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EFFECTS OF PHYSICAL TRAINING ON PHYSICAL PERFORMANCE IN FRAIL ELDERLY PEOPLE

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*Man does not **cease to play** because he grows old,*

*Man grows old because he ceases to **play.***

George Bernard Shaw

ABSTRACT

Aging is often accompanied by decreased muscle strength, aerobic capacity and balance, which can lead to impaired physical performance. Epidemiological data have demonstrated that low levels of physical activity are strongly related to functional decline. Frailty has been defined as a clinical syndrome comprised of unintentional body weight loss, self-reported exhaustion, muscle weakness, slow walking speed and a low level of physical activity in men and women over the age of 65. There is contradictory evidence regarding the effects of physical training on physical performance in frail elderly people.
The primary aim of this thesis is to describe the effects of physical training on physical performance i.e. muscle strength, aerobic capacity, balance, mobility and physical activity level as well as activities of daily living (ADL) and health-related quality of life (HRQL) in frail elderly people. Another aim is to investigate reliability with test re-test in one repetition maximum (1RM) in the arm/shoulder.

Ninety-six community-dwelling elderly people (58 women) were randomised to four different groups: i) physical training programme (aerobic, muscle strength, balance), ii) a nutritional intervention programme (individually targeted nutritional advice and group sessions), iii) a combination of these interventions and iv) a control group. At baseline the subjects were screened for physical performance as well as nutrition related variables. These measurements were repeated immediately after the intervention, which lasted for 12 weeks, and again six months later. During the last six months, the subjects in the training groups were encouraged to perform home-based exercises and to fill in training diaries. Two years after baseline, a third follow-up regarding ADL was conducted through telephone calls. The test re-test procedure with 1RM was conducted at one week-interval, comparing the reliability between test sessions, and also between subjects with or without previous muscle strength training experience.

A positive effect of the physical training programme was shown on leg muscle strength and habitual physical activity level for frail elderly people. Adding a nutritional intervention did not affect the results. There were no other significant differences between groups. Subjects with improvements in muscle strength, balance and mobility had significantly higher compliance compared to non-improvers. There were moderate significant correlations between compliance of the home-based exercises and improvements in personal ADL and HRQL.
There was a high correlation between the test sessions in 1RM, $r=0.97$ for both groups. An analysis of 95% limits of agreement for the mean difference was -4.3/+6.9 kg for the group without and -3.0/+6.4 kg for the group with previous muscle strength training experience, respectively.
In conclusion, the physical training programme showed a positive effect on leg muscle strength and habitual physical activity level. An individually tailored intervention is probably necessary to achieve a positive result on physical performance such as aerobic capacity, balance and mobility in frail elderly people. 1RM seems to be a reliable and safe method for dosing the intensity and evaluating a muscle strength training programme for elderly people.

SAMMANFATTNING

Vid stigande ålder försämras muskelstyrka, kondition och balans för de allra flesta personer. Detta kan leda till försämring av den fysiska funktionsförmågan. Epidemiologiska studier har visat att fysisk inaktivitet är starkt relaterat till fysisk funktionsnedsättning. Skörhet (frailty) har definierats som ett kliniskt syndrom bestående av ofrivillig viktminskning, självrapporterad uttröttbarhet, nedsatt muskelstyrka, långsam gånghastighet och låg fysisk aktivitetsnivå hos män och kvinnor över 65 år. Hittills genomförda studier visar på motsägelsefulla resultat avseende effekt av fysisk träning på fysisk funktionsförmåga för sköra äldre personer. Det övergripande syftet med avhandlingen var att beskriva effekterna av fysisk träning på fysisk funktionsförmåga, i detta fall, muskelstyrka, kondition, balans, förflyttningsförmåga och fysisk aktivitetsnivå samt aktiviteter i dagliga livet (ADL) och hälsorelaterad livskvalitet (HRQL) hos sköra äldre personer. Ett specifikt syfte var också att undersöka reliabiliteten av ett muskelstyrketest (1RM) i armen/skuldran.

Nittiosex sköra personer (58 kvinnor), i ordinärt boende, randomiserades till fyra olika grupper: i) fysisk träning (kondition, muskelstyrka, balans) ii) kostbehandling (individuellt riktade kostråd och gruppsammankomster) iii) kombination av träning och kostbehandling och iv) kontrollgrupp. Innan behandlingen startade undersöktes deltagarna med avseende på fysisk funktionsförmåga samt nutritionsrelaterade variabler. Mätningar upprepades sedan direkt efter avslutad behandling (12 veckor) samt sex månader senare. Under de sista sex månaderna uppmanades deltagarna i träningsgrupperna att träna på egen hand och att fylla i träningsdagböcker. Två år senare genomfördes att tredje uppföljningstillfälle, då deltagarna intervjuades på telefon med avseende på deras ADL-förmåga.
Reliabilitet (tillförlighet) av 1RM utfördes vid två tillfällen med en veckas mellanrum. Resultaten analyserades dels mellan de två tillfällena, dels mellan deltagare med respektive utan tidigare erfarenhet av styrketräning.

Fysisk träning visade på positiva effekter på benmuskelstyrka och fysisk aktivitetsnivå. Kostbehandling påverkade inte resultaten. Det fanns inga andra signifikanta skillnader mellan grupperna. Personer som förbättrades med avseende på muskelstyrka, balans och förflyttningsförmåga hade signifikant högre träningsnärvaro (compliance). Därutöver fanns det måttligt starka statistiska samband mellan träning på egen hand samt förbättring i ADL och HRQL.
Det fanns starka samband mellan testtillfällena i 1RM, r=0.97 för båda grupperna. En analys av ett 95% intervall för skillnaden i medeltal mellan testtillfällen visade -4.3/+6.9 kg för gruppen utan erfarenhet av styrketräning och -3.0/+6.4 kg för gruppen med erfarenhet av tidigare styrketräning.
Sammanfattningsvis: Träningsprogrammet visade en positiv effekt på muskelstyrka och fysisk aktivitetsnivå. Det är troligen nödvändigt att i högre grad individualisera fysiska träningsprogram för att kunna åstadkomma positiva resultat på kondition, balans och förflyttningsförmåga hos sköra äldre individer.
1RM verkar vara en reliabel och säker metod för att dosera intensiteten och utvärdera ett styrketräningsprogram för sköra äldre individer.

LIST OF PUBLICATIONS

I. Rydwik E, Lammes E, Frändin K, Akner G. Effects of a physical and nutritional intervention programme for frail elderly people over age 75. A randomised controlled pilot treatment trial. Accepted for publication in Aging Clin Exp Res, April 2007.

II. Rydwik E, Gustafsson T, Frändin K, Akner G. Effects of a physical training programme on aerobic capacity in frail elderly people and the influence of lung capacity, cardiovascular disease and medical drug treatment. Submitted.

III. Rydwik E, Frändin K, Akner G Effects of physical training in frail elderly people regarding habitual physical activity level and activities of daily living. Submitted.

IV. Rydwik E, Karlsson C, Frändin K, Akner G. Muscle strength testing with one repetition maximum in the arm/shoulder for people aged 75+ – test-retest reliability. Clin Rehabil 2007; 21: 258-65.

CONTENTS

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
BMD	Bone Mineral Density
BMI	Body Mass Index
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
DXA	Dual X-ray Absorptiometry
FIM	Functional Independence Measure
HBM	Health Belief Model
HRQL	Health-Related Quality of Life
IAM	Instrumental Activity Measures
ICF	International Classification of Functioning, Disability and Health
MFE	Modified Figure of Eight
OLS	One Leg Stance
TS	Tandem Stance
WHO	World Health Organization
1RM	One Repetition Maximum

1 INTRODUCTION

The population aged 65 and older will increase by 59% in the next 50 years in Sweden, and people above age 80 will represent half of this increase [1]. The World Health Organisation (WHO) has adopted the definition of Active Ageing of the Ministry of Health of Canada, which considers active ageing as a "*process of optimising opportunities for physical, social and mental well-being throughout life course in order to extend life expectancy"* [2]. However, these goals are difficult to fulfil for frail elderly people due to a lack of clinical research in this field [3].

The main focus of this dissertation is the effects of physical training on frail elderly people. The perspective is biopsychosocial, regarding a human being as a biological being, a psychological being and a social being and then add the entities together to form a whole [4, 5].
In the design of the studies included in the present thesis we have tried to cover as many aspects of life as possible including physical performance, nutritional state, morbidity, health-related quality of life and different aspects affecting life style changes. We also invited next of kin to all examinations and meetings in order to include them in the process.
When working with elderly people as a physiotherapist it is of importance to support and stimulate the older individual to set reachable goals in order to improve or preserve physical performance and in the extension avoid the threshold of dependence and to preserve or improve quality of life.

1.1 BACKGROUND

1.1.1 Framework

The framework chosen for this thesis is the International Classification of Functioning, Disability and Health (ICF) approved by the World Health Assembly of the WHO in May 2001 [6]. It is the successor of the International Classification of Impairments, Disabilities and Handicaps (ICIDH) and the ICF has moved on from "consequences of disease" to a classification of human functioning and disability [7]. This change has been seen mainly in the dual approach of two umbrella terms *Functioning* versus *Disability* including body function/structure versus impairment, activity versus activity limitation and participation versus participation restriction. The model is divided in two parts, part 1 – Functioning and Disability and part 2 – Contextual factors such as environmental and personal factors. This gives the ICF new dimensions compared to ICIDH i.e. all people can be included despite absence or presence of disease or injury and environmental and personal factors are taken into consideration [6].
A distinction between Activity and Participation has not been clarified in the last edition of the ICF [6]. Jette et al [8] have investigated the hypothesis that a distinction between Activity and Participation could be identified. This proved to be more difficult than the authors expected. However, they concluded that within physical functioning three distinct factors were identified – Mobility Activities, Daily Activities and Social Participation – where the two first corresponded to Activity and

the last to Participation. They also conclude that assessment instruments need to be constructed to be able to differentiate between the constructs of the ICF.
This framework has been chosen because it is known worldwide and among many different professions and the research in this thesis has been conducted in collaboration with other professions, i.e. physician, dietician and nutritionist [9-12].

In many studies referred to in this thesis, mixed groups of elderly people are examined. Therefore, it is difficult to distinguish between frail, healthy and other subgroups of elderly people with separate subheadings, but I will try to be as specific as possible when describing different cohorts or groups of elderly people.

1.1.2 Frailty

Frailty has been defined as a clinical syndrome comprised of unintentional weight loss, self-reported exhaustion, muscle weakness, slow walking speed and low level of physical activity in men and women over the age of 65 [13-15]. A combination of low physical activity and weight loss has been shown to be a significant predictor for disability and mortality [13].
Frailty as a physical state (intrinsic frailty) has been suggested to be distinguished from the consequences of frailty. Intrinsic frailty comprise impairments such as loss of muscle strength, body weight, balance and mobility and the consequences include changes in functional dependence, psychosocial factors and health care consumption. Global frailty includes intrinsic frailty as well as the consequences [16].
In the MESH terms of PubMed, frail elderly are defined as “Older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity” [17].

The understanding of the physiology and etiology of frailty was discussed at a conference of clinical and basic scientists from different fields and countries. A summary has recently been published, showing diverse causes such as

i) sarcopenia, with increasing fat infiltration in the muscles with metabolically active fat leading to a chronic inflammatory state,
ii) reduced number of alpha-motor neurons in the nervous system resulting in a lower electrical stimulation of the muscle fibre and
iii) pathophysiological deficits, such as higher levels of inflammatory cytokines leading to for example bone and muscle loss, anaemia, insulin resistance and decreased levels of insulin-like growth factors that are likely to be associated with the maintenance of muscle mass with increasing age, see Figure 1 [18].

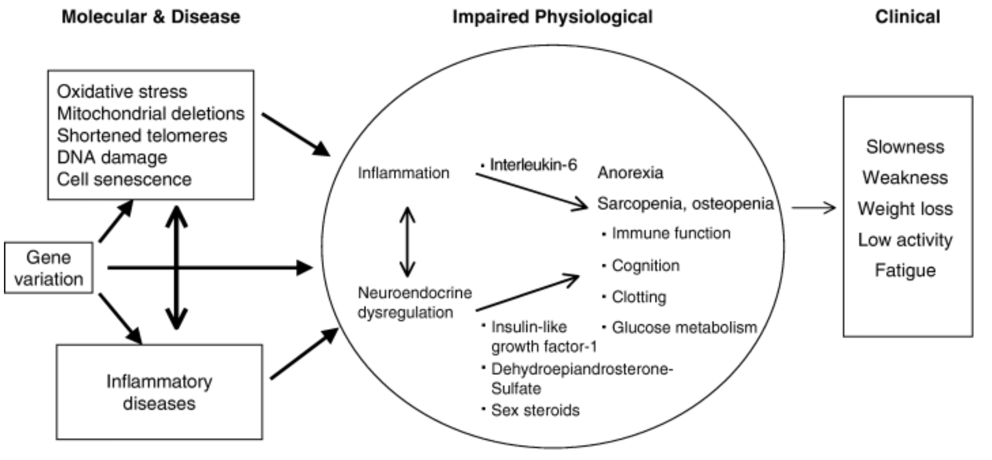

Figure 1. Possible causes of frailty. Printed with permission from Dr Walston [17] and Blackwell Publishing.

The Frailty Working Group discusses the difficulties designing a randomised controlled trial for a frail population in recent review [19]. They conclude that planning a study for frail subjects "requires a conceptual shift" compared to a traditional approach. The inclusion should be broader in order to increase generalisation, improved methodology including improved screening for frailty, improved statistical methods for managing missing data and unforeseen events and validation of objective measurements concerning disability.

In the present thesis **frailty** will be **defined** as a combination of

- unintentional body weight loss ≥ 5 % during the last 12 months and/or body mass index (BMI) < 20 kg/m^2
- low physical activity level (≤ grade 3 in the Classification of physical activity according to Mattiasson-Nilo et al and Frändin & Grimby [20, 21]).

1.1.3 Physical performance

Body function impairments

Sarcopenia has been defined as loss of *muscle mass and strength* due to a decline in skeletal muscle protein, cross-sectional area and infiltration of fat and connective tissue [22-24]. Muscle loss occurs at a rate of 5% per decade starting in the fourth decade and in people 80 years and older, muscle mass has on average declined 50% when compared to young controls [25]. However, decreases in voluntary muscle strength do not become apparent before the age of 60 [26]. Yarasheski et al [24] demonstrated that high-intensive progressive muscle strength training can activate the muscle protein synthesis in frail elderly people to the same extent as in young men and women given the same relative amount of muscle strength training.

Different studies show diverse body mass-adjusted decline in $VO_{2\ max}$ between 15-18% for men and 7-30% for women per decade after the age of 60 [27, 28]. Fleg et al [29] showed a similar decline after the age of 70 regardless of physical activity level.

However, the physically active subjects declined from a higher level [29]. The decline is partly explained by central mechanisms such as deficient sympathetic modulation leading to for example decreased myocardial contractility and reduced acceleration of heart rate. Peripheral mechanisms are mostly due to increased body fat, decreased muscle mass, and impaired oxygen extraction and redistribution of blood flow to working muscles [30].

Activity limitations/Participation restriction
Balance decreases with increasing age, for example, the ability to maintain a one-leg stance decrease by approximately 50% between the 6^{th} and 8^{th} decades [31]. Postural sway with normal sensory input (vestibular, vision and somatosensory modalities) on the body function level increases only marginally with increasing age. However, with a reduction of two modalities, postural sway increases greatly in comparison to younger people. This suggests that elderly people are more dependent on all three modalities compared to younger people. This is probably the reason why elderly people may produce an inefficient response to trips and slips resulting in a fall [32].

Therefore, in the present thesis, **balance** is **defined** as maintenance of postural control.

Maximum *walking speed* decreases more than habitual walking speed with increasing age [33]. This decrease in speed is associated with reduced stride length and single support time during the stance phase on the body function impairment level [32].

As mentioned above, the concepts of activity limitation and participation restriction are difficult to separate since they are dependent on each other and also on environmental and personal factors [6]. Different terminology has been used to describe these concepts and ICF also uses the umbrella term disability. Verbrugge [34] has defined disability as the gap between a person's capability and the environmental demands or a person's difficulties in pursuing his/her usual activities of daily living due to a chronic health problem. Disability can also be divided in physical, mental and social disability. A suggested distinction between physical disability and functional limitation is that disability is "do do" while functional limitation is "can do" meaning that "the words separate a person's capability from her/his ultimate patterns of behaviour" [35].
This is exemplified by a study that showed that 61% of the women aged 70-74 years reported *mobility deficits*, increasing to 82% in the ages 80-84. The corresponding numbers for men were 32 and 52% respectively. However the need for help was reported only by 38 and 62% of the women and 16 and 28% of the men respectively [36]. Limitations in *personal activities of daily living* (PADL) were reported by 15% of the women aged 70-74 increasing to 32% in the 80-84 age group, and by 13 and 30% of the men respectively. The corresponding numbers for reported need of help were 5 and 18% for women, and 6 and 14% for men respectively [36].

A study investigating various risk factors for instrumental ADL limitations found hierarchical components explaining the limitations, such as: mobility, balance, BMI (high), grip strength and physical activity in descending order [37].

1.1.4 Physical performance/activity and nutritional aspects

Results reported by the Nutrition and Function Study indicate a relation between low intake of micronutrients and low physical performance [38, 39]. Women have been shown to have a lower nutrient intake (calcium, vitamin D, magnesium and phosphorus) compared to men when controlled for age and sex. Women were also 2.9 times more likely than men to have a lower overall physical performance level (balance, gait and muscle strength) when demographic covariates, chronic health conditions and BMI were controlled for [38]. A higher intake of calcium, vitamin D, magnesium and phosphorus was associated with better lower extremity performance (i.e. balance, walking speed and muscle strength) and less reduction in activities of daily living (ADL) [39]. A few studies have investigated the effects of vitamin D and calcium supplementation, alone or in combination, on physical performance. Elderly women in geriatric care receiving a combination showed a small but significant effect on musculoskeletal function (muscle strength and Timed Up and Go) compared to subjects receiving only calcium [40]. Other studies have shown a non-effect of vitamin D alone on physical performance in healthy elderly men and in frail elderly people [41, 42].

A direct relationship between severity of disability, medication use and difficulty in shopping for food and an indirect relationship between lack of money and difficulty in preparing meals, suggesting an increased risk of weight loss or gain, eating few meals and low intake of fruit and vegetables per day (food insecurity) have been reported [43].
It has also been shown that elderly people (men and women) hospitalised for various medical reasons had lower quadriceps strength, lower bone mineral density at the femoral neck, and lower ability to climb stairs at discharge if they had a protein intake of <1 g/kg of ideal body weight at admission. They also had a lower total energy and calcium intake [44].
A cross-sectional study has shown no association between physical activity level and fat-free mass or fat mass for subjects over age 60, in contrast to younger subjects [45]. According to the same authors, no longitudinal studies have investigated this relationship. However, studies have shown that exercise can increase fat-free mass and to a certain degree decrease fat mass in healthy elderly people [46].

1.1.5 Physical performance and cardiovascular and lung diseases

A review has shown that older women with congestive heart failure (CHF) on average have a lower peak $VO_{2\ max}$ than are required for independent living [47]. However, variations in peak $VO_{2\ max}$ were not reported. It has also been shown that older women (m=62 years) with CHF have significantly smaller cross-sectional area of the vastus lateralis muscle compared to healthy age-matched women [48]. Women (m=77 years) with CHF had lower leg muscle strength compared to women with other chronic disabilities and women with severe CHF had smaller type 1 muscle fiber compared to women with less severity of CHF [49]. Apart from cardiac pathology, decreased skeletal muscle strength and oxidative capacity in the muscles may also play an important role for the reduced aerobic capacity in subjects with CHF [47]. Oxygen delivery to the muscles seems, however, to be the most important factor [50]. Another study showed that overall lung function explained approximately 30% of the variance in a maximal exercise test for patients with CHF [51].

It has been suggested that similar factors, mainly oxygen delivery to working muscles, affect maximal aerobic capacity in patients with chronic obstructive pulmonary disease (COPD) as well as patients with CHF [50]. This is often reported by the afflicted subjects as a sense of leg muscle fatigue [52]. Patients with COPD have a lower percentage of slow twitch muscle fibers and therefore a higher percentage of fast twitch muscle fibers in limb muscles compared to healthy subjects [53]. The opposite has been shown for the diaphragm muscle in patients with COPD. Consequences are e.g. limitations of muscle endurance in limb muscles and muscle strength in respiratory muscles [52]. There seems to be a competition between muscles in the limbs and respiratory muscles in both healthy people and patients with COPD during maximal aerobic exercise. However, for patients with COPD the higher oxygen cost of breathing may lead to a greater decrease of oxygen delivery to limb muscles [50].

The effects of ß-blockade on $VO_{2\ max}$ have been thoroughly examined and studies have shown a reduction of 5-15% but to a greater extent by non-selective compared to $ß_1$-selective blockade in healthy people [54]. Slow muscle twitch fibers seem to be more affected by ß-blockade compared to fast twitch fibers [54]. This may be of importance for elderly people since the muscle fibers of elderly people consist of a larger amount of slow twitch fibers compared to younger people [25]. However, even though ß-blockade reduces $VO_{2\ max,}$ it seems as though it does not affect training ability. Other studies, summarised in a review, have shown that a period of physical training provides similar relative improvement for both healthy subjects and subjects with various cardiac diseases, in both cases with or without ß-receptor blockade [55].

1.1.6 Physical training

Effects on frail elderly people

In preparation of this thesis a literature search was conducted on PubMed and Web of Science, using the keywords physical training and/or exercise, and frail with the limitations of randomised controlled trials and >65 years of age. Fifty-six articles were found and 27 articles were included after reading abstracts. Articles were excluded in this phase mainly due to targeting towards specific diseases and outcomes other than physical performance and health-related quality of life (HRQL).
Of the 27 articles, 13 were excluded due to institutionalised subjects/residential care units (n=11), non-randomised (n=1), and one only analysing the feasibility of and the adherence to a specific rehabilitation programme. A complementary search was conducted on AMED, CINAHL and PEDRO resulting in one additional article.
The descriptions of the remaining eleven studies (15 articles) are shown in Table 1 (page 8, 9) [42, 56-69]. The score rating methodology is based on a modified version of the Cochrane Collaboration procedures described previously [70] in which a study is scored as low (0-30 points), moderate (31-60) or high (61-100) methodological quality. The results of included studies are shown in Figure 2 and the conclusion is that there is strong evidence for the effect of physical training on muscle strength and balance, moderate evidence for mobility and contradictory effect on gait, endurance and emotional status/HRQL and limited evidence on range of motion. There is also strong evidence for a non-effect on both PADL and IADL (in Figure 2 labelled as ADL), which is in line with the conclusion of two reviews [71, 72].

The most common interventions in the studies were leg muscle strength training including weights as well as functional muscle strength training and balance training. A few studies combined physical training with either improved dietary intake or drug treatment, e.g. Megestrol acetate (aiming at appetite stimulation) and testosterone (aiming at anabolic stimulation) [60, 61, 66, 69]. Dietary intake with nutritional supplement did not affect physical performance [60] and appetite stimulation seemed to have a negative effect on leg muscle strength [69]. Testosterone injections positively affected leg muscle strength regardless of training intensity [66].

A recent published article describes the design of a randomised controlled trial for frail elderly people in primary care. The physical training programme consisted of stretching, muscle strength and balance training. The medical intervention was targeted toward individual needs and consisted mainly of improved control of medications, hypertension, diabetes, depression, and dietary prescriptions [73]. The results of the study have not yet been published.

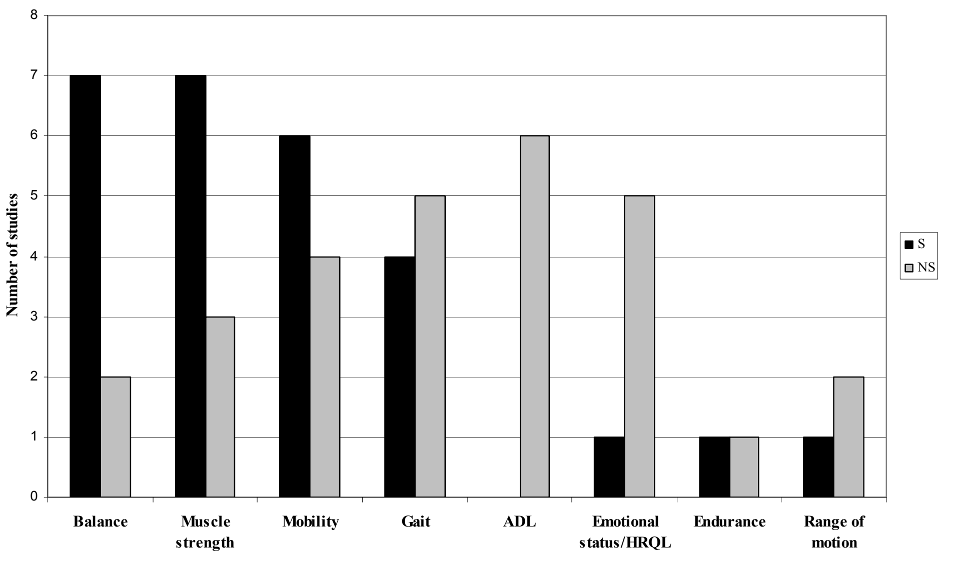

Figure 2. Number of studies with a significant (S) and a non-significant (NS) result on different physical performance measures and Health-Related Quality of Life (HRQL).

Table 1. Description of studies investigating the effects of physical training on physical performance and HRQL in frail elderly people.

Author	Included/ analysed	Age Sex	Frailty criteria	Method Quality	Length/ Frequency	Assessments	Intervention	Result (in comparison with control/comparable group)
Chandler et al 1998	100/87	m=78 50 men 50 w	Unable descend stairs without holding rail	53 p Moderate	10 wk, 3 t/wk	Leg muscle strength (LMS) Balance (FR, sway) Falls efficacy scale Endurance (6MW) Mobility (Mobility Skills Protocol, Chair rise) Gait (speed) HRQL (SF-36/PF)	1) Progressive leg muscle strength training 2) Control	LMS ↑ Significant associations between gains in strength and gains in mobility
Brown et al 2000	84/84 Dropout not described	m=83 37 men 50 w	PPT scores 17-32	49 p Moderate	36 session, 3 t/wk	Leg muscle strength (LMS), Range of motion Mobility (PPT) Balance (dynamic, static, Berg's Balance scale) Gait (analyses) Reaction time Sensation (feet with monofilament)	1) Exercise (mobility, balance, flexibility, speed of reaction) 2) Home-based flexibility exerxcies	Mobility ↑, LMS ↑, Balance (static) ↑
Chin A Paw et al 2001, 2002	217/157 217/139	m=79 70% w	Home care Physical inactivity Involuntary weight loss or BMI ≤ 25kg/m^2	63 p High	17 wk, 2 t/wk	Functional performance (tandem stance, gait speed, chair stand, range of motion) Physical fitness (GFT - isometric grip and knee extension strength, balance, reaction time, shoulder flexibility) ADL (mobility and self-care) Physical activity (PASE) Subjective well-being, Self-rated health Social involvement	1) Exercise (moderate intensity - muscle strength, flexibility, speed, coordination) and placebo nutritional supplement 2) Nutritional supplement and social program 3) Exercise and nutritional supplement 4) Control (social program and placebo nutritional supplement)	Functional performance (sum score) ↑ (group 1, 3) Balance ↑ (group 1, 3) Chair stand ↑ (group 1, 3) Gait speed ↑ (group 1, 3) Range of motion ↑ (group 1, 3)
Shimada et al 2002	34/32	m=81 5 men 29 w	Attending geriatric day hospital	60 p Moderate	12 wk, 2-3 t/wk	Balance (OLS, FR, MPT, FBS) Mobility (POMA, TUG, Stair climbing/descending)	1) Balance exercises 2) Gait exercises 3) Control	FBS ↑ for group 1 POMA ↑ for group 2
Binder et al 2002, 2005	119/115	m=83 55 men 60 w	1) Mobility/balance impairment 2) help in 2 IADL 3) Max VO_2 10-18 ml/kg/min Meet 2 of 3 criteria	57 p Moderate	9 months, 3 t/wk	Mobility (Mod PPT, FSQ) Leg muscle strength (LMS) Range of motion (lower extremity) Balance (FR, OLS, Berg's balance scale) Endurance (Max VO_2) Fat-Free Mass (FFM) ADL (OARS) HRQL (SF-36) Depression (GDS)	1) Exercise (flexibility, balance, muscle strength, endurance) 2) Home-based flexibility exerxcies	Mod PPT ↑, FSQ ↑, LMS ↑, OLS ↑, Berg's Balance scale ↑, Max VO_2 ↑, FFM ↑
Timonen et al 2002, 2006	68/57	m=83 68 w	Mobility/balance difficulties, discharge from geriatric clinic	59 p Moderate	10 wk, 2 t/wk	Leg muscle strength (LMS) Balance (Berg's Balance scale) Gait (maximal speed) ADL/IADL (Joensuu classification)	1) Progressive leg/arm muscle strength training, functional strength training 2) Home-based fumctional strength training	LMS ↑ Gait ↑ Balance ↑

Table 1 continued..

Author	Included/ analysed	Age Sex	Frailty criteria	Method Quality	Length/ Frequency	Assessments	Intervention	Result (in comparison with control/comparable group)
Hauer et al 2003	57/44	m=82 57 w	Age >75, recent history of injurious falls	55 p Moderate	12 wk, 3t/wk, 2-year follow-up	Leg muscle strength (LMS) Balance (POMA, Modified balance scores) Mobility (Chair rise, TUG) Gait (speed) ADL/IADL (Barthel, Lawton) Physical activity level Emotional status (GDS, PGCMS, Fear of falling)	1) Progressive leg muscle strength training, walking, balancing 2) Placebo (stretching, ball games seated)	LMS ↑, Chair rise ↑, TUG ↑ Gait speed ↑ (remained at 2 years), Balance ↑, Physical activity level ↑
Latham et al 2003	486/444	m=79 186 men 258 w	≥ 1 health problem, functional limitations after hospitalisation	96 p High	10 wk, 3 t/wk Single oral dose 6 x 1.25 mg calciferol	Leg muscle strength (LMS) Balance (Berg's Balance Scale) Mobility (TUG) Gait (habitual speed) ADL (Barthel) HRQL (SF-36/PF) Falls (Diary, Fear of falling)	1) Progressive moderate intensity quadriceps strength at home 2) Vitamin-D supplementation 3) Exercise control (placebo home visits) 4) Placebo tablets	No significant effect, except for an increased risk for musculoskeletal injuries of RR 3.6 in the exercise group.
Helbostad et al 2004 x2	77/66	m=81 15 men 62 w	1) least one fall last year 2) walking aid (in or outdoor)	68 p High	12 wk, 2 t/wk	Gait (speed, max step length) Mobility (Chair stand, TUG) Balance (Figure of Eight, postural sway) Leg muscle strength (LMS) ADL (Barthel) Walking habits (duration, frequency) HRQL (SF-36) Falls	1) Home-based training (functional strength training, balance training) 2) Combined training (progressive functional strength training with weights, balance training) + home-based training	Gait speed/step length ↑, TUG ↑, Figure of Eight ↑ (group 1, 2) HRQL ↑ (group 2 compared to group 1)
Sullivan et al 2005	71/61	m=78 71 men	Functional decline as a consequence of illness	76 p High	12 wk, 3t/wk Injections 1/wk	Muscle strength (leg press, chest press) Mobility (chair-stand, stair-climb) Gait (habitual and maximal speed) Midthigh fat-free mass Lean body mass (whole body)	1) High-intensity progressive leg/arm muscle strength training, testosterone injections 2) As group 1 but placebo injections 3) Low-resistance leg/arm muscle strength training, testosterone injections 4) As group 3 but placebo injections	↑ Muscle strength ↑ Midthigh area for testosterone injection regrardless of training intensity
Sullivan et al 2007	29/24	m=79 83% men	Functional decline as a consequence of illness	74 p High	12 wk, MA daily	Muscle strength (leg press, chest press) Mobility (chair stand, stair climb) Gait (habitual/maximal speed) Dietary intake (diary 7 days) Body weight, Body fat Lean body mass, Midthigh area (fat-free mass)	1) High-intensity progressive leg/arm muscle strength training, MA 2) As group 1 but placebo 3) Low-resistance leg/arm muscle strength training, MA 4) As group 3 but placebo	LMS ↓ Group 1 LMS ↑ Group 2 Dietary intake ↑ group 1, 3 Body weight/fat ↑ group 3

Abbreviations: m=mean, w=women, p=point, wk=week, t=times, Leg Muscle Strength= LMS, FR=Functional Reach, 6MW=6-minute walk, HRQL=Health-Related Quality of Life, SF-36=Short Form-36, PF=Physical Functioning, PPT=Physical Performance Test, BMI=Body Mass Index, GFT=Groningen Fitness Test for Elderly, ADL= Activities of Daily Living, PASE=Physical Activity Scale for the Elderly, OLS=One-leg stance, MPT= Manual Perturbation Test, FBS=Functional Balance Scale, POMA=Performance-Oriented Mobility Assessment, TUG=Timed Up and Go, FFM=Fat-Free Mass, Mod=Modified, FSQ=Functional Status Questionnaire, OARS=The Older American Resources and Services instrument, IADL=instrumental ADL, GDS= Geriatric Depression Scale, PGCMS=Philadelphia Geriatric Center Morale Scale, MA=Megestrol Acetate ↑=significant positive result, ↓=significant negative result, RR=relative risk

Other types of physical training

Weight-bearing exercises with weight vest/belt have been conducted in a few randomised controlled studies for community-dwelling elderly people [74-80]. Main outcomes have been bone mineral density (BMD) and muscle strength. The results of the studies showed an increase in BMD in two out of five studies [77, 80]. Three of four studies reported improvements in leg muscle strength [74, 78, 79]. The intervention in the study showing a non-significant result did not include exercise training; the subjects were only instructed to wear the weight vest two hours daily, four days per week [76]. Three studies examined the effect on balance and all of them showed improvements [77-79]. One study examined the effect on HRQL and showed a decrease of bodily pain, improved physical functioning and increased internal health locus of control [75]. Another study showed no effect on self-efficacy [77]. None of the above-mentioned studies investigated the effect on frail community-dwelling elderly people.

One randomised controlled study with weight-belt training was conducted in residential care focusing on lower extremity muscle strength, walking and balance, according to the resident's mobility deficits [81, 82]. The result showed improvements in walking speed at 1st follow-up and walking speed, balance and lower extremity muscle strength at 2nd follow-up [82].

Functional training such as chair rise, walking in different directions, and flexibility was compared to muscle strength training with moderate intensity using elastic bands in elderly people with more than one impairment [83]. Both groups improved but the functional training group improved significantly more in gait speed. During chair rise the functional strength training group significantly improved knee torque indicating that they performed a more controlled and efficient movement strategy during chair rise compared to the muscle strength training group.

Both prospective and retrospective studies have shown that falls are related to frailty [84-86]. According to a Cochrane review approximately 30% of people over 65 years of age fall each year and 10% of those falls result in a fracture. The review describes a number of interventions that are likely to be beneficial in preventing falls, for instance individually prescribed training of muscle strength and balance as well as Tai Chi group exercise [87]. Two randomised controlled studies have been conducted within the FICSIT Group (Frailty and Injuries: Cooperative Studies of Intervention Techniques) examining the effect of Tai Chi, however subjects in the Tai Chi studies were not regarded as frail [88, 89]. One of the studies showed that Tai Chi can help to maintain significant gains after an exercise intervention consisting of muscle strength training and balance training [89]. The other study compared computerised balance training (centre of mass feedback) with Tai Chi and found that Tai Chi significantly reduced the risk for falls, as well as fear of falling, compared to computerised balance training [88]. A follow-up study of the latter study [88] was conducted to evaluate whether the programme had affected the subjects' activities in daily life and their physical activity level. Only the Tai Chi group reported that they had experienced a noticeable effect on life and that their daily activities had been affected, and many of these subjects had incorporated Tai Chi in their normal physical activities [90]. Two randomised controlled studies examined the effect of Tai Chi on balance for community-dwelling elderly, and both showed significant improvements [91, 92]. One of the studies also showed that improved balance led to a significant reduction in

number of falls [91]. Another study examined the effect of Tai Chi on transitionally frail adults living in sheltered living, but could not detect a 50 % reduction of falls in favour of the intervention group [93].
The effects of Qigong for elderly people have been reported in a few controlled randomised studies [94-98]. Significant improvements were shown in outcomes such as subjectively improved physical health in chronically ill persons [97]; decreased pain and associated mood disturbances in chronic pain patients [98]; decrease in motor symptoms and daytime sleepiness in Parkinson patients [95] and similar decrease in hypertension of both Qigong exercises and conventional exercises such as stretching and walking [94]. Only one study analysed the effects on physical performance and showed an improvement on balance and mobility as well as an increase in self-estimated physical activity level for cardiac patients i.e. with previous heart infarction or bypass surgery etc. [96]. No studies investigated the effect of Qigong on frail elderly people.
In general, there are three main features of Qigong: postures and movement, state of mind and breathing [97]. It can also be divided in passive and active Qigong [99]. Both active Qigong and Tai Chi involves slow movements, weight shifting and breathing [99, 100] but Qigong has been suggested to be less physically and cognitively demanding compared to Tai Chi [97].

In this thesis, **physical training consists of** muscle strength training, aerobic training and balance training in the form of Qigong.

Intensity/dose/frequency
No studies were found that investigated optimal intensity, dose and frequency for frail community-dwelling elderly people. One study conducted in a long-term setting concludes that once a week is not enough, but twice a week may not be feasible due to limited capacities, ill-health etc. at least not in a long-term perspective [101].
The American College of Sports and Medicine (ACSM) recommends high intensity, 60-100% of one repetition maximum (1RM) regarding *muscle strength training* and conclude that it is clear that if the intensity is low the increases are modest for young as well as elderly individuals [102]. A meta-analysis showed that to achieve maximal effect sizes, untrained subjects are recommended to train 3 days/week at an intensity of 60% of 1RM with four sets per muscle group; however subjects over the age of 55 were only included in a few studies [103]. Galvão & Taafee [104] showed that three sets gave significantly better effect than one set concerning both dynamic muscle strength as well as muscle endurance in healthy elderly people. However, another review suggests that since one set gives similar muscle strength gains compared to multiple, one set should be recommended for non-athletes since they are less time-consuming and might lessen the drop-out rates [105].
Regarding frequency, one study showed no difference between one, two or three times weekly in high-intensive muscle strength training in healthy elderly people [106], which is in contrast to the meta-analyses described above [103].
One study reported that muscle power (speed x force) showed equal effect of different intensity levels (20-80% 1RM), however a dose-response relationship with high training intensity was found regarding dynamic muscle strength and muscle endurance [107]. In conclusion, there seems to be a consensus in the scientific

literature regarding intensity level affecting muscle strength and muscle endurance but contradictory recommendations regarding dose (number of sets) and frequency.

Regarding *endurance*, it has been concluded that >80% intensity and duration >30 minutes gives significantly higher effect sizes in $VO_{2\ max}$ for people aged 46-90 [108]. There were no differences between less than or more than 15 weeks of training duration. In most of the studies, the frequency was $\geq$ 3 times/week.
The ACSM recommends that moderate to high intensity levels are required to affect the cardiovascular system of elderly people; however light to moderate intensities may reduce the age-associated decline [102].

To my knowledge there are no recommendations regarding *balance* training, concerning either frequency or dose. The intensity is usually described as increasing in difficulty such as decreasing the base of support and number of sensory input and moving the centre of mass in different directions close the postural limits through weight shifting [109]. Programmes consisting of individualised static and dynamic balance training in different environments have also been suggested [110]. Dual tasks (for example, adding cognitive tasks) during balance training have been recommended to reduce falls [111]. A recent study has shown that muscle power training (described as rapid concentric movements followed by slow eccentric movements in this study) of low intensity (20% of 1RM) had a significantly larger impact on balance compared to moderate (50% 1RM) or high (80% 1RM) intensity [112].

Regarding frail and very old people the recommendations are to focus on muscle strength and balance training before aerobic training should be an option, especially if a subject is unable to get out of a chair and maintain balance while moving [102].

1.1.7 Testing of physical performance

To determine the necessary intensity level for planning a progressive muscle strength training programme, different types of measurements are important.
Muscle strength is defined as a maximum isometric contraction [113] or as the maximal force that a muscle or muscle group can generate [114]. Dynamic muscle strength can be measured by 1RM, defined as the maximum weight a person can lift only once in a complete range of motion [115].
1RM has been shown to be reliable for experienced weight lifters in the upper and lower extremities [116]. Elderly people appear to need 2–3 test sessions to achieve a reliable test [117-119]. Movements tested in these studies were mainly leg press, bench press [117, 119] and in one study knee extension [118].

A recent review of maximal *aerobic testing* for elderly people found only four studies using bicycle ergometry for testing maximal aerobic capacity in people over the age of 65 [120]. Only one of these studies included subjects with some dependency in activities of daily living [121]. The use of treadmill testing has advantages such as familiarity to the subjects (e.g. walking) and ease of data comparison since a lot more research has been conducted on treadmill. On the other hand, older people may have difficulties with the minimum speed on a treadmill as well as balance problems; therefore a bicycle ergometry test may be an option for safety reasons. The authors of the review conclude that there is a need for refinement of testing protocols and a consensus on the criteria for $VO_{2\ max}$ for elderly people [120].

The information of *balance testing* can be divided into task and performance parameters. The information from task parameters is obtained from clinical measures – clinical testing measuring what a person does, not how the task is performed [122]. According to Huxham et al [123], available clinical measures have limitations. There are yet no instruments available that include tasks in an open environment (such as picking up an object from a purse while crossing a busy street), thereby evaluating the highest level of balance.

Adverse events/contraindications/side effects
Studies have reported injuries during 1RM testing in a range of 2.4–19% in elderly people [124, 125]. One study reported muscle soreness in 70% of the subjects, however, without affecting daily living [125]. One study showed that no abnormal heart rate/rhythm responses occurred in a diverse cardiac rehabilitation population (m=62 years) [126]. Another study showed that it was safe to conduct 1RM in patients (m=63 years) with chronic obstructive pulmonary disease regarding heart rate, blood pressure and oxygen saturation [127].

There is no difference in contraindications for maximal aerobic testing or training for younger or older people. The major absolute contraindications are recent ECG changes, myocardial infarction, unstable angina, uncontrolled arrhythmias, third degree heart block and acute congestive heart failure [102].

The risk of falls must be considered when testing and training balance. Fear of falling can be one reason for avoiding limits of postural control, which is essential for evaluating balance or achieving a positive effect of balance training. It is therefore important to create safe environments to reduce fear and the risk for falls [109]. Hip protectors could be another way of reducing fear for the individual as well as the instructor(s), both during testing and exercises [128].

1.1.8 Physical activity
Epidemiological data demonstrate a strong relation between low levels of physical activity and functional decline [129-131]. Some studies have shown that the total physical activity level, measured with accelerometer, did not increase during an aerobic and/or strength training intervention for healthy elderly, especially not during training days [132, 133]. This suggests a compensatory decline. However, a long-term effect was not investigated.
On the other hand Fujita et al [134], showed an increased physical activity level, measured with physical activity diary, both directly after a six-month intervention and after another six months for healthy elderly people. A study on geriatric patients after discharge showed an increase in habitual physical activity level directly after a physical training intervention but this increase did not remain at 2-year follow-up [62].

Several studies have shown differences between men and women regarding levels of physical activity for elderly people [21, 135, 136]. One study showed that men exhibited more variation in types of physical activity and they also reported longer activity duration compared to women, but there were no differences regarding frequency of physical activity or walking habits. Women were more active in household activities [135]. This in line with a Swedish study showing that when including household activities in the physical activity scale, women were equally physically active as men [21]. Another Swedish study has shown that participation in leisure physical activities increased from 1992 to 2002 when comparing two different cohorts with a mixed group of elderly people. Participation in leisure activities was more common among those living with someone, however, significant only for women. Educational level and no reported mobility deficits were also significantly related to high physical activity level [136].

In this thesis, **physical activity** is **defined** as "any bodily movement produced by the contraction of a skeletal muscle" [137].

1.1.9 Compliance/Motivation

Compliance

Knowledge of individual compliance to the treatment programme is vital in order to be able to draw conclusions from a clinical study [138, 139]. In the Swedish dictionary "Terminology of Medicine", compliance is defined as "*a patient's ability to follow a prescription*" (author's translation) [140].

Compliance is in this thesis, **defined** as the number of sessions attended or the number of times the subjects conducted home-based exercises by themselves. The prescription will consist of both participation in the physical training sessions and conduction of home-based exercises.

A number of risk factors for non-compliance in elderly people have been identified in the literature, such as illness and feelings of vulnerability [141, 142]. Positive factors for compliance can be high level of mobility, positive attitudes and strong self-efficacy [143-145]. Factors associated with maintaining a higher level of physical activity after an intervention can be self-reported improvement or incorporation of the activities in daily living [90, 146, 147]. Telephone calls for support and encouragement from health staff also improved compliance [148-151].

Health Belief Model

The Health Belief Model (HBM) was created as a conceptual theoretical framework for understanding the influences of people's engagement in health-related activities. Original factors included in the model were perceptions of susceptibility, severity, benefits and barriers [152]. A review examining studies that have used the model found that perceived barriers was the most powerful dimension of the HBM across various study designs [153]. Perceived benefit was also a strong contributor overall, but especially for explaining sick-role behaviour.

Self-efficacy

The self-efficacy theory is based on the principal assumption that psychological procedures create and strengthen expectations of personal efficacy [154]. Expectations of personal mastery affect both initiation and the persistence of certain

behaviours. Four main principal sources have been suggested as affecting self-efficacy:
- Performance accomplishment relates to earlier success or failure in accomplishing a certain task and has been suggested to be the strongest source of self-efficacy. Success with minimal effort reinforces the sense of self-efficacy. To strengthen a person's sense of self-efficacy it is important to gradually limit external aids, otherwise it is likely that the person will credit external factors rather than their own capabilities.
- Vicarious experience relates to how people in the surrounding accomplish certain tasks.
- Verbal persuasion relates to suggestions from the surroundings or self-instructions. This is also affected by the trustworthiness and credibility of the suggested person(s).
- Emotional arousal relates to how threatening a situation or task is experienced.

It has also been suggested that efficacy expectations should be differentiated from outcome expectations, because an individual can expect certain outcomes of an action, but if they have serious doubts whether they can perform the action it will negatively affect the behaviour [154].

A meta-analysis has shown that organised physical activity had the highest impact on self-efficacy compared to other subjective well-being variables such as overall well-being, life satisfaction and physical symptoms for healthy elderly people [155]. There are also differences between men and women regarding psychological factors influencing physical activity. One study has shown that women had less self-efficacy and more barriers towards performing physical activity compared to men [135]. Self-efficacy has been shown to be a strong predictor for behavioural changes regarding cardiovascular diseases and diabetes for older adults [156]. Rosenstock et al [157] suggested that self-efficacy should be added to the HBM, since self-efficacy has been shown to be such a strong predictor for behavioural change. The authors suggest that this would provide a more powerful and thorough understanding of health-related behaviour [157].

Social support

Social support can include backing from family and friends as well as professional support [158]. Social support from spouses, relatives, friends and exercise staff has been shown to be related to high physical activity level [159-162]. However, it can also be experienced as obligating and intrusive [163]. Social support has been suggested to have an indirect effect on exercise behaviour through a higher sense of pleasure during training and through self-efficacy. The study also suggested that social support within the exercise group is of importance [164]. Another study supports this indirect effect of social support on self-efficacy and also on internal and external motivation [165].

A Swedish study showed that elderly people with high estimated HRQL also reported satisfactory social support, good self-rated health and high physical activity level compared to those with low estimated HRQL [166].

It has also been suggested that social support should be added to the HBM [167].

1.1.10 Health Related Quality of Life

The WHO has defined health as a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [168]. According to Ware [169] the concept "quality of life" (QOL) has been adopted to distinguish the old health definition "absence from disease" from the new definition described by the WHO including mental and social well-being dimensions. However, QOL encompasses many things not related to health [169]. HRQL may be seen as the parts of QOL related to an individual's health [170]. Ware [169] suggests five distinct dimensions to be included when measuring HRQL: physical health, mental health, everyday functioning in social and in role activities, and general perceptions of well-being.

Hays et al. [171] operationalised important concepts based on the Medical Outcome Study (MOS), and define HRQL as "the extent to which health impacts an individual's ability to function and his/her perceived well-being in physical, mental and social domains of life". The HRQL rating scale SF-36 was developed from the MOS-study [172] and contains eight subscales: Physical Functioning, Bodily Pain, Role Physical Functioning, Role Emotional Functioning, General Health, Vitality, Mental Health and Social Functioning. There have been attempts to conceptualise the SF-36 into the ICF model. It is suggested that Bodily Pain should be mapped to *Body function & structure*, Physical Functioning, General Health, Mental Health and Vitality to *Activities*, and Role Physical, Role Emotional and Social Functioning to *Participation* [171, 173].

A high physical activity level has been shown to be related to HRQL in healthy elderly people [131, 174]. Rejeski et al. [175] showed that physical activity influences several domains of HRQL, but not all of them. The amount of physical activity associated with HRQL, however, is still unclear [176]. A meta-analysis has shown that aerobic training in comparison to muscle strength training was most beneficial in regard to psychological well-being for healthy elderly people [155]. There is however a lack of evidence for the effect of a physical training intervention on HRQL for elderly people [72, 131].

1.2 RATIONALE FOR THE THESIS

There are several reasons to study physical performance and the effect of physical intervention in frail elderly people:

- There is lack of evidence of the effects of physical training in elderly people with many concurrent diseases and in frail elderly people. It is more difficult to conduct research on this group due to large heterogeneity and the necessity to control for the many variables that can affect the outcomes of different interventions.
- There seems to be limited combined effect of nutrition and physical training for frail elderly people. So far, no studies have combined aerobic training and Qigong with high-intensity muscle strength training. Additionally, individualised nutritional treatment has not been part of the interventions.
- There is very limited evidence regarding the amount, especially dose and frequency, and types of physical training necessary to achieve clinically relevant improvements in frail elderly people. The importance of high intensity during muscle strength training has, however, been stated and it is therefore important to establish reliable clinical tests for measurements of muscle strength.

- There are many different instruments available in the literature for measuring physical performance in elderly people, but it is difficult to find instruments that can detect clinically relevant changes concerning different baseline levels. Clinically relevant changes or cut-off limits are seldom reported. There is also the problem of floor and ceiling effects that needs to be taken into consideration.
- Several factors affecting compliance for physical training/activity are identified in the literature, but this has not been specifically investigated in frail elderly people. There is a need for a deeper understanding of the underlying causes of various compliance and how this can be addressed in a clinical setting, in order to target interventions towards the needs of individual patients to prevent further functional decline.

1.3 AIMS

The general aim of this thesis is to describe the effects of physical training on physical performance in frail elderly people.

The specific aims were to investigate

- the impact of a physical and nutritional intervention programme for frail community-dwelling elderly people. A secondary aim was to describe the difference between subjects who improved and subjects who did not improve and between compliers and non-compliers (paper I).

- whether a physical training programme can affect aerobic capacity in frail elderly people including the influence of compliance, leg muscle strength, lung capacity, and cardiovascular diseases and drugs (paper II).

- the effects of a physical training and a nutritional intervention programme on physical activity level, ADL and HRQL from a long-term perspective in frail elderly people. A second aim was to describe the relationships between:
  - increases versus non-increases in physical activity level with ADL and HRQL respectively,
  - doses and intensity of home-based exercises with ADL and HRQL respectively (paper III).

- the reliability of test-retest of 1RM of the arm/shoulder in elderly people, aged 75 and older, and to compare subjects with or without previous muscle strength training experience (paper IV).

2 MATERIALS AND METHODS

2.1 SUBJECTS

2.1.1 Paper 1-3

Subjects over the age of 75 were recruited through a questionnaire regarding nutrition and physical activity, advertisement in the local newspaper, primary care and the local authorities. Subjects were screened by telephone interview and were included if they fitted the chosen definition of frailty (see above section 1.1.2), lived independently and could walk with or without assistive devices. A total sample of 96 subjects was included (Figure 3).

2.1.2 Paper 4

An invitation letter was sent to a random sample of elderly people, who had previously answered a questionnaire (see above). Subjects were included if they had no previous experience of muscle strength training and if they had not experienced recent cardiac problems (group 1). A second group was recruited from a physical training project for frail elderly people (see 2.1.1) (group 2). This was done in order to allow comparison between subjects with and without previous muscle strength training experience. A total sample of 40 subjects were included, 27 in group 1 and 13 in group 2.

2.2 PROCEDURES

2.2.1 Paper 1-3

The subjects were randomised consecutively in batches into four different groups. The randomisation procedure was conducted in an open manner by the study personnel with the instructions of a statistician. For each new group included, randomisation started with the oldest individual to avoid age differences between groups.

Randomisation was done to the following treatment groups:

1. Training (T) (n=23): Specific physical training plus general diet advice
2. Nutrition (N) (n=25): Specific individualised diet counselling and group session education plus general physical training advice
3. Training and nutrition (T + N) (n=25): Specific physical training plus specific individualised diet counselling and group session education
4. Control (C) (n=23): General physical training advice and general diet advice

The subjects were assessed at baseline (0 months), 1st follow-up (3 months) and 2nd follow-up (9 months, i.e. 6 months after the end of the intervention) and for some outcome measures at 3rd follow-up (24 months).

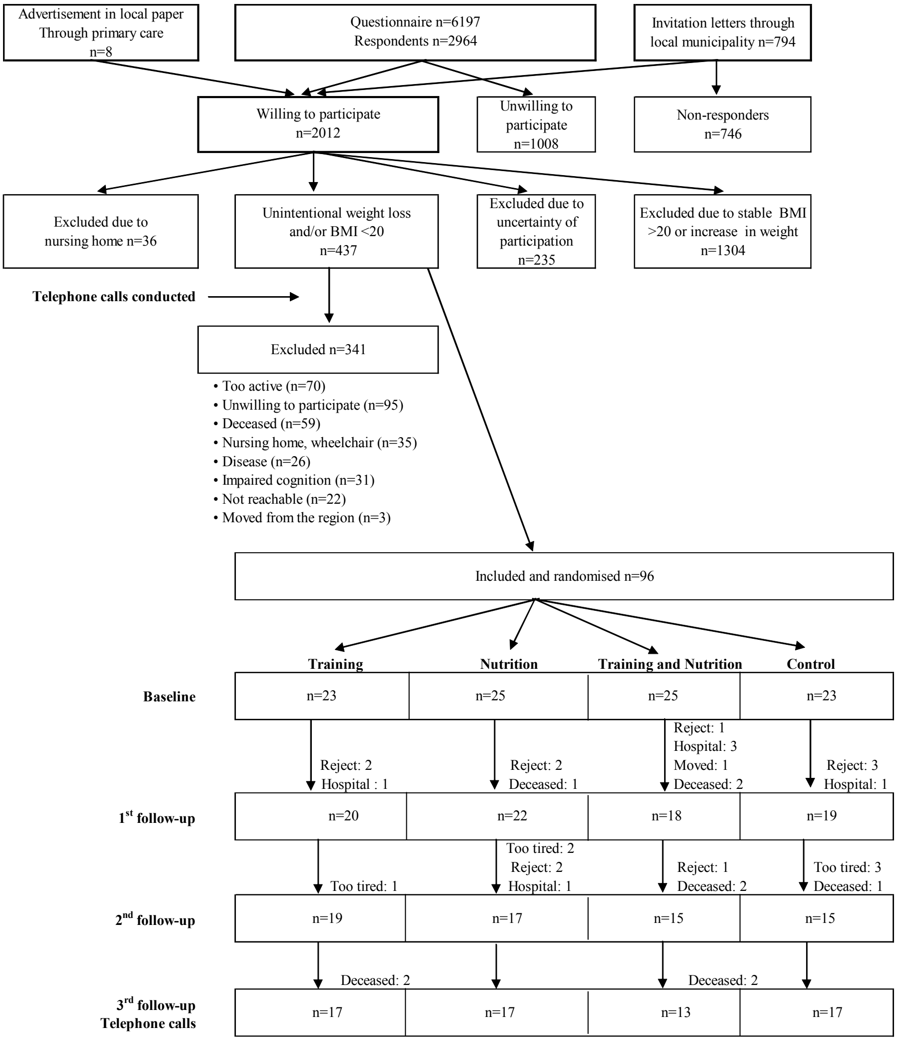

Figure 3. The flow of recruitment, inclusion/exclusion and drop-out of subjects from baseline to 3rd follow-up.

2.2.2 Paper 4

One repetition maximum was measured using a muscle strength training device for the arm/shoulder (Pull Down, Norway). The 1RM measurement was in accordance with the recommendation of the American College of Sports Medicine [177].
The test leader conducted the measurements on each subject in two different test sessions, approximately one week apart. To avoid fluctuations in daily condition, the measurements were performed at about the same time of day.

2.3 MEASURES

2.3.1 Baseline characteristics

The subjects were examined by a geriatrician for medical history, medication and physical status (paper 1-4). Body weight and height were measured by standard procedures and BMI was calculated by dividing the body weight (kg) by height^2 (m) (paper 1-4). Blood haemoglobin was analysed according to standard procedure at the Dept. of Clinical Chemistry at the Karolinska University Hospital (paper 2). Education (paper 1) and type of walking aids (paper 1, 3) were recorded. Smokers and tobacco consumption, total number of years with smoking as well earlier smokers and years after smoking cessation were recorded (paper 2).

A combined electrocardiography (ECG) and spirometry (AT-2PLUS, Schiller AG, Switzerland) was used for registration of ECG and lung capacity. Total slow (SVC) and forced (FVC) vital capacity and forced expiratory volume during the first second (FEV_1) as well as peak expiratory flow (PEF) was measured. The lowest ratio between FEV_1 /SVC or FEV_1 /FVC was calculated and expressed as FEV%. The tests were performed seated and the best of three attempts was recorded. The subjects were categorised as having normal, obstructive or restrictive lung function. The results of these tests were used as baseline characteristics and analysed as possible influences on maximal work load/time in paper 2.

2.3.2 Body structure/function

Muscle strength

Muscle strength was measured in the lower extremities with 1RM in combined knee and hip extension (Leg Press Scandinavian Mobility, Norway), and in the upper extremity with elbow extension (Dips, Scandinavian Mobility, Norway) and shoulder extension (Pull down, Scandinavian Mobility, Norway) [117].

The tests were used as outcome measures in paper 1 and Leg Press also in paper 2. Grip strength was measured with a Jamar dynamometer. Both hands were tested and the best result out of three trials was recorded [178-180]. The subjects were sitting with the shoulder in a neutral position and the elbow in 90° flexion. The result of this test was used as basis for baseline description.

Aerobic capacity

A bicycle ergometry test was conducted according to Wetterqvist et al [181]. The resting ECG was recorded and evaluated by a geriatrician before the subjects were allowed to start the test. All subjects started at 25 Watt (W) and the load was increased with 25 W every four minutes if possible. Every three minute the subjects were checked for heart rate, systolic blood pressure and estimated effort, breathlessness and pain according to the CR-10 scale [182].

The test was interrupted when the subject i) could no longer perform at a speed sufficient to maintain load, ii) refused to continue due to fatigue, breathlessness and/or pain, iii) reported chest pain, iv) or for safety reasons determined by the geriatrician. The ECG recording continued throughout the test.

If the subjects interrupted the test before the end of a four-minute stage, the maximal load was calculated as follows: if the subject worked for $\leq$2 minutes on the maximal load, the difference between the last loads was divided by half and added to the lower load. This resulted in maximal loads such as 37.5, 62.5, 87.5 and 112.5 W [181]. These measurements were used as outcome measures in paper 2.

Body composition
Body weight was measured by standard procedures. Four skin folds were measured using a Harpenden calliper (British Indicators Ltd, Bedfordshire, UK) [183] over biceps brachii, triceps brachii, subscapular region and crista iliaca using the mean of three measurements to the nearest 0.1 mm from each location. Fat mass was calculated from the sum of these four skin folds using prediction equations [184, 185]. Fat-free mass (FFM) was calculated as body weight minus fat mass. Body weight and fat-free mass was used as outcome measures in paper 1.

Bone mineral density, fat mass and lean body mass were also measured with Dual X-ray Absorptiometry (DXA) measurement at baseline. The results of the tests were used as a basis for baseline description and predictions.

Energy intake
Energy intake was analysed using a four-day food record, where the participants reported all foods eaten. The food intake data were computerised, and the energy content was calculated using StorMATS (version 4.06, 2002, Rudans lättdata, Västerås, Sweden) and the Swedish national nutrient database, PC-kost (version 02_1, National Food Administration, 2002). Measurement of energy intake was expressed as kcal per kg body weight and was used as an outcome measure in paper 1.

Adverse events
Subjective (chest pain, dizziness) and objective (pathological ECG recording) adverse events were recorded (paper 2) and muscle soreness affecting ADL were recorded (paper 4). A portable defibrillator, oxygen equipment and the Karolinska University Hospital Pharmacy standard drug emergency kit containing adrenalin, atropine, hydrocortisone etc were available in case of adverse events.

2.3.3 Activity/Participation
Balance
Balance was measured in four different ways:

- tandem stance (TS) where the subjects were allowed 1-2 trials before the time-keeping started [186]. The time-keeping ended if the subject's foot/feet changed position or after 30 seconds. The subjects were instructed to wear comfortable shoes and the arm position was self-selected. The test was performed with eyes open.
- one-leg stance (OLS) where the subjects were allowed 1-2 trials before the time-keeping started [186, 187]. The time-keeping ended if the subject's foot changed position or after 30 seconds. The subjects were instructed to wear comfortable shoes and the arm position was self-selected. The preferred leg was used and recorded at baseline. The same leg was then tested at follow-ups. The test was performed with eyes open.
- the Modified Figure of Eight (MFE), where the subjects walk in a figure of eight, on two 4 cm wide circles with an inner diameter of 163 cm, placing

their feet on the line if possible [188], at a self-selected speed [189]. The number of complete steps outside the line was recorded.
- step test, where the subjects were instructed to place the whole foot onto a 15 cm high block and down again, alternating left and right foot during 30 seconds. This was conducted only without support and the number of steps was recorded [190].

The balance measurements were used as outcome measures in paper 1.

Functional muscle strength testing

A 30-second chair-stand test was conducted and the number of stands was recorded [191]. The subjects were instructed to rise from a chair (height 44 cm) with the arms folded across their chest, as many times as possible in 30 sec.
The number of step-ups in 30 seconds with or without support was recorded. The subjects were instructed to step up with both feet to a standing position on a 15 cm block and then down again, alternating left and right starting foot. The type of support was self selected by the subjects and was recorded.
These tests were used as outcome measures in paper 1.

Mobility

Timed Up and Go (TUG) and TUG manual were measured [187, 192, 193]. The subjects were instructed to rise from a chair (height 44 cm), walk three meters, turn around at a mark on the floor and walk back to be seated again. This activity was timed. The residents were allowed to use their usual walking aids. This procedure was conducted twice with (TUG manual) and without (TUG) carrying a tumbler of water.
Walking speed was measured indoors with timed 10-meter walk tests at habitual and maximal walking speed (adding one meter for acceleration and deceleration respectively) [194]. The subjects were allowed to use their usual walking aids.
The tests were used as outcome measures in paper 1 and as a basis for baseline prediction.

Physical activity level

Physical activity level was estimated according to a six-graded activity scale including both physical training/exercises and household/domestic activities [20, 21] and was used as baseline characteristics in paper 1, 2 and 4 and as an outcome measure in paper 3.
The subjects were also asked about walking habits concerning the frequency (days per week or month) and duration (minutes, hours) of their walks outdoors and this was used as outcome measures in study 4 [195].

Activities of daily living

Personal ADL was estimated by the test leader using the Swedish Functional Independence Measure (FIM) form with a maximum score of 91 points [196, 197].
Instrumental ADL was estimated by the test leader using the Instrumental Activity Measure (IAM) with a maximum score of 56 points, developed as a supplement to FIM [198, 199]. Both scales consist of different items using a 7-graded ordinal scale where 6 and 7 indicate independence with or without devices.

The instruments were used as an outcome measure in paper 1 and 3 and as baseline characteristics in paper 4. In paper 3 the scales were dichotomised in dependency/independency.

Health-related quality of life (HRQL)
HRQL was estimated with SF-36 [200-202]. The questionnaire consists of eight subscales: Physical Functioning, Bodily Pain, Role Physical Functioning, Role Emotional Functioning, General Health, Vitality, Mental Health and Social Functioning. Each ordinal subscale has a maximum of 100 points indicating, for example, high Physical Functioning or low Bodily Pain. The instrument was used as an outcome measure in paper 3.

2.3.4 Clinical relevance

As an attempt to define clinical relevance, a limit of 15% improvement was chosen as suggested by the Philadelphia Panel for evidence-based clinical practice [203].

According to the Swedish Road Administration, different red light crossings for pedestrians require different limits of walking speed. To be able to pass a zebra crossing on time, different time dimension are required, low >1.4 m/s, moderate 1.0-1.4 and high <1.0 m/s [204]. According to these limits a clinical relevance has been set to ≥ 1.0 and >1.4 m/s, meaning that a subject has shown clinically relevant improvement if he/she moves from a lower category to a higher at 1st follow-up.
Podsiadlo et al [193] have reported cut-off limits for performance of TUG where subjects scoring <10 sec are freely independent and subjects scoring <20 sec are independent in personal activities of daily living and to walk outdoors alone. According to these limits a clinical relevance has been set to <10 and <20 sec, meaning that a subject has shown clinically relevant improvement if he/she moves from a higher category to a lower at 1st follow-up.
Regarding maximal work load, 25 W equals slow walking speed or driving a car, 50 W – normal walking speed or light household work, 75 W – heavy household work or gardening and 100 W – fast walking speed or carpeting/construction work [205], so moving from a lower to a higher category is suggested to be clinically relevant in this thesis.
Regarding the physical activity scale, each category level is quite large, so moving from a lower to a higher category is suggested to be clinically relevant in this thesis.

2.4 INTERVENTION

2.4.1 Physical training

The subjects randomised to the physical training programme participated in organised regular physical group training of approximately one hour, twice a week for twelve weeks.
The programme consisted of three sections performed in groups of 5-8 subjects:

- aerobic training including warm-up
- individually prescribed muscle strength training (60-80% intensity)
- Qigong including cool-down

The warm-up/aerobic training section consisted of standing exercises, such as walking/jogging on the spot, walking forwards/backwards and sideways, and arm movements. Arm and leg exercises were performed separately to increase the intensity rather than the difficulty in coordination. The 20-minute section also included a short cool-down period halfway for range-of-motion activities and stretching. The subjects were allowed to use their ordinary walking aids if needed.

The 20-minute muscle strength training section consisted of two separate stations: strength training on stationary equipment and functional strength training. During the first two weeks, most of the subjects performed at 60% intensity with repetition 1x8 on the stationary equipment (leg press, dips and pull down, see Muscle strength 2.3.2). In the third week, the intensity was increased to 80% of 1RM. At the sixth and tenth weeks, the 1RM procedure was repeated to ensure 80% intensity. Two subjects started the training programme on the stationary equipment at 50% and increasing to 70% due to diseases such as post polio syndrome and myasthenia gravis.
The functional strength training station consisted of chair stand, step-up and toe raise. According to their baseline values, the subjects performed the exercises with or without a weight belt. If possible, the amount of kilograms added was 10% of the subjects' individual initial body weight. This was increased during the 12 weeks up to 20% of body weight according to the subjects' abilities and scored effort. These exercises were repeated 2x10. The subjects who could not perform one chair stand from a chair (height 44 cm) performed the exercise from a bunk, adjustable to different heights in a vertical position; this was progressed by lowering of the height of the bunk or by switching to a chair.

The balance training section consisted of different Qigong exercises performed on different degrees of supporting area combined with arm and trunk movements. These exercises progressed with increasing difficulty. The subjects were encouraged to stand without support during all these exercises. Those with a poor balance function stood in front of a chair or bunk and had their walker in front of them to create a safe surrounding. The exercises ended with a short cool-down period.

After each section the subjects were asked to score the effort on the CR-10 scale according to Borg [182] and the heart rates were registered. Mean training intensity assessed as predicted heart rate (220 minus age) was 73% (sd=14), 72% (30), and 70% (13) for the aerobic, strength training and Qigong sections respectively.
The subjects estimated effort during the different sections was md=3 (q1-q3=3-5), 4 (3-5), 3 (3-5) for the different sections respectively.

The training programme was planned by a physiotherapist and led by a trained instructor with the help of a trained physiotherapy assistant. The trained instructor was not involved in assessments of outcome measures. The trained physiotherapy assistant helped the instructor with registration of heart rate and scored effort, as well as ensuring correct load and safety during balance training etc.

This period of physical training was followed by six months of home-based exercises without supervision. The subjects were encouraged to perform Qigong and functional muscle strength training (see above) and to take regular walks. They were also instructed to fill in physical training diaries, noting minutes and intensity (Borg CR-10 scale) for each activity, to be sent in every month in pre-stamped envelopes. The procedure was followed up at three months and at six months (2nd follow-up).

2.4.2 Nutritional treatment

The nutritional treatment consisted of individual dietary counselling based on baseline food record data. Using the results of the food record, a dietician/nutritionist tested different options that would cover the estimated needs of each individual, and then gave advice on food intake at an individual session lasting about one hour. Results of the baseline tests were explained and changes in daily eating patterns and food choices were suggested and discussed. The nutritional treatment included five group sessions that covered such topics as nutritional needs for elderly people, meal frequency and cooking methods. At each session an example of a nutritionally well-balanced between-meal snack was served.

The N and T+N groups did not receive systematic specific advice regarding nutrition after completion of the 12-week programme, but those who had been given nutritional supplementation (n=3) during the intervention period did receive nutritional supplement until 2nd follow-up.

2.4.3 General advice

The general physical training advice for the control group was to walk three times per week for at least 20 minutes, to use staircases instead of a lift from time to time and the WHO's recommendation of a total amount of 30 minutes of physical activity/day. The general diet advice was to eat three main courses and 2-3 between-meal snacks including meat, fish or egg, fruit and vegetables, dairy products, and fibre in combination with fluid every day.

2.5 THE HEALTH BELIEF MODEL (PERSONAL FACTORS) - ATTEMPT TO DEVELOP A "MOTIVATION SCALE"

As mentioned above, dimensions suggested to be included in the Health Belief Model are barriers, benefits, self-efficacy and social support [152, 157, 167].
These dimensions were put into four different statements: barriers – "*I experience major difficulties in changing my physical activity level"*; benefits – *"I can see major advantages with changing my physical activity level"*; self-efficacy – *"I have high confidence in my ability to change my physical activity level"* and social support – *" I have very great social support for changing my physical activity level".* An overall statement *"I am very motivated to perform physical activities regularly",* was also used.
Each of these statements were ranked on a scale of 1 to 10 where 1 equals "definitely false" and 10 equals "definitely true", except for the statement *"I experience major difficulties…"* where 1 equals "definitely true" and 10 equals "definitely false".
The estimated scores were used in paper 1 as outcome measures and as possible predictors for improvements in physical performance as well as for compliance.

2.5.1 Reliability

Precision

An item-analysis of the different statements was conducted according the Classical Test Theory to test for normal distribution but the analyses resulted in very low and non-significant kappa values [206].

Test re-test reliability

The statements were estimated twice at baseline approximately one week apart using face-to-face interviews and showed a significant but moderate test re-test reliability of r=0.46 for barriers, r=0.33 for benefits, r=0.66 for self-efficacy, r=0.66 for social support and r=0.64 for the overall statement. The statements were also administered at 1st and 2nd follow-up.

2.5.2 Validity

Construct validity

There were no significant correlations between on the one hand compliance during the supervised physical training programme or number of occasions, duration and intensity of the home-based exercises and on the other hand the estimated scores of the different statements.

Content validity

There were low but significant correlations between the overall statement and self-efficacy and barriers of r=0.43 and r=0.34, respectively. There was a moderate correlation between self-efficacy and barriers of r=0.65.

2.6 STATISTICAL ANALYSES

In all papers, continuous data are presented by mean (m) and standard deviation (sd), ordinal data and continuous data with "ceiling effect" or data where fixed levels were analysed (i.e. maximal load in watt) are presented with median (md) and first and third quartiles (q1-q3) using the statistical software JMP 5.0 and 6.0.0 (SAS Institute, USA).

2.6.1 Paper 1-3

Scatter plots for baseline variables against change in outcome variables were used to investigate whether baseline values had any impact on the magnitude of change. The between-groups analyses were conducted with an intention-to-treat analysis, including all subjects regardless of compliance, with One-way ANOVA analyses. Tukey-Kramer HSD was used as post hoc tests for continuous data with normal distribution and Wilcoxon/Kruskal-Wallis tests for ordinal data and continuous data with skewed distribution. The within-group analyses were conducted with the Matched Paired T-test for continuous data while the Wilcoxon Sign test was used for ordinal data and continuous data with skewed distribution.

Pearson's correlations analyses were used for continuous data and Spearman's Rho for ordinal data. All analyses were conducted in JMP 5.0 and 6.0.0 (SAS Institute, USA).

Subjects were regarded as *improvers* if they had a positive difference between baseline and 1st follow-up, and subjects were regarded as *non-improvers* if there was no change or a negative difference. Compliance was regarded as either a continuous variable or dichotomised, where subjects were regarded as *compliers* if they had attended >65% of the training sessions (according to average compliance during the intervention, see section 3.2.5). The analyses of improvers/non-improvers and compliers/non-compliers were conducted with Student's t-test for continuous data, Wilcoxon Kruskal-Wallis tests for ordinal data and Fischer's Exact Test for nominal data.

In paper 3, ADL scores were dichotomised in independency and dependency, where a 6 or 7 in the FIM and IAM scales were classified as independence and 1-5 as dependence. Changes in ADL (with baseline values included in the model) were analysed with a proportional-odds logit model for ordinal data, separately for each follow up in Stata 8.0 (Stata corporation, Texas, USA) [207].

2.6.2 Paper 4

Pearson correlation analyses were conducted, as well as Bland & Altman´ s 95% limits of agreement [208-210] in JMP 5.0 (SAS Institute, USA) and Excel 2000 (Microsoft, USA). To analyse the variance between groups in 1RM, an F-test was conducted in SAS v. 8.2 (SAS Institute, USA).

2.7 BASELINE DESCRIPTION

2.7.1 Baseline characteristics

Paper 1-3

Data regarding baseline characteristics are shown in Table 2. Women had had more previous myocardial infarctions compared to men but there were significantly more men with congestive heart failure. Men had significantly larger values of all used measures of pulmonary function compared to women. These differences were not affected when correcting for body weight.

Table 2. Baseline characteristics, significant differences between women and men are indicated with grey colour

	Women n=58	**Men** n=38	**Total** n=96
Age, m	83.1 (3.9)	83.3 (4.3)	83.2 (4)
Education, n			
Secondary school or lower	43 (n=57)	26	69 (n=95)
High school or higher	14 (n=57)	12	26 (n=95)
BMI, m	21.9 (3.7)	21.6 (3.2)	21.8 (3.5)
Heart and lung diseases, n			
No heart disease	16	8	24
Congestive heart failure (certain)	6 (4)	12 (11)*	18 (15)
Previous myocardial infarction (certain)	28 (13)**	9 (8)	37 (21)
Arrythmia (intermittent)	11 (5)	8 (2)	19 (7)
Angina pectoris (certain)	14 (0)	6 (3)	20 (3)
No lung disease	41	24	65
Obstructive	10	8	18
Restrictive (probable)	3 (0)	7 (3)	10 (3)
Medication, n			
Continuous (m)	7 (3)	6 (3)	6 (3)
Cardiovascular drugs (m)	2 (1) n=30	2 (1) n=23	2 (1) n=53
Non-selective ß-blockade (n)	3	4	7
Selective ß-blockade (n)	18	15	33
Spirometry			
SVC (m)	1.92 (0.5) n=54	2.69 (0.7)** n=35	2.22 (0.7) n=89
FVC (m)	1.86 (0.5) n=54	2.8 (1)** n=35	2.23 (0.9) n=89
FEV_1 (m)	1.38 (0.5) n=54	2.03 (0.7)** n=35	1.63 (0.6) n=89
FEV% (m)	68.9 (12.8) n=54	70.1 (13.7) n=35	69.4 (13.1) n=89
PEF (m)	3.15 (1.3) n=54	4.82 (2.2)** n=35	3.81 (1.9) n=89
Smoking			
current smokers (n)	10	3	13
1-10 cigarettes per day (n)	5	2	7
11-20 cigaretts per day (n)	5	1	6
total number of years (m)	44 (21)	34 (19)	39 (20)
stopped smoking (n)	15	21	36
number of years after smoking cessation (m)	28 (14)	35 (16)	32 (16)
Walking aids outdoors, n			
no aid	24 (n=57)	13	37 (n=95)
stick	9 (n=57)	10	19 (n=95)
walker	24 (n=57)	15	39 (n=95)
Walking aids indoors, n			
no aid	43 (n=57)	28	71 (n=95)
stick	7 (n=57)	6	13 (n=95)
walker	7 (n=57)	4	11 (n=95)

m=mean (sd), n=number *<0.05, **<0.01

Paper 4

The groups with or without previous muscle strength training experience differed significantly regarding BMI, physical activity level and both PADL and IADL. However, this was expected due to inclusion criteria.

2.7.2 Baseline levels

Table 3 shows the baseline levels of the various outcome measures. The women had lower bone mineral density, lean body mass and body weight, and higher fat mass compared to the men. The women were also significantly weaker in muscle strength and reached lower maximal work load/time in aerobic capacity compared to the men. The women scored significantly less in PADL and the subscales Vitality and Bodily Pain in SF-36 compared to the men. Seventeen of the 96 subjects (18%) were dependent in one or more categories of PADL. The most common categories for dependency in IADL were cleaning (80%), heavy shopping (71%) and washing (68%).

There were low significant correlations between maximal workload (bicycle ergometry) at baseline for the whole group combined and SVC/total year of tobacco consumption of $r=0.39$ ($p<0.01$) and $r= -0.28$ ($p<0.05$) respectively. When analysing women and men separately, there were only significant correlations for men between maximal work load and SVC [$r=0.42$ ($p<0.01$)], FVC [$r=0.50$ ($p<0.01$)] and FEV1 [$r=0.35$ ($p<0.05$)], respectively. There were no significant correlations between maximal workload and lung capacity measurements for women or leg muscle strength for both sexes.
There was a significant difference in maximal workload at baseline between men with lung disease and/or obstructive pulmonary function capacity compared to men without lung disease [md=37.5 W (37.5-50) vs. 62.5 W (50-75); $p<0.05$], but no differences for women or for the whole group. Heart diseases or blood haemoglobin count did not correlate to maximal workload at baseline.

Figure 4 shows the performance (load in kg) in Leg Press minus kg body weight, and Chair Stand. Twenty-one of 91 subjects performed poorer in Leg Press in comparison to their body weight. However, eight of those 21 subjects could still lift their own body weight during chair stand. Seven of the 70 subjects that performed better in Leg Press in comparison to their body weight, could not lift their own body weight during chair stand.

The results of one-leg stance and tandem stance are shown in Figure 5. The correlation between tandem stance and one leg stance was $r=0.72$ ($p<0.0001$).

Habitual and maximal walking speed are shown in Figure 6. Women and men walked on average 41% (sd=20) and 49% (28) faster during maximal walking compared to habitual walking.

Table 3. Results of outcome measures at baseline, significant differences between women/men and drop out/non-drop out respectively, are indicated with grey colour.

	Total (n=96)	**Women** (n=58)	**Men** (n=38)	**Drop out** (n=14)	**Non-drop out** (n=82)
Muscle strength (m)					
Leg Press (kg)	74 (24) (n=91)	66 (19) (n=54) **	85 (26) (n=37)	64 (22)	76 (24) (n=77)
Dips (kg)	17 (7) (n=93)	13 (4) (n=56) ‡	22 (6)	15 (5) (n=13)	17 (7) (n=80)
Pulldown (kg)	23 (8) (n=92)	19 (5) (n=54) ‡	28 (9)	18 (7)* (n=13)	24 (8) (n=79)
Grip strength, strongest hand (kg)	20 (7)	16 (5) ‡	26 (5)	20 (6)	20(7)
Aerobic capacity (md, m)					
Maximal load in watts	50 (37.5-62.5) (n=93)	50 (37.5 -56)* (n=56)	50 (50-62.5) (n=37)	50 (41-62.5)	50 (37.5-62.5) (n=79)
Maximal time in minutes	8 (3) (n=93)	7 (2)* (n=56)	9 (3) (n=37)	8 (3)	8 (3) (n=79)
Body composition					
Body weight (kg)	59 (11)	55 (9) ‡	64 (10)	58 (13)	59 (10)
Fat-free mass, antropometry (kg)	43 (8)	38 (5) ‡	51 (6)	44 (10)	43 (8)
Bone mineral density (DXA) (g/cm^2)	0.98 (0.14) (n=91)	0.93 (0.14) ‡ (n=55)	1.06 (0.11) (n=36)	0.95 (0.11) (n=9)	0.98 (0.14)
Fat mass (DXA) (%)	28 (9)	32 (8) ‡ (n=55)	21 (6) (n=36)	25 (10) (n=9)	28 (9)
Lean body mass (DXA) (%)	67 (9)	64 (9) ‡ (n=55)	72 (7) (n=36)	71 (10) (n=9)	67 (9)
Energy intake (m)					
4-day food record (kcal/kg)	27 (8) (n=93)	27 (8) (n=55)	28 (8)	30 (9) (n=11)	27 (8)
Balance (m, md)					
Tandem stance (sec)	3 (0-17)	3 (0-14)	3 (0-18)	0 (0-1)**	4 (0-19)
One-leg stance (sec)	3 (2-6)	3 (1-5)	3 (2-6)	2 (1-3)	3 (2-6)
Modified Figure of Eight (step)	17 (15) (n=90)	15 (14) (n=54)	19 (17) (n=36)	23 (13)*	16 (16) (n=76)
Step test (number)	12 (8)	12 (8)	13 (8)	9 (5)	13 (8)
Functional muscle strength (m)					
Chair Stand (number)	6 (4)	6 (4)	6 (4)	4 (5)	6 (2)
Step-ups (number)	7 (2)	7 (2)	7 (2)	6 (4)	7 (2)
Mobility (m)					
TUG (sec)	15 (7)	15 (6)	15 (7)	16 (6)	15 (7)
TUGmanual (sec)	16 (6) (n=88)	16 (5) (n=53)	17 (7) (n=35)	20 (7)** (n=13)	16 (6) (n=75)
Habitual walking speed (m/s)	0.9 (0.2)	0.8 (0.2)	0.9 (0.2)	0.7 (0.2)	0.9 (0.2)
Maximal walking speed (m/s)	1.2 (0.4)	1.2 (0.3)	1.3 (0.4)	1.0 (0.3)*	1.3 (0.4)
Physical activity level (md)					
Last summer	2 (2-3) (n=69)	2 (2-3) (n=41)	2 (2-3) (n=28)	2 (1-2) (n=9)	2 (1-3) (n=60)
Last winter	2 (2-3) (n=93)	2 (2-3) (n=57)	2 (2-2) (n=36)	2 (2-2)*	2 (1-3) (n=79)
Walking habits (frequency)	5 (4-6)	5 (3-6)	6 (4-6)	4 (2-6)	5 (4-6)
Walking habits (duration)	2 (2-2)	2 (2-3)	2 (1-2)	2 (1-2)	2 (2-2)
Activities of daily living (md)					
Personal (FIM, points)	88 (83-89)	88 (83-89) *	88 (84-90)	84 (78-84)*	86 (83-89)
Instrumental (IAM, points)	42 (35-48)	43 (37-48)	40 (33-47)	30 (27-42)**	42 (37-49)
Health-Related Quality of Life (SF-36, points, md)					
Physical Functioning	50 (30-65)	40 (31-60)	52 (31-69)	38 (25-54)	50 (35-65)
Role Physical Functioning	25 (0-75)	25 (0-50)	25 (25-75)	25 (0-75)	25 (0-75)
Bodily Pain	56 (41-88)	51 (41-82)*	79 (41-100)	52 (34-88)	61 (41-100)
General Health	51 (34-70)	48 (35-65)	56 (31-72)	39 (75-70)	55 (33-70)
Vitality	45 (29-61)	40 (26-55)*	58 (45-65)	40 (21-61)	50 (30-65)
Social Functioning	69 (50-100)	75 (50-100)	63 (50-100)	44 (38-100)**	75 (50-100)
Role Emotional Functioning	100 (33-100)	100 (33-100)	100 (33-100)	83 (33-100)	100 (33-100)
Mental Health	72 (52-88)	72 (56-84)	70 (49-88)	66 (53-88)	72 (52-88)

m=mean (sd), md=median (q1-q3), * p<0.05, ** p<0.001, ‡ p<0.0001, DXA=Dual X-ray Absorptiometry, TUG=Timed Up and Go, FIM=Functional Independence Measure, IAM=Instrumental Activity Measure

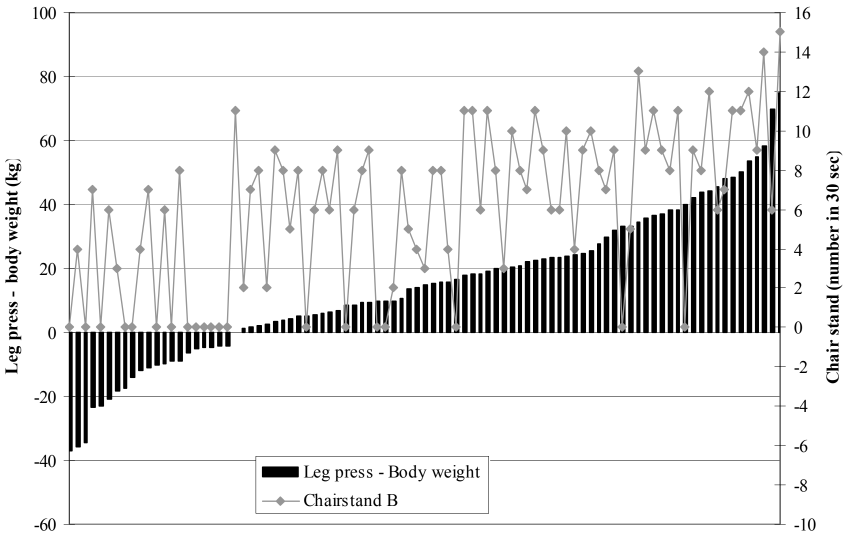

Figure 4. The subjects performances (load in kg) in Leg Press minus (-) body weight and their ability to rise from a chair without arm support, lifting their own body weight at baseline (B).

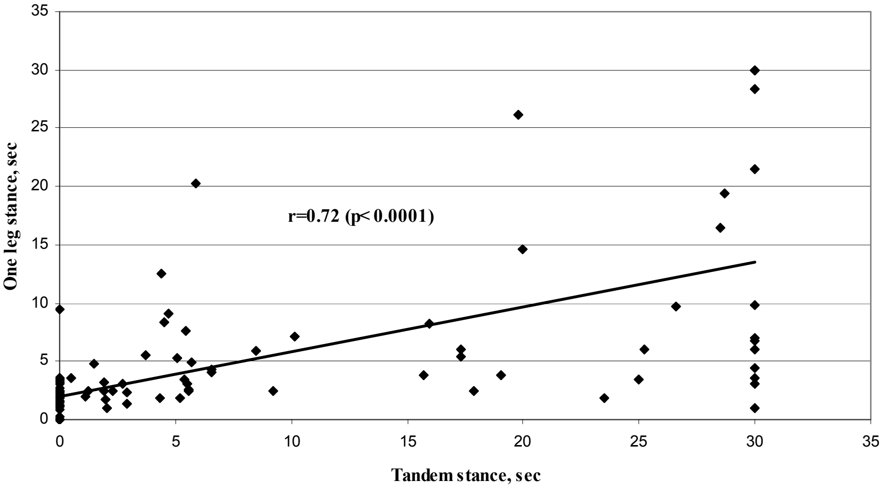

Figure 5. Tandem stance in relation to one-leg stance at baseline.

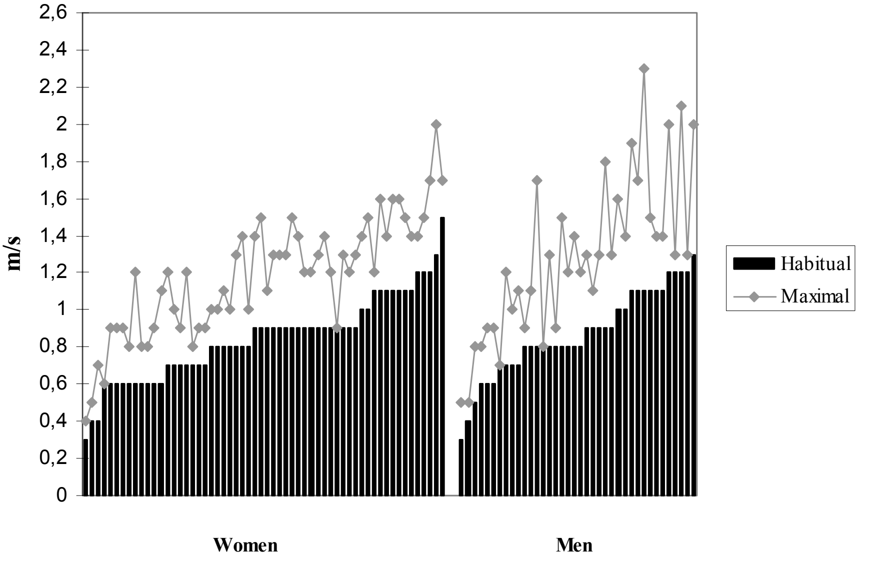

Figure 6. Habitual and maximal walking speed for women and men.

2.7.3 Comparison to reference data

Physical performance

The results of various physical function assessments in our studies were compared to the following reference data:

- Leg Press: Women with an average age of 72.2 [211] and for men 60+ [177]. Hand grip strength: An age group between 80 and 89 assessed with a similar device [212].
- Chair Stand: Subjects aged 75-90 reported by the authors who presented the test originally [191].
- One-leg stance, maximal walking speed and maximal work load during bicycle ergometry: A Swedish population (H-70) of men and women aged 76 [21, 181, 189].
- Maximal heart rate: Men and women with an average age of 87 [213].

In our population of frail elderly people, physical performance was on average 81% for women and 69% for men compared to reference data. The lowest performance compared to reference data was in one-leg stance and chair stand (Figure 7).

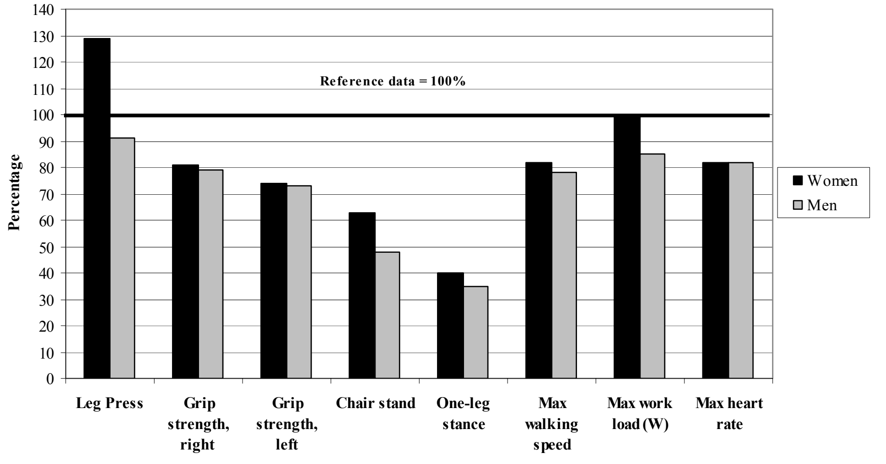

Figure 7. Physical performance in relation to reference data set to 100%.

Activities of daily living

Reference data regarding PADL and IADL comes from the same Swedish H70-population described above of 76 year olds [214]. Since we and Sonn et al [214] used different assessment instruments, the data were dichotomised in dependency/independency as in paper 4.

Regarding PADL, both men and women in our group of frail elderly performed equally or slightly better compared to reference data (data not shown).

For IADL, independency was on average 52% for both women and men compared to reference data. The lowest performance was in shopping and cleaning (Figure 8).

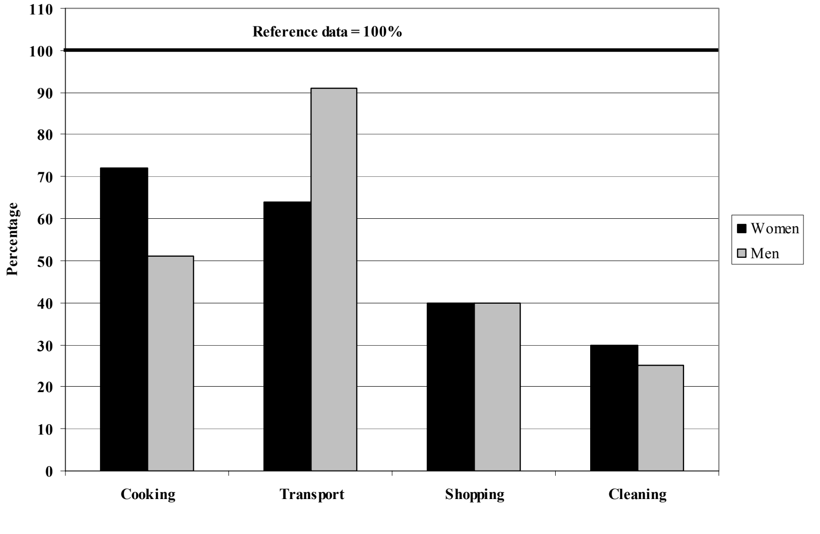

Figure 8. IADL in relation to reference data set to 100%.

Health-related quality of life
Reference data regarding SF-36 comes from a Swedish population aged 75+ [215]. Our sample scored on average 90% for women and 88% for men compared to reference data. The lowest scores were in Physical Functioning and Role Physical for both women and men (Figure 9).

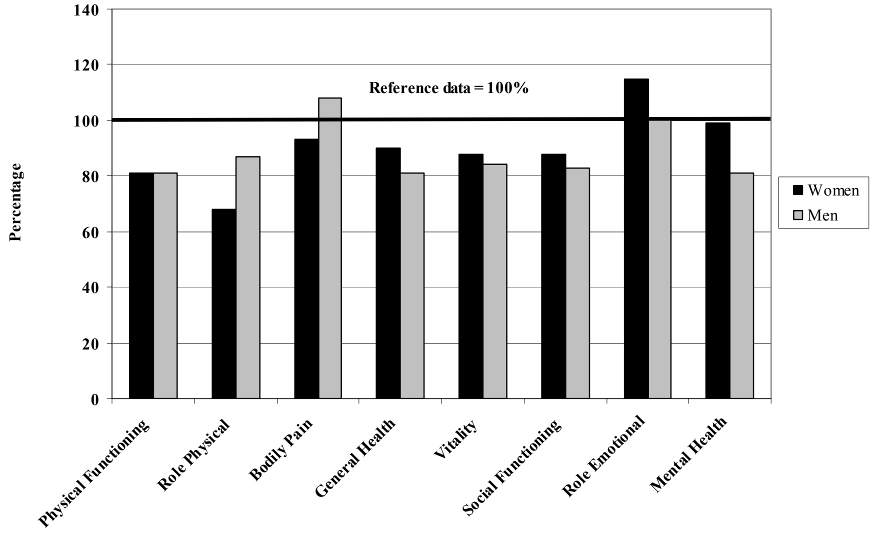

Figure 9. The different subscales of the SF-36 in relation to reference data set to 100%.

2.7.4 Predictions of three selected outcome using baseline data

Mortality
Handgrip strength ≤18 kg in women has been shown to predict an independent relative risk of 1.73 for mortality in a 5-year period compared with women with a handgrip strength >22 kg [216]. In our frail population, 76% of the women performed ≤18 kg in handgrip strength.
Disability in one or more categories in PADL in men has been shown to significantly increase the relative risk for mortality by 1.9 over a 6-year period [217]. In our frail population 13% of the men had disability in one or more categories of PADL

Falls
The cut-off score for predicting fallers versus non-fallers has been reported to be ≥13.5 s for TUG (sensitivity 80%, specificity 100%) and ≥14.5 s for TUGmanual (sensitivity 88%, specificity 90%) [218]. In our frail population 50 and 46% of the subjects performed more than 13.5 sec on TUG and 14.5 sec on TUGmanual, respectively, indicating that approximately 50% of the subjects were fallers with a sensitivity of 80-88%.
The odds ratio (OR) for an increased risk of falling has been reported to be 4.7 for subjects with a diffTUG (TUG minus TUGmanual) of ≥4.5 sec [192]. In our frail population 13% of the subjects had a diffTUG of ≥4.5 sec.

Hip fracture
Having more than two risk factors, such as slow habitual walking speed < 0.69 m/s, diabetes mellitus, Parkinson's disease, null parity, age over 80, and any type of fracture after age 50, have been shown to increase the risk for hip fracture in women with osteoporosis (T-score ≤ -2.5 sd) with 35 % and osteopenia (T-score -2.5 to 1.0 sd) with 18% over a 10-year period [219].
In our frail population, 22 women had established osteoporosis [220] and 18 of those had more than two risk factors indicating that 33% of the women had a 35% increased risk of hip fracture in a 10-year period. Twenty-two women had a diagnosis of osteopenia and 17 of those had more than two risk factors indicating that 31% of the women had an increased risk of 18% of hip fracture in a 10-year period.

2.7.5 Non-responding/Dropout analyses

The questionnaire was sent to all individuals over age of 75 (Figure 3).
The non-responding group (those who did not answer the questionnaire) comprised slightly more women (68%) compared to responders (63%).
The average age was similar in both groups, 81.8 years for non-responders and 81.2 years for responders.
However, we observed an age-dependent difference in non-response rate as follows:

- 75-79 years: 48 %
- 80-84 years: 48 %
- 85-89 years: 56 %
- 90-94 years: 56 %
- > 95 years: 65 %

Of the 96 included subjects, seven women and seven men dropped out after baseline assessments and did not attend any of the follow-up assessments. Of those 14 subjects, six died within nine months from baseline and additionally two within 20 months. Significantly, more subjects died in the drop-out group compared to non-drop-outs within 24 months. Subjects dropped out from all four groups; 3, 3, 6 and 2 subjects from the T, N, T+N and C group respectively.
Table 3 shows that in comparison to the non-dropout group, the subjects in the dropout group had significantly lower/poorer results regarding:

- muscle strength in the upper extremities (Pulldown)
- balance, both static and dynamic
- mobility
- ADL, both personal and instrumental, indicating more dependence
- HRQL, Social Functioning
- self-efficacy for changing physical activity level (Health Belief Model), data not shown

compared to non-drop-outs.

There were no significant differences between drop-outs and non-dropouts regarding age, sex, BMI, lung and heart diseases and continuous prescription medicine (data not shown).

3 RESULTS

3.1 BODY FUNCTION

3.1.1 Physical performance

Between groups analyses

There were significant improvements regarding:

- Muscle strength in the legs (Leg Press) for the T+N and T groups compared to the N group at 1st follow-up, with a mean difference of 11.4 kg [CI 95% 0.8 ; 21.9] and 14.3 kg [4.4 ; 24.1], respectively ($p<0.01$), see Figure 10
- Muscle strength in the arms (Dips) for the T+N and T group compared to the C group at 1st follow-up with a mean difference of 2.9 kg [0.2 ; 5.5] and 3 kg [0.4 ; 5,5] respectively ($p<0.01$)

There were no other significant between-group differences between baseline and 1st follow-up. There were no significant between-groups differences between baseline and 2nd follow-up.

Moreover, there were no significant differences between groups regarding body weight, lean body mass and energy intake.

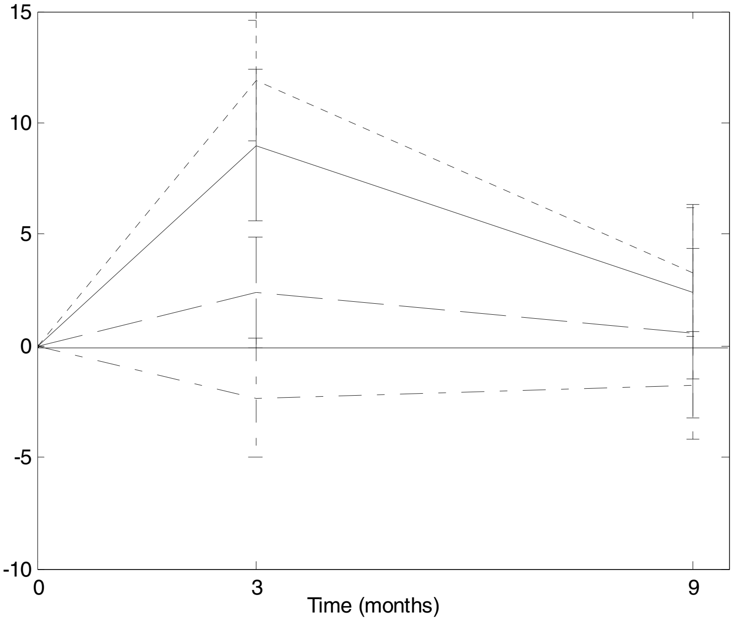

Figure 10. Mean differences (SEM) for Leg press between baseline (0 months) and 1st and 2nd follow-up (3 and 9 months) for the four groups. There was a significant increase for the T and T+N group compared to the N group ($p<0.01$).

-------- = T-group, —— = T+N-group, – – – = C-group, – - – - – = N-group

Within groups analyses

There were significant improvements for both the T and T+N groups, regarding:

- Muscle strength in the legs (Leg Press) with 11.9 kg [CI 95% 6.3 ; 17.5] and 9 kg [1.8 ; 16.2] for the T and T+N group, respectively.
- Muscle strength in the arms (Dips) with 1.8 kg [0.8 ; 2.8] and 1.7 kg [0.04 ; 3.4] for the T and T+N group respectively.
- Muscle strength in the arms (Pulldown) with 3.4 kg [0.9 ; 5.8] between baseline and 1st follow-up and with 2.7 [0.9 ; 4.6] between baseline and 2nd follow-up for the T group

Regarding aerobic capacity, there were no significant differences within groups on maximal workload (watt) or time (minutes) between baseline and follow-ups. A similar analysis excluding subjects with ongoing ß-receptor blockade showed the same result.

There was a small, but significant, decrease in FFM within the T group with -0.9 kg [-1.7 ; -0.2].

Analyses of the combined training group (T and T+N)

There were no differences in the outcome of maximal workload/time in relation to sex, ß-blockade, tobacco consumption or presence or absence of heart disease between baseline and follow-ups for the combined training group.

There was a significant difference ($p<0.05$) between subjects with or without lung disease regarding changes in work time with 1.5 min [0.3 ; 2.8] between baseline and 1st follow-up in the combined training group, with no sex differences.

In the combined training group, improvers in the outcome variables leg muscle strength (leg press) see Figure 11, and arm muscle strength (dips, pull down) had significantly higher compliance compared to non-improvers. The correlation between compliance and difference in work time between baseline and 1st follow-up was $r=0.31$, however, non-significant ($p<0.07$).

In the combined training group there were no significant differences between on the one hand age, sex, educational level, BMI, FFM, energy intake/kg body weight, physical performance including spirometry measures, presence of heart and/or lung disease and number of continuous prescription medications at baseline and on the other hand compliance.

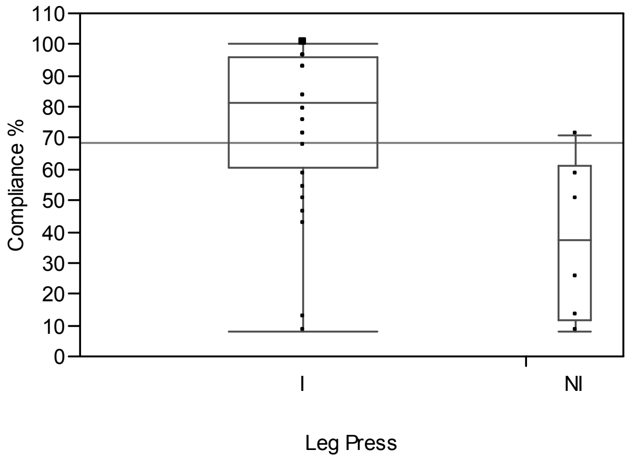

Figure 11. Improvers (I) in muscle strength (Leg Press) had significantly higher compliance in percentage compared to non-improvers (NI).

3.1.2 Test re-test reliability

In paper 4, there was a high test re-test correlation between the measurements of 1RM for both groups respectively (r=0.97) and for the combined group as well. The 95% limits of agreement for the mean difference were -4.3/+6.9 kg for group 1, -3/+6.4 kg for group 2 and -2.6/+5.6 kg for the combined group
The systematic bias was, on average, 1.3 with a 95% confidence interval [0.09 ; 2.5] for group 1, 1.7 [0.2 ; 3.3] for group 2 and 1.4 [0.5 ; 2.4] for the combined group, possibly indicating a small, but statistically significant, learning effect for both groups.
The F-test showed no significant difference between the groups.

3.1.3 Adverse events

Subjective
During the bicycle ergometry test at baseline, four subjects experienced dizziness and two subjects chest pain during or directly after the test. At 1st follow-up, two subjects experienced dizziness and one chest pain. Of those, one subject experienced dizziness both at baseline and 1st follow-up and one chest pain at the same two measurements. At 2nd follow-up, one subject experienced dizziness and one chest pain. None of the subjects experiencing chest pain or dizziness at baseline and/or 1st follow-up had pathological ECG recordings (see below). One subject experiencing chest pain at 1st follow-up had a non-assessable ECG-recording due to pacemaker.

In Paper 4, three subjects in group 1 and two in group 2 reported muscle soreness after the first test session, but not to the extent that it affected their daily lives. No injuries were reported.

Objective
During the bicycle ergometry test at baseline, 4 subjects had certain and 5 probable pathological ECG recordings (mainly non-specific ST-T changes, in three cases occurrence of atrial fibrillation, AV-block 2 and sinus arrest), 10 subjects were non-assessable due to bundle branch blocks or pacemaker treatment. This may be summarised as 4/5/10. The corresponding results for 1st and 2nd follow-up were 2/5/10 and 1/5/7.
No adverse events occurred that required emergency equipment (e.g. defibrillator, oxygen or medication) during or after the tests.

3.2 ACTIVITY/PARTICIPATION

3.2.1 Physical performance

Between-groups analyses
There were significant improvements in:

- Balance (Step test) for the T group compared to the T+N group with a mean difference of 4.3 steps [0.2 ; 8.5] ($p<0.05$).

Within-groups analyses
There were significant improvements for both the T and T+N groups regarding functional muscle strength:

- Functional muscle strength (Chair Stand) with 1 [0.004 ; 2], 1.2 [0.07 ; 2.3] and 0.6 [0.05 ; 1.1] for the T, T+N and N group, respectively
- Functional muscle strength (Step-ups) with 2.2 [1.1 ; 3.3] between baseline and 1st follow-up and with 1.1 [0.3 ; 1.8] between baseline and 2nd follow-up for the T group.

The T group also had a small, but significant, improvement in balance (step test and MFE) with 3.2 [0.9 ; 5.5] and -4.3 [-7.8 ; -0.8], respectively, see Figure 12-13.

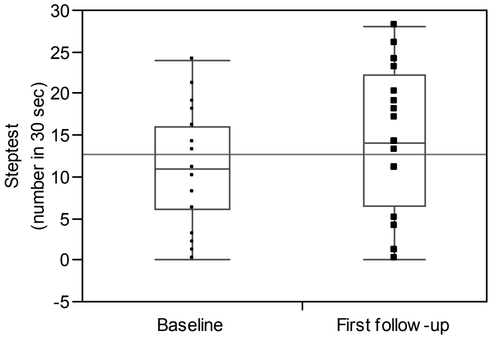

Figure 12. Subjects in the T group significantly increased the number of steps in the Step test between baseline and 1st follow-up.

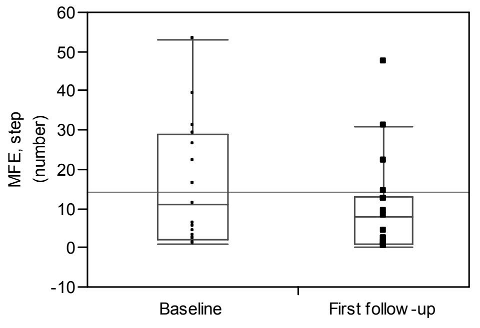

Figure 13. Subjects in the T group significantly decreased number of steps outside the line in the Modified Figure of Eight (MFE) between baseline and 1st follow-up.

3.2.2 Physical activity level

The N and C groups were significantly more physically active at baseline compared to the T and T+N groups.

The T and T+N groups significantly increased their physical activity level between baseline and 1st follow-up compared to the C group (Figure 14). The changes between baseline and 1st follow-up were on a median level 0 (0-1), 0 (0-1), 0 (0-0) and 0 (-1-0) for the T, T+N, N and C group, respectively. This increase remained significant at 2nd follow-up for the T group compared to both the N and C groups. An additional analysis showed that the baseline values explained 27% of the variance in change between baseline and 1st follow-up.

There was a near-significant increase for the T and T+N group compared to the N and C group regarding walking duration between baseline and 1st follow-up ($p<0.08$) and between baseline and 2nd follow-up ($p<0.06$). However, when comparing the combined T and T+N group with the combined N and C group, there was a significant increase in walking duration for the combined training group between baseline and 1st follow-up. This change was on a median level 0 (0-1) for the combined T and T+N group and 0 (0-0) for the combined N and C group. Corresponding data between baseline and 2nd follow-up were with a median change; 0 (0-1) and 0 (-1-0), respectively ($p<0.01$). Baseline values explained 21% of the variance in change regarding duration between baseline and 1st follow-up.

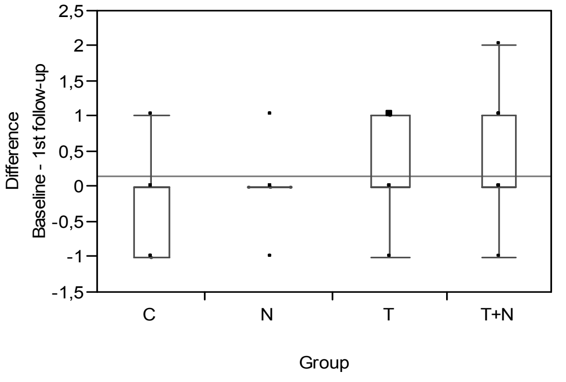

Figure 14. Changes in physical activity level between baseline and 1st follow-up for the four groups. There were significant increases for the T and T+N groups compared to the C group ($p<0.05$).

3.2.3 Activities of Daily Living and Health-Related Quality of Life

There was no effect on PADL, IADL and HRQL, between groups at any of the follow-ups.

3.2.4 Associations in the combined training group

In the combined training group, improvers in the outcome variables balance (step test) and mobility (TUG) had significantly higher compliance compared to non-improvers.

There were several significant correlations between increase in physical activity and improvement in ADL:

- physical activity (baseline–2nd follow-up) – PADL r=0.36 (baseline–2nd follow-up) and r=0.44 (1st follow-up–2nd follow-up)
- physical activity (baseline–2nd follow-up) – IADL r=0.36 (baseline–2nd follow-up)
- frequency of walking (baseline–2nd follow-up) – PADL r=0.42 (1st follow-up–2nd follow-up).

There was also a significant correlation between increase in physical activity and improvement in HRQL:

- physical activity (baseline–2nd follow-up) – Physical Functioning r=0.41 (baseline–1st follow-up).

There were several significant correlations between home-based exercises and improvements in PADL:

- number of occasions and months of home-based exercises – PADL r=0.53 and 0.50, respectively (baseline–2nd follow-up)
- hours, number of occasions and months of home-based exercises – PADL r=0.47, r=0.65 and r=0.47, respectively (1st follow-up–2nd follow-up).

There were no significant correlations between home-based exercises and improvements in IADL.
There were several significant correlations between home-based exercises and improvement in HRQL:

- intensity in home-based exercises – General Health r=0.43 (baseline–2nd follow-up)
- months and number of occasions of home-based exercises – Role Emotional r=0.53 (baseline–2nd follow-up) and r=0.44 (1st follow-up–2nd follow-up) respectively.

3.2.5 Compliance

The mean compliance rate of the 12-week organised physical training programme was 65% (range 4-100%).

Twenty-seven of the 40 subjects in the T and T+N groups who completed the 1st follow-up sent in the training diaries for, on average, 5 (sd 2) home-training months. Outdoor walks, functional muscle strength training and Qigong were the most common activities, performed on average 12 (8) occasions/months for an average of 7 (6) hours, 9 (10) occasions/months for 1.5 (1.6) hours and 8 (7) occasions/months for 1 (1) hour, respectively. The activities were performed with a median intensity of 3 (3-3) and the intensity was similar between subjects as well as between activities.
If all types of activities were summarised, only 5 subjects fulfilled the WHO's recommendation of 30 minutes of physical activity per day on average.
Forty-six out of 49 eligible subjects (one was excluded due to missing data on energy intake) completed the individual dietary counselling, and the mean compliance rate for the N and T+N group during group sessions was 73% (range 20-100%).

3.3 CLINICAL RELEVANCE

Table 4 shows the proportion of subjects that improved >15% in the different physical performance variables for the combined T and T+N groups and the combined N and C groups respectively. The largest difference regarding average change and proportion of subjects improving >15% between groups was observed for muscle strength and functional muscle strength (Leg Press, Dips, Pulldown and Chair Stand) which is in line with the significant differences in the between and within-groups analyses (see above). The difference increased in the sub-group of >65% compliance, which is also shown in Figure 15 and 16.

Table 4. Proportion of subjects improving between baseline and 1st follow-up and the average change.
For example there was an average change of 16% in Leg Press in the combined T and T+N group and 50% of the subjects improved ≥15%; the average increase of those subjects was 28%.

	Combined T, T+N	Combined T, T+N (>65% compliance)	Combined N, C
Muscle strength/Functional muscle strength			
Leg Press			
Average change %	16	21	0
Proportion of subjects with improvements ≥15%	50	64	11
Average increase (≥15%)	28	29	23
Dips			
Average change %	13	18	-1
Proportion of subjects with improvements ≥15%	33	43	28
Average increase (≥15%)	32	32	25
Pulldown			
Average change %	13	22	3
Proportion of subjects with improvements ≥15%	46	73	16
Average increase (≥15%)	28	28	27
Chair Stand			
Average change %	14	23	3
Proportion of subjects with improvements ≥15%	47	58	29
Average increase (≥15%)	42	40	25
Balance			
Tandem stance			
Average change %	6	6	45
Proportion of subjects with improvements ≥15%	26	21	27
Average increase (≥15%)	113	107	249
One leg stance			
Average change %	56	56	50
Proportion of subjects with improvements ≥15%	42	46	46
Average increase (≥15%)	149	136	135
Modified figure of eight, step			
Average change %	-3	-9	12
Proportion of subjects with improvements ≥15%	50	62	27
Average increase (≥15%)	-50	-51	-60
Step test			
Average change %	17	26	6
Proportion of subjects with improvements ≥15%	50	63	37
Average increase (≥15%)	56	55	51
Mobility			
Timed Up and Go			
Average change %	-2	-9	0
Proportion of subjects with improvements ≥15%	29	29	24
Average increase (≥15%)	-30	-36	-21
Maximal walking speed			
Average change %	4	6	2
Proportion of subjects with improvements ≥15%	26	29	12
Average increase (≥15%)	27	26	23
Habitual walking speed			
Average change %	-2	-2	2
Proportion of subjects with improvements ≥15%	18	21	15
Average increase (≥15%)	25	24	24

Only a small number of subjects moved from one category to another (Table 5) and the differences between groups were very small, except for physical activity level, which is also in line with the significant difference in the between groups analyses.

Table 5. Number of subjects changing between different categories/levels between baseline and 1st follow-up. For example 8 of the 28 subjects in the combined T and T+N groups that performed Timed Up and Go between 11 and 20 sec at baseline, performed Timed Up and Go in less then 10 sec at 1st follow-up.

	Combined T, T+N	**Combined T, T+N** (>65% compliance)	**Combined N, C**
Aerobic capacity			
Maximal load in watt			
Increase ≥ 1 level	7 (n=36)	6 (n=22)	7 (n=40)
Mobility			
Timed Up and Go			
Change to <10	8 (n=28)	4 (n=17)	6 (n=29)
Change to <20	3 (n=6)	3 (n=5)	1 (n=3)
Maximal walking speed			
Change to ≥ 1.0 m/s	1 (n=9)	1 (n=7)	1 (n=9)
Change to ≥1.4 m/s	5 (n=21)	5 (n=14)	3 (n=21)
Habitual walking speed			
Change to ≥ 1.0 m/s	1 (n=30)	1 (n=21)	3 (n=23)
Change to ≥1.4 m/s	2 (n=7)	2 (n=3)	1 (n=18)
Physical activity level			
Increase ≥ 1 level	16 (n=38)	13 (n=24)	5 (n=41)

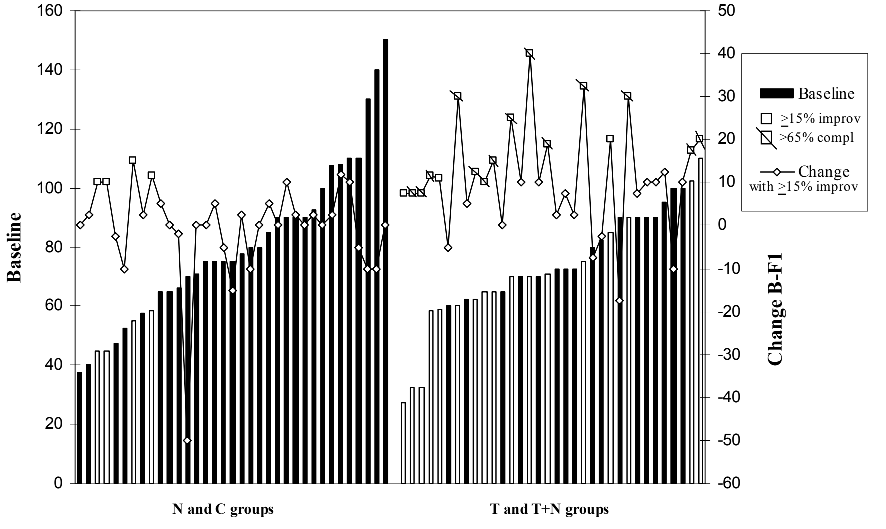

Figure 15. Change in Leg Press results between baseline (B) and 1st follow-up (F1) in relation to compliance and >15% improvement (improv). Both black and white bars indicate baseline levels, but the white bars also indicate subjects with >15% improvement. The boxes with a line across indicate subjects with improvement >15% and with a compliance (compl) of >65%.

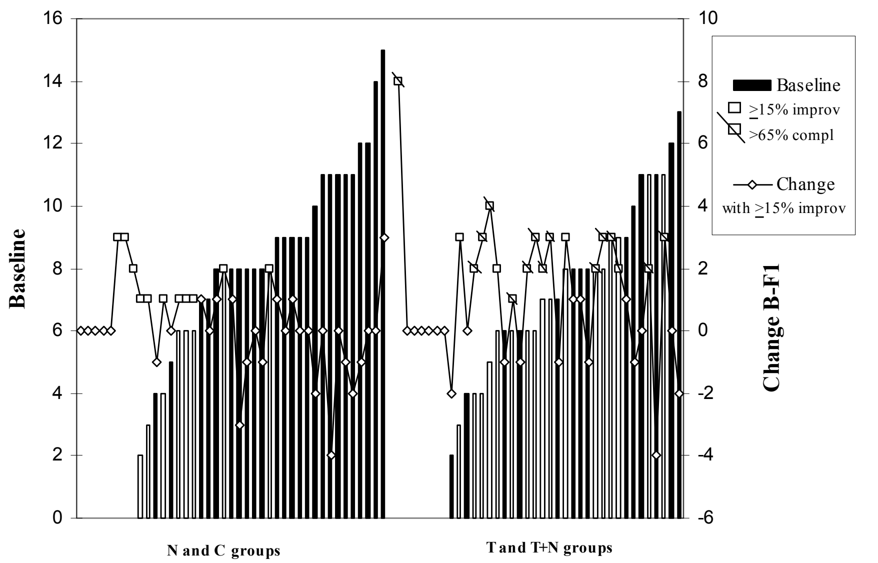

Figure 16. Change in Chair Stand results between baseline (B) and 1st follow-up (F1) in relation to compliance and >15% improvement (improv). Both black and white bars indicate baseline levels, but the white bars also indicate subjects with >15% improvement. The boxes with a line across indicate subjects with improvement >15% and with a compliance (compl) of >65%.

3.4 PERSONAL FACTORS

3.4.1 Health Belief Model

All four groups were comparable at baseline except for the benefits and self-efficacy items. There were no differences between groups regarding the statements between baseline and both follow-ups.

The within-group analyses showed that the N group significantly increased the estimated ratings for benefits by md=1 (0-3) and the T group for self-efficacy by 2 (0-3) between baseline and 1st follow-up. The T+N group significantly increased the estimated ratings of the overall statement *"I am very motivated…"* between baseline and 1st follow-up by 1 (0-4). There were no within-group differences between baseline and 2nd follow-up.

There were no differences between compliers and non-compliers regarding the different statements in the Health Belief Model (HBM) at baseline. Moreover, there were no changes in estimated HBM ratings between baseline and 1st follow-up in the combined T and T+N group.

4 DISCUSSION

This thesis has shown a positive effect of a physical training programme on leg muscle strength and habitual physical activity level for frail elderly people. Adding a nutritional intervention did not affect the results.
There was a high reliability of r=0.97 in test re-test of 1RM in the Pulldown device for the upper extremities with 95% limits of agreement of approximately -4/+6 kg.

4.1 RESULTS

4.1.1 Muscle strength

Progressive muscle strength training, especially when performed with stationary equipment, was particularly effective in the lower extremities. This finding was also expected, since this section was the most individualised part of the training programme and the lower extremities were more subjected to training through the functional strength training section. The significant difference in lower extremity strength was only observed in comparison with N group, but not the C group. However, both the C and the N group received the same physical training advice, and as has been shown in this study, a combination of treatment did not add any extra benefit.
The significant increase in muscle strength did not remain at 2nd follow-up, indicating the need for continuous physical training for this group of frail elderly people. This confirms the well-known fact that muscle strength decreases with physical inactivity and that specificity of physical training is of importance.
The small improvements within groups concerning Dips and Pulldown are probably too small to be clinically relevant. As shown in paper 4 there is a variability of -4/+7 kg in the pull-down device, which cannot be explained as an effect of strength training, but rather by fluctuating daily condition and/or motivation. In addition, there are conflicting results in the literature regarding dose and frequency. Perhaps the subject in this study could have improved more in arm muscle strength if the dose had been set to 3x8 repetitions instead of 1x8.

Test re-test 1RM

The reliability was equally high in both groups, despite the fact that there were significant differences between the groups at baseline. Furthermore, there was no significant difference in 1RM between the groups indicating that previous muscle strength training experience does not affect the results; however, this interpretation must be tested in a larger study.

The analysis of 95% limits of agreement showed that when 1RM was performed in a second session, about 95% of the repeated measurements fell within -4/+7 kg of the first session. The limits of agreement were asymmetrically distributed around zero, due to a mean systematic bias of 1.3 and 1.7 kg for group 1 and group 2, respectively. This finding may indicate a learning effect or differences in motivation and daily condition rather than a true change in muscle strength.
The observed difference of -4/+7 kg may seem large, but one must consider the many muscles and muscle groups involved in the movement. When measuring only one muscle group, for example elbow flexors, a difference of -4/+7 kg would be much too high to consider the method reliable.

4.1.2 Aerobic capacity

No increase in aerobic capacity measured as maximal workload or time during bicycle ergometry was observed. An exception was subjects in the combined training group without lung disease, who significantly increased work time between baseline and 1st follow-up compared to subjects with lung disease. This highlights the influence of diseases in evaluating the outcome of a physical training program.

The physical training program consisted of three different sections to ensure diversified training effects. The aerobic section lasted for 20 minutes in which the subjects on average reached 73% of predicted maximal heart rate. Exercise training at this intensity level is well documented to enhance oxygen uptake in young individuals. Nonetheless, no increase was observed in aerobic capacity measured as workload or time during bicycle ergometry in either of the two training groups. A meta-analysis concluded that physical training of >80% intensity and duration >30 minutes for people aged 46–90 yields a significantly greater effect on $VO_{2\,max}$ compared to lower intensity and duration [108]. Despite the effort to facilitate heart rate increases, the intensity of the aerobic section of the training programme may still have been too low and the duration too short [108] to produce any effects.

4.1.3 Balance

There was a small, but significant, difference between the T and T+N group, in favour of the T group, regarding step test. The groups were comparable at baseline and the compliance was similar in both groups, so this cannot explain the difference. The most probable cause is a statistical significance by chance, due to the many different outcome variables [221]. There were no other differences between groups regarding the four different balance measures. We did find, however, that the T group exhibited significant, but clinically limited, improvement in two measures of balance: Modified Figure of Eight and Step test. Halfway through the physical training intervention (after 6 weeks) the difficulties of the movements of Qigong were increased. This was however not enough to affect the balance measures. In addition, frail elderly people probably need much more individualised and targeted balance training to be able to challenge their limits, which is necessary to improve balance [109]. This could not be provided for in the training groups for the participants due to available number of instructors per subject.

4.1.4 Physical activity level

The habitual physical activity level significantly increased in both training groups and this increase remained at 2nd follow-up. This is in contrast to a previous study of frail elderly people [62], where the subjects were not encouraged to continue home-based exercises, which may explain the difference. The method to measure physical activity was, however, similar to our study, including both leisure and household activities. The subjects in our study were included based on low physical activity level, but there was still a small, but significant difference between the groups at baseline due to larger range, i.e., there were more subjects scoring 1 (hardly any physical activity) in the training groups compared to the other groups. Baseline values explained 27% of the changes between baseline and 1st follow-up, possibly because it is easier to "move" from grade 1 to 2 than from grade 3 to 4. However, we still think the results are valid. This interpretation is also supported by the significant increase in walking duration for the combined training group. Thirty-seven and 39% of the subjects in this group increased ≥1 category between baseline and 1st follow-up and between baseline and 2nd follow-up, respectively. Corresponding data for the combined N and C group were 15 and 13%. In addition, more subjects in the combined N and C group decreased walking duration compared to the combined training group, 20% and 8% respectively, between baseline and 1st follow-up. Corresponding numbers were 13% and 3% between baseline and 2nd follow-up.

4.1.5 ADL and HRQL

We observed no effect on ADL and HRQL, which is in line with previous studies [71, 72, 131]. However, we found low to moderate correlations between on the one hand increases in physical activity levels and walking habits and on the other hand improvement in ADL and HRQL (subscale Physical Functioning).
There are many possible explanations for a lack of effect of physical training on ADL or HRQL. First, ADL is very much dependent on environmental barriers and personal factors. Even though a physical intervention programme may succeed in improving muscle strength and balance, the elderly participants might still keep their home service assistance either due to habit or due to a fear that they might not receive it again if the need were to arise in the future. Environmental barriers can also affect IADL; if, for example, the closest grocer's shuts down, which was the case for one of the subjects in our study. This led to increased dependence in heavy shopping regardless of change in the physical performance level.

Second, HRQL, a concept difficult to define and to measure, is affected by several factors and may imply many different things for each individual. It has been shown that disabled people found physical health less important compared to non-disabled people [171]. It has also been suggested that a functional limitation leading to a disability in e.g. social functioning can be due to environmental barriers rather than a person's physical performance capability [171]. This may be one explanation for the lack of effects of a physical training programme aiming at improving just that. To be able to affect ADL and HRQL, it may be of importance to address other issues together with a physical training programme e.g. behavioural factors, including social support by the individual's partner or family members, and to target interventions at environmental barriers as well.

4.1.6 Compliance

We observed a significant difference between improvers and non-improvers regarding compliance in several outcome variables, e.g. muscle strength. These findings are not surprising, since both specificity and a certain minimum amount of training are necessary to achieve improvements [102, 103].
In the analysis of compliers/non-compliers, the other analysed variables showed no significant differences, regardless of a compliance limit of >65% or >80%. There may certainly be other factors involved, such as combinations and degrees of diseases and injuries etc.
We found moderate correlations between performance of home-based exercises and PADL/HRQL, showing an association between physical training and improvements in ADL/HRQL, respectively for those who actually performed the exercises. Intention-to-treat analyses are of importance since they reflect a larger population

regarding, for example, compliance. However, one cannot expect to reach a positive result from a physical training programme unless it is actually performed regularly.

4.1.7 Clinical relevance

The Philadelphia Panel suggest that ≥15% improvement should be required for A and B recommendations meaning "fair or good evidence to support the recommendation that the intervention be specifically considered" [203]. The 15% improvement is calculated for the difference between the intervention and the control group.
Only the result for leg muscle strength and physical activity level fulfilled these criteria in our study (Table 4, 5). However, the subgroup with compliance >65% showed increases of ≥15% regarding arm muscle strength, Chair Stand, balance (MFE and Step test) in comparison to the combined N and C group. The panel suggests that increases of ≥15 % without statistical significant difference could be regarded as evidence C+ recommendation, where C equals "poor evidence regarding inclusion or exclusion of an intervention, but recommendations may be made on other grounds". However, this will not alter our conclusion.

If the A and B recommendations were applied to the systematic review described in Figure 2, the results would have been altered. Both balance and mobility would have been regarded as contradictory evidence instead of strong and moderate evidence as significant improvements were <15% in 4 out of 7 studies and 2 out of 6 studies for balance and mobility respectively. However, there is no consensus among researcher in different fields and professions that ≥15% improvement is clinically relevant and very few studies address this issue. The methodological procedure used in the systematic review (see section 1.1.6) is well established by the Cochrane Collaboration. Therefore, I think the conclusion described in Figure 2 is valid until further research results in this area are available.
Studies included in the review comprise many different definitions of frailty, mainly focusing on physical frailty. If a strict definition as applied in this thesis would have been used, very few studies would have been included and no conclusion could have been drawn. In addition, there is no consensus of a definition of frailty in the literature [19]; therefore, an extensive exclusion of studies was not an option.

4.1.8 Health Belief Model

An attempt was made to explore and measure the concept motivation, resulting in four different statements based on the HBM plus an overall statement about motivation. However, the data analysis revealed non-valid results, especially regarding construct validity for measuring motivation. The statements created from the dimensions in the HBM were probably too superficial to be able to predict compliance or outcome. Maybe several sub-questions are of importance in each dimension in order to fully capture the concept of motivation. Resnick & Jenkins [222] have done this by exploring only the dimension of self-efficacy. Other important dimensions to explore could be vulnerability, locus of control and expectation outcomes.
Based on this, we decided to analyse each different statement separately as the HBM has been validated in other studies. However, behavioural attitudes were not addressed during the intervention; therefore it is not surprising that there were no

change between groups. The small significant within-groups changes are not regarded as clinically relevant.

4.2 METHODOLOGY

4.2.1 Study Design

There is no consensus regarding the definition of frailty [19] and different definitions are presented in the literature [13-15]. The definition of frailty used in this study was chosen based on the published literature at that time, but also for logistical and financial reasons. Due to low budget, we had to screen subjects through telephone calls and therefore had to have a definition that was possible to asses without meeting the subjects. The results of the recruitment procedures of the FICSIT studies have shown that it is approximately six times more costly to recruit frail elderly people compared to young healthy people [223]. The increased cost was mostly due to the extensive screening process, interaction with family members and transport arrangements [223]. A more narrow definition would probably have resulted in a more homogeneous group. On the other hand, it has been suggested that a broad definition increases generalisation [19].

The BMI cut-off score for elderly people has been discussed [224]. In relation to loss of body function, a cut-off score of 18-20 kg/m^2 has been recommended [224]. A previous study analysing the criteria for frailty suggested a BMI cut-off score of 21.7 kg/m^2 in combination with a low level of physical activity [13]. In the present study a cut-off score of BMI <20 kg/m^2 was set for those without weight loss during the last 12 months to make sure that we included possible underweight.

The original physical activity scale [225] has been modified to include household/domestic work [20, 21], which was the version used here as an inclusion criteria. In a population of 76-year-olds both scales, with and without household activities, were compared. Women showed the greatest difference, and the major transfer occurred from grade 3 to grade 4 [21].

In this study, grade 3 or below was set as a limit for physical inactivity. To be placed on grade 3, the subjects must either fulfil the requirements regarding light domestic work or light physical exercise, or both. Although the duration of light physical exercise is in accordance with the recommendations of the WHO of a minimum of 30 minutes physical exercise per day, the subjects on grade 3 cannot manage all domestic work themselves. Based on this, we find that this can be considered as a low physical activity level.

As shown in Figure 3, a total number of 6.999 potential subjects were contacted for potential recruitment and only 96 subjects (1%) were randomised. This gap may seem much but is in line with other studies enrolling elderly people [223, 226].

4.2.2 Measurements

Specificity is of importance when measuring and training muscle strength. One repetition maximum was chosen because it measures dynamic muscle strength, it is a clinical test and therefore easier to implement in a clinical setting and because it gives the opportunity to standardise and dose the intensity of a muscle strength training programme. One of the disadvantages of 1RM is that it measures muscle strength at the weakest point in the range of motion of a joint [227]. However, isokinetic strength testing with for example Cybex are fare more expensive and rarely used in clinical settings; therefore, we chose the 1RM instead. The reliability of 1RM in elderly people has been questioned [118]; it is therefore important to interpret results with caution.

Unfortunately, due to the clinical setting and research conditions, a maximal oxygen uptake test could not be performed. The 4-minute stages and 25 W intervals were suggested by Wetterqvist et al. [181], who reported hemodynamic responses and average work loads in 355 participants aged 70-75, both male and female. However, the utility of this test for measuring training-induced changes may be questioned due to the subjects' estimated maximal work capacity in relation to the size of suggested incremental workload steps [228]. An indirect support for this possibility is that the participants' estimated effort during the tests was quite low, which is in line with a previous study in healthy elderly people showing that only 41% of the women and 36% of the men who exercised less than 8 minutes rated their maximal effort as "hard" to "very, very hard" [229]. An alternative explanation could be that the applied scale is difficult for elderly people to understand and that it is difficult to rate perceived exertion when participants are not used to experience total fatigue.

There are several ways of measuring balance. The validity of measuring OLS and TS for 30 sec has been questioned in a recent thesis [122]. It was shown that the first 5 seconds of OLS and TS were very important if the subjects were to remain in this position. The ability to stand for longer than five seconds, it was suggested, may be affected by other factors such as muscle strength. Improvement over 5 seconds may therefore not be regarded as improvement of balance, but of other factors. The author suggested assessing the weight-shifting transfer when taking position rather than the length (in seconds) one's position has been accomplished [122]. However, no such assessments are available at present.

At the start of the study, the physical activity scale was used mainly for screening fulfilment of inclusion criteria; however, during the trial we decided to repeat these assessments at all follow-ups. The physical activity was not originally constructed for measuring change over time [225]. Still, we could show a significant increase in habitual physical activity level.

Regarding PADL, most of the subjects scored high at baseline (near the ceiling) and therefore improvements were not detectable; however, a possible decline in PADL during the 2-year period might have been detectable, if this would have occurred. When estimating IADL we asked the subjects what they did perform, not what they could perform. Differences in contribution, ability and habits between men and women regarding domestic activities could therefore affect the results more in this age group. However, the same questions were asked at all follow-ups and may therefore not affect change over time.
The reason for dividing the score in independency/dependency was to set clinically relevant limits. Further, we also wanted to analyse the different subcategories of ADL, not just the total score. If we had found differences between groups, it would then have been easier to interpret and implement the result in a clinical setting.

Adverse events
From a safety perspective, it is important to note that very few adverse events was observed and no severe complication occurred during the bicycle ergometry test, even though many participants had confirmed heart disease. In fact, only 34 of 93 participants had a normal ECG but further pathological changes were uncommon during the tests. Two participants experienced slight to moderate chest pain during the test; however, without any simultaneous ECG signs of coronary ischemia. Thus, even though these frail elderly subjects certainly constitute a population at substantial cardiac risk, it was safe to conduct the submaximal bicycle ergometry presented here.

After the first session in the test re-test study of 1RM only 5 of 34 (15%) subjects reported muscle soreness and none of them reported that it had affected their daily living. No subject reported an injury. These observations suggest that it is safe to use the Pulldown device to conduct 1RM measurements in both healthy and frail elderly subjects. Our clinical experience in care of the elderly has shown that professional staffs are frequently reluctant to motivate elderly people to push their limits, despite evidence of effect of high-intensive muscle strength training. As our results show that 1RM in the arm/shoulder is safe to conduct, we believe that this study will contribute to a necessary change in attitudes.

Reference data
The women in our frail group performed better in leg muscle strength compared to reference data. The Leg Press test in our study and in the cited reference studies were all performed seated in an upright position, but the equipment and the instructions may differ, which may explain the difference in results.
One of the lower performances was in OLS; however, the instructions to the subjects differed in our study compared to e.g. the study by Frändin et al [189]. Our subjects were allowed to place their arms and the non-supported leg in a self-selected position. In the study by Frändin et al [189], the subjects were instructed to place their arms on their back and with the hip joint in a neutral position and the knee flexed to 90°. If these instructions had been used in our study, very few subjects would have been able to perform the test and the performance in regard to reference data would have been even worse. Lack of standardisation is of course a disadvantage when comparison data with other studies; in addition, it could also have decreased our ability to evaluate changes over time.

4.2.3 Intervention
Physical training
One of the challenges when designing the present physical training programme was to standardise the different sections, both in order to describe training intensity and for the readers to be able to understand how the programme was executed in detail to be able to reproduce the study. This is rarely the case in many published studies, which has been discussed in a recent review [70].
The subjects were asked to score their effort after each section and they usually scored a 3 or a 5 on the CR-10 scale, meaning “somewhat tiring” or “tiring”. However, some of the subjects scored a 3 even though they had to sit down and rest during the aerobic section. Maybe these types of scales are difficult for frail elderly

people to understand and interpret. There may also be a difference in attitudes towards the feeling of effort, which may very well be gender related.
The heart rate may also have been affected by treatment with beta-blockers and problems like cardiac arrhythmias. The method for predicting maximal heart rate (220 minus age) is well established, but has disadvantages due to the large variations in the applied prediction formula at the individual level [230]. In addition, the heart rate levels were similar during the aerobic and balance training sections. Thus, the use of heart rate for evaluating training intensity in this age group may be questioned.
Tai chi has been shown to decrease the risk for falls and also to preserve the effect of a strength and balance training programme for elderly people [88, 89]. When contacting different organisations in Sweden to find instructor classes for Tai Chi, it became clear that Tai Chi is considered more difficult to perform than Qigong, especially for elderly people. This has also been suggested in the scientific literature, where the movements of Qigong are regarded as less complex and challenging to perform; however, both Qigong and Tai Chi include training in different standing positions (support areas) [97, 99, 100]. In addition, Qigong is more widespread in Sweden, especially for the elderly. Therefore, we chose Qigong instead of Tai Chi.
Physical training and physical activity is often organised in groups by different organisation in Sweden. We chose to imitate this procedure to reflect reality in clinical settings. Therefore, the aerobic and the balance sections were not individually tailored. The results of this study have shown that individually tailored programmes are probably necessary to achieve a positive effect in frail elderly people.

Nutritional intervention

To our knowledge, this is the first RCT in community-dwelling frail elderly people, aged 75 and over, that has applied individualised dietary counselling and tried to work with food choices and eating patterns instead of standardised supplements. This approach resembles clinical routine practice and serves educational and participatory purposes. However, the chosen method of nutritional treatment was difficult to standardise, making it difficult to tie clinical effects at follow-up to the actual treatment. This might be one reason for the lack of positive results concerning outcome of the nutritional measurements.
The within-group analyses showed that the T group significantly improved in 7 of 12 physical performance variables and the T+N group in 3 of 12. This could be interpreted as if the nutrition intervention programme negatively affected the results; however since there were i) no significant differences between the two groups in the different variables (except for one balance measure) between baseline and 1st follow-up and ii) a rather small sample size, we do no find this interpretation valid.

General advice

The C group received both general diet and physical training advice, while the T and N groups only received general diet or general physical training advice, respectively, which may explain the lack of improvement in most of the variables. Besides serving as a control intervention, the reason for including the advice was that it might resemble the advice given in primary care. The C group had a significantly higher education level, which might have had an impact on compliance with given advice. It has been shown that health literacy is of importance in the understanding of health advice [231].

4.3 LIMITATIONS

4.3.1 Paper 1-3

The small sample size and the large heterogeneity regarding both physical performance and nutritional measurements may be the most important limitations of this study, as well as the fairly high dropout rate. This heterogeneity and the unknown treatment effect(s) for various outcome variables made it difficult to perform a power calculation. We therefore decided to conduct this pilot RCT to provide both methodological and clinical information as a basis for future studies in frail elderly. Another limitation of the study is that the test leaders were not blinded to randomisation due to logistical and financial reasons.

It is well known that all subjects included in a treatment trial almost never respond to a particular treatment. In this thesis we tried to examine more closely the concept of improvers/non-improvers in relation to compliance and other background factors, and to treatment with physical training and/or nutrition. However, the analysed background factors did not show any consistent pattern in this group. This could be due to the small sample size and also, there may certainly be several others factors involved in this process.

The dropout group had significantly lower physical performance and higher mortality rate but no difference in heart and lung disease or continuous prescription medication. Dropout occurred from all four groups, even though there were slightly more dropout from the T+N group. However, The T+N group did not improve more compared to for example the T group. Therefore we do not think that this invalidates the results of the thesis.

4.3.2 Paper 4

One limitation of the 1RM testing is that the subjects performed an average of six attempts before reaching 1RM, indicating a possible risk of exhaustion before reaching the maximum weight. This possibility constitutes an intrinsic problem when measuring 1RM. To circumvent exhaustion and decrease the risk of injuries, the American College of Sports Medicine suggests that after warm-up the initial load should amount to 60–80% of the predicted 1RM and reach 1RM within 3–5 attempts [177]. This study fulfilled these requirements for only some of the subjects, mainly because it is more difficult to estimate the starting load for this group of elderly people.
Another limitation is the small sample size in group 2. Altman [232] argues that there should be at least 50 subjects in an analysis of 95% limits of agreement; otherwise there might be a risk that the ranges vary too much.

4.4 CONCLUSIONS

- Leg muscle strength and the habitual physical activity level increased as an effect of a supervised physical training programme followed by home-based exercises.
- The combination of physical training and nutrition did not improve the results compared to physical training alone.
- No increase in aerobic capacity measured as maximal workload or time during bicycle ergometry was observed. An exception was subjects in the combined training group without lung disease, who significantly increased work time compared to subjects with lung disease.
- Subjects who improved muscle strength, balance and mobility had significantly higher compliance compared to non-improvers. There were moderate significant correlations between compliance of the home-based exercises and improvements in PADL and HRQL.
- There were no significant differences between on the one hand compliance and on the other hand age, sex, educational level, BMI, FFM, energy intake/kg body weight, heart and/or lung disease including spirometry measures and number of continuous prescription medications.
- 1RM evaluated by the Pulldown device seems to be a reliable and safe method for dosing and evaluating a muscle strength training programme for elderly people. The observed variation of approximately -4/+7 kg cannot be interpreted as an effect of muscle training, but is more likely an effect of learning, fluctuations in daily condition and/or motivation.

4.5 CLINICAL IMPLICATIONS

The results of this thesis show that targeted interventions are probably necessary to achieve a positive result for frail elderly people. Most likely, balance and aerobic training need to be more individualised and thereby more demanding in order to achieve improvements in balance and aerobic capacity. Many issues must be addressed in assessing and managing a frail elderly person's whole life situation. Therefore, a geriatric team approach is necessary, integrating health assessment with disease management. This frequently includes multiple interventions such as physical training, nutrition, medical drug prescriptions, technical aids, social support etc. In clinical settings, and where there is a lack of scientific evidence, the judgment of clinical relevance probably has to be set individually in relation to the particular elderly person's whole life situation.

When implementing assessment methods in clinical settings, it is important to strive for simplicity, minimal device cost and a non-time consuming procedures. The 1RM procedure presented here meets all of these requirements. The test can be conducted on existing equipment and is simple, highly reliable and safe for elderly people. Since progressive muscle strength training has been shown to be effective for elderly people, the importance of monitoring and dosing the intensity of a muscle strength training programme is vital for high-quality management, while at the same time considering the effects of learning, fluctuating daily condition and motivation.

4.6 FUTURE OUTLOOKS

Further research is needed in this area using targeted interventions compared to a control groups receiving ordinary care. This is e.g. supported by significant differences in physical performance between drop-outs and non-drop-outs, shown in this thesis. There is also a strong need for research regarding clinically relevant levels of outcome effects in multimorbid, frail elderly people. The lack of such studies may be explained by many potential confounding factors and difficulties in setting the "relevance limits"; such limits may also differ from person to person. However, measures for capturing relevant changes need to be explored more for frail elderly people.

To affect life-style attitudes, ADL and HRQL, behavioural and environmental barriers need to be addressed within the intervention.

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