectiveness of once a-week exercise in combination with lifestyle activity promotion, and measurement and standardization of exercise intensity in frail populations. Finally, implementation, initiation and maintenance of these programs should receive a high priority.

Epilogue

Both physical exercise and adequate nutrition are recognized as essential and mutually interacting factors for optimal health. We have tried to develop an exercise and nutritional intervention program feasible for widespread implementation among frail older people. Because of the interacting effects of physical activity and nutrition we hypothesized that simultaneous intervention with both training and nutrient dense foods would provide synergy, but no evidence of interaction was detected in our trial. However, the results do propose the combination of physical exercise and micronutrient enriched foods for optimal health promotion, as both interventions exert different effects. Summarizing the findings described in this thesis and the complementary thesis of Nynke de Jong,[2] we conclude that consumption of nutrient dense foods improves blood vitamin levels, homocysteine concentration, and bone mass and density. Exercise improves physical functioning and fitness and preserves muscle mass, energy intake and delayed-type hypersensitivity. Whether the observed effects on bone parameters, blood vitamins and delayed-type hypersensitivity are relevant for the prevention of fractures, maintenance of bodily functions and morbidity respectively, remains to be confirmed in longer-term interventions. Neither intervention was effective in improving subjective well-being, appetite and self-rated disabilities. A plausible explanation is that the questionnaires chosen were not sensitive enough to measure changes in time. As subjective feelings may explicitly reflect life satisfaction, they are extremely relevant for future research in this field.

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Summary

An impressive increase in life expectancy in the Western world has resulted in a shift toward an emphasis on improving quality of life rather than prolonging it. Two promising strategies for improving quality of life or health status are physical exercise and nutritional supplementation. Both regular physical activity and adequate dietary intake are recognized as essential and mutually interacting factors for optimal health. Dependency and disability are essential components of quality of life. Because of their limited reserves, frail older persons have an increased susceptibility to dependency and disability. For this reason they may particularly benefit from preventive interventions. Due to the frailty element, the design of possible preventive interventions deserves special attention: programs need to be tailored to their specific needs and capabilities.

This thesis focuses on the effectiveness of a specifically designed exercise and nutritional program. The effects of these programs on functional status and psychosocial well-being have been studied in a large-scale randomized controlled trial. Effects on immune response are also addressed. The objectives of this thesis are to investigate:

1. Criteria for identification of frail elderly people;
2. The effects of a specific exercise and nutritional program on physical functioning, psychosocial well-being and immune response in frail elderly people who live independently;
3. The development of an exercise program for frail elderly people.

The introductory *Chapter 1* explains the concept of frailty, the preventive interventions and the different outcome measures.

The term frailty is frequently used in geriatric medicine and gerontology. However, no generally accepted definition or standardized criteria to identify frailty exist. In this thesis frailty is defined as a state of reduced physiologic reserves that leads to a decline in physical performance and functional independence. Besides biological aging and chronic diseases, the main contributors to physical frailty are physical inactivity and dietary inadequacies. Both an inadequate nutritional state and

inactivity have been associated with a loss of muscle mass and muscle function, resulting in functional limitations and an even further decline in activity levels, consequently evolving into a downward process.

Physical exercise and micronutrient supplementation may therefore be preventive strategies with great potential. Because of the limited capabilities of frail individuals, the design of interventions deserves special attention: programs need to be tailored to their specific needs and abilities. A specific comprehensive exercise program was developed, aimed at the maintenance or improvement of mobility and performance of those daily activities essential for independent functioning. The nutritional program consisted of food products enriched with vitamins and minerals at 25 to 100% of the Dutch Recommended Daily Allowances (RDA), for which the intake is frequently low in the elderly.

The effects of both interventions on physical functioning, psychosocial well-being and cellular immune response were studied.

Objective 1: *Examination of possible criteria for identification of frail older people.* In *Chapter 2.1* three different working definitions for selecting a frail elderly population were compared in 450 independently-living men aged 69-89 who participated in the Zutphen Elderly Study. Frailty was defined as inactivity combined with 1) low energy intake, 2) weight loss or 3) low body mass index (BMI). Differences according to the inactivity/weight loss criterion were more pronounced than according to the other two criteria. Inactivity/weight loss was associated with lower subjective health and performance as well as more diseases and disabilities. Three-year relative risks of mortality (Odds ratio [OR] = 4.1, 95% confidence interval [CI]: 1.8-9.4) and functional decline (OR = 5.2, CI: 0.04-25.8 for disabilities, OR = 3.7, CI: 0.8-16.2 for performance) were also higher. Inactivity in combination with weight loss seems to be a workable definition for selecting a frail elderly population.

The usefulness of inactivity and weight loss as a screening criterion was further investigated in the SENECA study, a longitudinal study on nutrition, lifestyle and health of elderly Europeans (*Chapter 2.1*). Again, inactivity combined with weight loss was associated with an unfavorable health profile: inactive, weight-losing elderly people had significantly more chronic diseases (2.2 versus 1.1), were on more medications (2.3 versus 1.1), and had a lower physical performance score, self-rated and relative health when compared to the weight-stable, more active reference group. They also reported disabilities (81 versus 43%) and received supportive services (26 versus 6%) more often. Few social contacts, inadequate micronutrient intakes and biochemical deficiencies were also more prevalent in these frail elderly subjects.

It was concluded that physical inactivity in combination with weight loss seems to be a practical and inexpensive screening criterion for identifying functionally vulnerable persons among non-institutionalized elderly people.

Objective 2: *Examination of the effects of a specific exercise and nutritional program on physical functioning, psychosocial well-being and cellular immune response of frail elderly people.*
To fulfill objective number two, a randomized controlled trial was developed based on a two-by-two factorial design that permitted an assessment of the independent effects of the exercise and nutritional intervention as well as possible interaction effects. Because there was no evidence of interaction, the analysis was performed according to factor. In other words, exercise was compared to no exercise and nutrient dense foods to regular foods.

Independently-living frail elderly people were recruited by mail from senior housing complexes, Meals-on-Wheels programs, home care organizations and general practitioners. The most important inclusion criteria were: requiring care such as home-care or Meals-on-Wheels, not being a regular participant in physical activities of moderate to high intensity; and a self reported BMI ≤ 25 kg/m^2 or recent (past year) involuntary weight loss. Eligible subjects, 56 men and 161 women with a mean age of 78.9 years (range: 67-96), were randomly assigned to: a) twice weekly, moderate intensity, progressive exercise (n=55); b) food products enriched with vitamins at 100% the RDA and minerals at 25-100% the RDA (n=58); c) both (n=60) or d) neither: control (n=44). Subjects not assigned to exercise followed a social program. The non-supplemented groups received identical regular food products. The intervention period was 17 weeks. Fifty-six subjects dropped out. The main reasons for dropout were health problems, including disease, hospital stay and recent falls or fractures.

Chapter 3.1 describes the effects on functional performance, fitness and self-rated disabilities. Three scores were constructed: a performance score based on 7 performance tests, a fitness score based on 7 fitness tests, and a disability score based on the self-rated ability to perform 16 daily activities. Functional performance had significantly improved (+8%) in trained compared to non-trained subjects (-8%) (difference in change = 1.9 points, 95%CI: 0.9-2.9 adjusted for baseline performance). The beneficial effect on fitness scores was smaller (adjusted difference in change = 0.9 points, 95%CI: 0.01-1.8). This beneficial effect of exercise was stronger in a subgroup with lower BMI and activity scores at baseline, and in a highly compliant subgroup that attended more than 75% of the exercise sessions. No exercise effects on self-rated disability were observed. Consumption of nutrient dense products did not affect performance, fitness or disability scores. The exercise program thus proved to be of functional benefit within 17 weeks, while daily consumption of micronutrient enriched foods at 25-100% of the RDA did not.

The focus of *Chapter 3.2* is psychological well-being. General well-being was measured by a questionnaire on health, self-respect, morale, optimism and contacts (SSWO score). At baseline, the SSWO score was significantly correlated with physical fitness ($r=0.28$, $p<0.001$), blood vitamin B6 and D status (correlation coefficient of $r=0.20$ and 0.23, respectively, $p<0.05$), but not with physical activity levels and other blood vitamin concentrations. The SSWO score and self-rated health (on a 10-point scale) had not changed after 17 weeks of either intervention. A possible explanation is that perceived psychological well-being in frail elderly people is a rather stable concept which is not responsive to 17 weeks of exercise or to nutritional intervention. It is also possible that the selected questionnaire was not suitable for measuring changes over time. The number of participants with social contacts less than twice a week declined, but this was not different between the exercise and social program, or between enriched and regular foods. The significant correlation between well-being and physical fitness and several blood vitamin concentrations at baseline suggests that long-term interventions may be beneficial.

Chapter 3.3 examines the effects on cellular immune response as measured by a delayed-type hypersensitivity skin test response (DTH) against 7 recall antigens expressed as the total number of positive reactions and the sum of diameters of all positive responses. Non-exercising subjects showed on average a decline of 0.5 responses (-26%) compared to an unchanged responsiveness among exercising subjects (difference in change = 0.5 responses, 95% CI: 0.04-0.89 adjusted for baseline DTH, activity level and micronutrient status). The difference between non-exercising and exercising subjects in change in the sum of diameters of all positive responses was smaller and non-significant. Again, no effects of micronutrient-enriched foods were observed. These results suggest that exercise may prevent or slow down the age-related decline in immune response in frail elderly people. As infectious diseases can have debilitating or even fatal consequences for the elderly, prevention of the age-related decline in cellular immune response could significantly improve their quality of life.

Objective 3: *Development of an exercise program feasible for frail elderly.*
Chapter 4 describes design and feasibility of the 17-week, twice-weekly comprehensive progressive exercise program for frail elderly . The main objective of the program was maintenance or improvement of mobility and performance of daily activities essential for independent functioning. An emphasis was placed on skills training: motor actions such as walking, scooping and chair stands were trained in the context of motor behavior such as daily activities and games. Exercises included strength, coordination, flexibility, speed and endurance training. The feasibility of the exercise program was studied in participants who were randomized to exercise in the intervention trial.

Seventy-two percent (83 of a total of 115 subjects) completed the 17-week program. Program appreciation and attendance were high. Seventy-three percent of those who completed the program reported wanting to continue participating - most of them only once a week, though. Thirty percent were still participating in an exercise program twelve to eighteen months after program termination.

It was concluded that the exercise program was enjoyable and acceptable to a population of frail, previously inactive elderly people. Initiation and maintenance of physical activity remain important topics for future research.

In *Chapter 5* the main findings are summarized, followed by a discussion of general methodological considerations and the main conclusions ending up with public health implications and recommendations for future research.

Our trial was the first to study the effectiveness of an exercise and nutritional program that emphasizes feasibility in independently-living frail older people. The main conclusions of this thesis are:

- Physical inactivity alone or in combination with weight loss seems to be effective and inexpensive for measuring a screening criterion for the identification of these vulnerable persons among non-institutionalized elderly people.

- Exercise programs can be developed which are acceptable and enjoyable for frail, previously inactive elderly people, as well as effective in preventing, slowing down or reversing age-related decline in physical functioning and cellular immune response.

- Seventeen weeks of consumption of micronutrient enriched foods at physiological doses (25-100% the RDA) did not affect functional status or cellular immune responses despite an improvement in blood vitamin concentrations.

- Neither intervention established a measurable effect on psychological well-being, self-rated health or self-rated disabilities. However, further research using sensitive measurement instruments validated for this specific population is necessary before definite conclusions can be drawn.

The use of standardized criteria that identify frail populations can facilitate recruitment and the implementation of effective, preventive strategies. It also facilitates a more effective allocation of limited health care resources and improves comparability between studies. We recommend physicians and home care workers as well as older people to document weight histories.

Convincing frail elderly people to initiate and sustain an exercise program appeared a difficult task. However, once they became participants, subjects highly appreciated the exercise program and the majority favored a continuation of program participation. Important conditions for widespread participation in exercise programs are: education of the target population on the beneficial effects of appropriate exercise programs, the deleterious effects of inactivity and the different available alternatives of exercise programs, and the training of exercise professionals in the implementation and coordination of appropriate programs. Active counseling by home health care workers, general practitioners, family and friends may be an efficient means of contacting and motivating this vulnerable group.

The assessment of the outcome measure is a critical aspect in the evaluation of the effectiveness of preventive programs. The development of measurement instruments that are valid and reliable for frail populations and sensitive for distinction of subtle changes in time is something that will need further attention.

Important topics for future research are the most effective and appropriate training prescriptions and their implementation, as well as the adoption and maintenance of an active lifestyle.

Samenvatting

Met het stijgen van de levensverwachting is de aandacht voor de gezondheid en met name de kwaliteit van leven van ouderen toegenomen. Regelmatige lichaamsbeweging en voedingsmiddelen die rijk zijn aan voedingsstoffen zijn twee mogelijk effectieve strategieën die de kans op een gezonde oude dag kunnen verhogen. Voldoende voedingsstoffen en voldoende lichaamsbeweging worden gezien als belangrijke factoren voor een optimale gezondheid.

Negatieve spiraal

Met het ouder worden wordt men vaak minder actief. Een minder actief leven kan leiden tot een slechtere eetlust waardoor men minder gaat eten. Wanneer men weinig eet (minder dan ongeveer 6,3 Megajoule of ±1500 kilocalorieën per dag) dan bestaat het gevaar op tekorten aan verscheidene vitaminen en mineralen. Zowel een tekort aan lichaamsbeweging als een tekort aan voedingsstoffen hangt samen met een achteruitgang in het lichamelijk functioneren op allerlei niveaus waardoor men moeite krijgt met bijvoorbeeld het uitvoeren van de dagelijkse activiteiten zoals zich wassen of boodschappen doen. Er kan gewichtsverlies optreden (mede door weinig gebruik van de spieren). Tenslotte zal het aantal activiteiten nog verder afnemen. Op deze manier ontstaat er een negatieve spiraal.

Met name ouderen die weinig eten en weinig bewegen zouden dus kunnen profiteren van preventieve strategieën. Omdat de meerderheid van de ouderen zelfstandig woont en dat ook graag zou blijven doen, is het in dit proefschrift beschreven onderzoek gericht op zelfstandig wonende ouderen.

De doelstellingen van het onderzoek waren:

1) Onderzoeken met behulp van welke kenmerken ouderen met een verhoogde kans op een achteruitgang in functioneren en hulpbehoevendheid kunnen worden geïdentificeerd;
2) Het evalueren van de effecten van een specifiek bewegings- en voedingsprogramma op de gezondheidstoestand van deze groep ouderen;
3) Het evalueren van de praktische haalbaarheid van het bewegingsprogramma.

Doelstelling 1: *Het onderzoeken van selectiecriteria*

Verschillende methoden voor de selectie van ouderen met een verhoogde kans op een achteruitgang in functioneren en op hulpbehoevendheid zijn bestudeerd in de gegevens van de Zutphen Ouderen Studie en de SENECA studie. In de Zutphen studie werd gekeken naar inactiviteit in combinatie met 1) een lage energie-inneming, 2) gewichtsverlies of 3) een laag lichaamsgewicht voor de lengte. In de SENECA studie werden inactiviteit, gewichtsverlies of de combinatie van beide bestudeerd. Met name de combinatie van inactiviteit en gewichtsverlies identificeerde een groep met een ongunstig gezondheidsprofiel: een geringere subjectieve gezondheid en lichamelijk functioneren en meer ziekten en zelfgerapporteerde beperkingen. Uit de gegevens van de Zutphen studie bleek ook het risico op sterfte en achteruitgang in lichamelijk functioneren verhoogd bij inactieven met tevens gewichtsverlies. Inactiviteit gecombineerd met gewichtsverlies lijkt dus een eenvoudig en goedkoop te meten criterium voor de identificatie van een risicogroep onder zelfstandig wonende ouderen.

Doelstelling 2: *De effectiviteit van het voedings- en bewegingsprogramma*

Het effect van een specifiek ontwikkeld voedings- en bewegingsprogramma apart aangeboden of in combinatie, is bestudeerd in een interventie studie. Ruim 7000 brieven zijn verstuurd naar service flats, aanleunwoningen, en via thuiszorgorganisaties, huisartsen en maaltijdleveranciers (tafeltje-dek-je). Van de 854 geïnteresseerden werden via een telefonische vragenlijst 217 personen geselecteerd voor deelname. De belangrijkste kenmerken waarop deelnemers geselecteerd werden waren:

- gebruik maken van hulp (bijvoorbeeld thuiszorg of maaltijdvoorziening)
- weinig lichaamsbeweging
- ongewenst gewichtsverlies of geen overgewicht

De deelnemers (gemiddeld 79 jaar) werden door loting ingedeeld in vier groepen:

1) bewegingsprogramma + verrijkte voedingsmiddelen: combinatie (60 personen)
2) educatief programma + verrijkte voedingsmiddelen: voeding (58 personen)
3) bewegingsprogramma + reguliere voedingsmiddelen: beweging (55 personen)
4) educatief programma + reguliere voedingsmiddelen: controle (44 personen)

Het bewegingsprogramma: In het bewegingsprogramma werd gedurende 17 weken, tweemaal per week gedurende 45 minuten in groepen van 10 à 15 personen geoefend met verschillende materialen (bijvoorbeeld pittenzakken, ballen, gewichten, elastische banden). Het programma richtte zich op het verbeteren van het lichamelijk functioneren door het trainen van spierkracht, lenigheid, coördinatie (balans, handvaardigheid), snelheid en uithoudingsvermogen.

Het educatieve programma: Voor het educatieve programma werden eenmaal per veertien dagen diverse activiteiten georganiseerd zoals lezingen, creatieve activiteiten of een voedingsquiz.

Het voedingsprogramma: Aan alle deelnemers werd gevraagd gedurende deze 17 weken tweemaal daags één van de door de onderzoekers verstrekte produkten te eten. Er was een keuze uit vanillevla, vruchtenkwark, vruchtenyoghurt, en vruchtencompote. De verrijkte voedingsmiddelen waren verrijkt met de vitaminen D, E, B_1, B_2, B_6, foliumzuur, B_{12} en C en de mineralen calcium, magnesium, ijzer, zink en jodium. Twee verrijkte produkten leverden ongeveer 50 tot 100% van de dagelijks aanbevolen hoeveelheden voor ouderen. De reguliere produkten waren qua uiterlijk identiek maar niet verrijkt.

In de week voor en na het 17 weken durende programma werden diverse metingen verricht bij de deelnemers, zoals spier- vet- en botmassa, lichamelijk functioneren (bijvoorbeeld loopsnelheid en opstaan uit een stoel), fitheid (bijvoorbeeld spierkracht, lenigheid en balans), ervaren gezondheid en welbevinden, eetlust en voedingspatroon, immuunrespons (weerstand tegen ziekten) en diverse laboratoriumbepalingen in het bloed. In dit proefschrift worden de effecten op het lichamelijk functioneren, de fitheid, de ervaren gezondheid, het welbevinden en de immuunrespons beschreven. Mijn collega Nynke de Jong beschrijft in haar proefschrift de effecten op de spier- vet- en botmassa, de eetlust, het voedingspatroon en diverse bloedwaarden.

Een kwart van de mensen (56) heeft het 17-weken durende programma niet afgerond. De belangrijkste redenen voor uitval waren gezondheidsproblemen waaronder klachten door reuma, ziekenhuisopname en het (her)ontdekken van kanker.

De resultaten van het onderzoek lieten zien dat het bewegingsprogramma een gunstig effect had op lichamelijk functioneren, fitheid, en de immuunrespons. Geen van beide programma hadden een meetbaar effect op zelfgerapporteerde problemen met dagelijkse activiteiten, de ervaren gezondheid en het welbevinden. De verrijkte voedingsmiddelen hadden geen meetbare gezondheidseffecten op de hier genoemde aspecten.

Doelstelling 3: *De praktische haalbaarheid*
Om iets over de praktische haalbaarheid te kunnen zeggen is na afloop van de 17 weken aan de deelnemers gevraagd of ze een uitgebreide evaluatielijst wilden invullen. Bijna driekwart van alle deelnemers die aan het bewegingsprogramma waren toegewezen hebben het programma ook volbracht. De presentie was hoog (gemiddelde 90% van alle lessen) en men was zeer enthousiast over de inhoud van het programma en de begeleiding: het gemiddelde rapportcijfer was een 9^-. Ook zou bijna driekwart indien mogelijk graag door willen gaan met het bewegingsprogramma. Bij navraag één tot anderhalf jaar later was echter slechts 30% nog actief in een bewegingsprogramma. Gezien het feit dat van de 7000 verstuurde brieven uiteindelijk slechts 854 (12%) personen geïnteresseerd waren in deelname, blijft het motiveren van ouderen tot een actieve levensstijl een moeilijke maar belangrijke taak.

Samenvattend kan geconcludeerd worden dat het mogelijk is bewegingsprogramma's te ontwikkelen die plezierig zijn om te volgen en eveneens de gezondheid gunstig beïnvloeden.

Dankwoord

Ruim vier jaar skatend naar de frisse lucht van Wageningen. Niet alleen spierkracht maar ook veel ervaring en papierwerk rijker. Iedereen die aan het tot stand komen van dit proefschrift heeft bijgedragen wil ik op deze plek bedanken, een aantal van hen wil ik graag persoonlijk noemen.

Nynke, je bent een supercollega!! Ik was en ben heel blij met jou als projekt-, veldwerk-, kamer- en promotiegenoot. Bedankt voor de geweldige samenwerking!

Mijn promotoren Frans Kok en Wija van Staveren, en mijn co-promotor Evert Schouten: bedankt voor jullie bijdragen aan het onderzoeksproject, ik heb een enorme en diverse hoeveelheid ervaring opgedaan. Evert, fijn dat je ondanks je volle agenda altijd rustig de tijd voor me nam en knap dat je de manuscripten altijd zo snel en tot op de komma van commentaar voorzag. Ook in de begeleiding van studenten vond ik onze samenwerking heel prettig! Frans, bedankt voor je waardevolle opmerkingen met name in de laatste fase van het onderzoek.
Wija, ik heb erg prettig onder je supervisie gewerkt!
Ook de overige leden van de begeleidingscommissie: Lisette de Groot, Kees de Graaf en Gert Jan Hiddink wil ik bedanken voor hun inbreng en samenwerking. Jacqueline Dekker, bedankt voor het wegwijs maken tijdens het eerste jaar van mijn aanstelling en het leuke contact daarna. Ik vind je een goede begeleider, jammer dat je wegging!

Alle veldwerkers wil ik bedanken voor hun hulp bij de enorme hoeveelheid werkzaamheden tijdens de interventieperiode:
Het verzamelen van deelnemers kostte vele uren, weken en uiteindelijk maanden extra dan gepland. Caroelien Schuurman en Sabine Neppelenbroek, dankzij jullie rekruteringskunsten zijn uiteindelijk toch ruim tweehonderd deelnemers aan onze intensieve interventie begonnen!

Marga, Saskia, Els en Karin bedankt voor al het prikken, meten, wegen, coderen, schminken....
De sportdocentes, Isabella Borburgh, Anne Bout, Joke van de Kaa, Karin Samson, Joke Seinen, Rita Wubbels and Tineke Zwijnen. Jullie enthousiaste inzet bij niet alleen de ontwikkeling van het bewegingsprogramma maar ook de uitvoering daarvan was geweldig! Mede door jullie enthousiasme oefenden de deelnemers zo gemotiveerd met gewicht, isolatiebuis of pittenzak!
Even gemotiveerd waren de deelnemers aan het educatieve programma dankzij het enthousiasme van Nellie van Amersfoort. Nellie, bedankt voor je creatieve en educatieve inzet.
De hulp van de vele studenten en vrijwilligers bij de voorbereidingen, het testen, meten, wegen, plakken, vragen, ontvangen, produkten inpakken, rondbrengen, meebewegen, data invoeren, analyseren, rapporteren en alle andere activiteiten was onmisbaar: ontzettend bedankt Almi, Astrid, Carolien, Danielle, Gitte, Ingeborg, Liselotte, Margriet, Mariska, Marleen K, Marleen M, Michiel, Mieke, Nancy, Nienke, Patrick, Renate, Saskia E, Saskia v G, Sigrid en vele anderen.
Dirk en Ben bedankt voor de computerhulp en het scannen van plaatjes en Dirk ook nog voor het maken van posters en regelen van wat we maar nodig hadden.
Hans van Es bedankt voor het ontwerpen van het logo voor de interventiestudie!

De bewegingswetenschappers in Groningen: Martin Stevens en Petrus Bult: heel erg bedankt voor de prettige samenwerking bij de ontwikkeling van het bewegingsprogramma.
Koen Lemmink: bedankt voor het lenen van de fitheidstesten!

Hoofstuk 2.1 is tot stand gekomen in samenwerking met het RIVM. Edith Feskens en Daan Kromhout bedankt voor het ter beschikking stellen van de data van de Zutphen studie en de samenwerking bij het schrijven van het daarop gebaseerde artikel. Nancy Hoeymans en Fransje Bijnen bedankt voor het wegwijs maken in de Zutphen data en jullie zeer nuttige input. Angelika, Claudia en Margje bedankt voor het lenen van jullie werkplek en vrolijke gezelschap!!

Alle Aio's en andere collega's op LUW, RIVM en TNO-PG jullie ook bedankt voor jullie bijdrage in de vorm van gezelligheid, peptalk, lunches, uitjes etc! Esther

Pallast, Jantine Schuit en Louise Mennen jullie nog eens extra bedankt voor de ervarings-tips met betrekking tot het ouderenonderzoek en ook voor de afleiding daarvan.

Amika en Frouwkje: twee sterke persoonlijkheden als paranimf die mij terzijde staan tijdens de aanval en verdediging: bedankt voor jullie hulp, afleiding en gezelligheid in de afgelopen jaren en hopelijk ook daarna!

Mijn zeer actieve ouders, lieve pap en mam, bedankt voor al jullie steun, adviezen, aanmoedigingen en het meedenken.

Lief Lars, een dikke knuffel voor jou persoon, je mooie tekeningen, dia's, lay-out adviezen en je steun en aanwezigheid van ver of dichtbij!!

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