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Maximal step-up height as a novel assessment of leg muscle strength and function – methodological and clinical studies

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Maximal step-up height as a novel assessment of leg muscle strength and function – methodological and clinical studies

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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With love to my wonderful family,
to all making this research possible,
to all doing daily maximal step-up,

to all searching further knowledge by exploring daily slow knee-bending.

CONTENTS

ABSTRACT

Physical performance is a strong predictor for morbidity and premature death and there is an increasing interest in the role of sarcopenia in many chronic diseases. There is a need for simple, robust and valid tests for assessing muscle strength and function in clinical practice. A novel maximal step-up test (MST) was developed and standardised to fulfil this need.

The aims of this thesis were to study the repeatability and validity of MST (Study I) and to study the associations to age, anthropometric variables, maximal oxygen uptake (VO_2 max) and self-reported physical function before and after a 3-month group training intervention programme (Study II). Furthermore, the aim was to study the long-term effects of the intervention programme on maximal step-up height (MSH) after an average of 22 months (Study III).

In Study I, MSH was tested with MST on middle-aged women and men (30/30) with capacity to work. 178 female patients were recruited from primary health care for Study II, all of whom had joint and muscular problems and most of whom also had reduced capacity to work, metabolic risk factors and other chronic diseases. For Study III, 101 out of these female patients were recruited. They participated in a 3-month group training intervention programme, which included three sessions per week of mixed aerobic fitness and strength training.

The repeatability of MSH between test occasions and between testers was 6 cm in Study I and 4 cm between testers at 22-month follow-up in Study III. In Study I, MSH was significantly correlated to isokinetic knee extension peak torque ($r=0.68$, $p<0.001$), self-reported physical function ($r=0.29$, $p=0.03$) as well as sex, age, weight and body mass index (BMI). MSH above 32 cm discriminated subjects with no limitation in self-reported physical function. In Study II, at baseline and after the 3-month intervention MSH was negatively correlated to age, body weight and waist circumference and positively correlated to self-reported physical function, VO_2 max and height. MSH correlated to training intensity at follow-up. Changes in MSH were significantly correlated to changes in waist circumference and physical function regardless of age and changes in VO_2 max. MSH below 24 cm discriminated female patients with self-reported severe limitation in physical function.

The long-term investigation in Study III showed that MSH increased significantly from 27.2 (5.7) cm at baseline to 29.0 (5.5) cm after three months and thereafter decreased to 25.2 (5.5) cm at the long-term follow-up. Time to follow-up (B=-0.42, p<0.001) and change in BMI (B=-0.29, p=0.012) correlated significantly to changes in MSH. Waist circumference, VO_2 max, physical function and exercise/physical activity levels were significantly improved at long-term follow-up, while BMI did not change. In a univariate logistic regression model, maintenance of MSH correlated to the extent of mixed training (OR 3.33, 95% CI 1.25-8.89). In a multivariate logistic regression model adjusted for important factors, the correlation was not significant. However, MSH was significantly higher in individuals participating in 2-3 sessions of exercise per week compared to one session.

In conclusion, the novel maximal step-up test assessing maximal step-up height is considered to be a useful and reliable test for leg function in clinical practice. It may also function as an indicator of metabolic health. The results of a 3-month group training intervention programme with 2-3 sessions per week of mixed aerobic fitness and strength training demonstrated increasing maximal step-up height, improved fitness and decreased risk in female patients with elevated cardio-metabolic risk. After an average of 22 months without regular group training, maximal step-up height was reduced again, while positive effects remained for waist circumference, VO_2 max, physical function and physical activity. However, regular group exercise 2-3 times per week with mixed aerobic fitness and strength training was associated with maintenance of maximal step-up height in a subgroup of women. Brisk walking for at least 150 minutes per week was not sufficient to maintain maximal step-up height in a subgroup of women.

SAMMANFATTNING PÅ SVENSKA

Fysisk förmåga är en stark prediktor för sjuklighet och för tidig död, och det finns ett ökande intresse för betydelsen av minskad muskelstyrka (sarkopeni) för uppkomst av kroniska sjukdomar. Därför finns det behov av enkla, stabila och pålitliga tester av muskelstyrka och benfunktion i klinisk vardag. Ett nytt maximalt klivhöjdstest (maximal step-up test, MST) utvecklades och standardiserades med denna intention.

Syftet med detta avhandlingsarbete var att studera upprepbarheten (repeatability) och betydelsen (validiteten) av MST (Studie I) och att studera sambandet mellan den maximala klivhöjden (maximal step-up height, MSH) och ålder, kroppsmått (längd, vikt, kroppsmasseindex (BMI) och midjemått), maximal syreupptagningsförmåga (VO_2-max), typ av gruppträning (intensitet), fysisk aktivitet (PA) och självskattad fysisk funktion (formulär SF-36, delskalan Physical function (PF)) före och efter ett interventionsprogram med gruppträning under tre månader (Studie II). Syftet var också att studera långtidseffekten av interventionen på MSH och övriga variabler efter en genomsnittlig tid av 22 månader (Studie III).

I Studie I testades MSH med hjälp av MST på medelålders kvinnor och män (30/30) med arbetsförmåga. Till Studie II rekryterades från primärvården 178 kvinnliga patienter med besvär i rörelseapparaten samt, i de flesta fall, nedsatt arbetsförmåga, led- och muskelbesvär, metabola riskfaktorer och andra kroniska sjukdomar. Till Studie III rekryterades 101 av dessa kvinnor. De deltog i ett tre månader långt gruppträningsprogram som innefattade tre pass per vecka med kombinerad konditions- och styrketräning.

Upprepbarheten av MSH mellan testtillfällen och mellan testare var 6 cm i Studie I och 4 cm mellan testare vid 22-månadersuppföljningen i Studie III. I Studie I korrelerade MSH till maximal isokinetisk knästräckningsförmåga ($r=0{,}68$; $p<0{,}001$), självskattad fysisk funktion ($r=0{,}29$; $p=0{,}03$) och till kön, ålder, vikt och BMI. MSH över 32 cm kunde urskilja personer utan begränsning i självskattad fysisk funktion. I Studie II kunde MSH under 24 cm urskilja kvinnliga patienter med minst en uttalad begränsning (SF-36, PF items). Vid studiestarten och efter 3 månaders intervention korrelerade MSH negativt till ålder, kroppsvikt och midjemått, samt positivt till självskattad fysisk förmåga, kondition (VO_2-max) och kroppslängd. MSH korrelerade till träningsintensitet vid uppföljningen. Förändringar i MSH var korrelerade till förändringar i midjemått och fysisk funktion oberoende av ålder eller förändringar i VO_2-max.

Långtidsuppföljningen i Studie III visade att MSH ökade från 27,2 (5,7) cm vid studiestart till 29,0 (5,5) cm efter 3 månader, och sjönk sedan till 25,2 (5,5) cm vid långtidsuppföljningen. Tid till långtidsuppföljning (B=-0,42; p<0,001) och förändring i BMI (B=-0,29; p=0,012) korrelerade till förändringar i MSH. Midjemått, VO_2-max, fysisk förmåga och motions-/fysisk aktivitetsnivå var signifikant förbättrade vid långtidsuppföljningen medan BMI var oförändrat jämfört med vid start. I en univariat logistisk regressionsmodell korrelerade bibehållandet av MSH till antalet pass/vecka med blandad konditions- och styrketräning i grupp (OR 3,33; 95% CI 1,25-8,89). I en multivariat logistisk regressionsmodell justerad för andra viktiga faktorer var korrelationen inte signifikant. Dock var MSH signifikant högre hos individer som deltog i 2-3 pass per vecka jämfört med ett pass.

Sammanfattningsvis anses det nya maximala klivhöjdstestet som mäter maximal klivhöjd vara ett användbart och pålitligt test av benfunktion i klinisk vardag. Det fungerar också som en indikator för metabol hälsa. Resultaten av ett 3 månader långt gruppträningsprogram med 2-3 pass per vecka med blandad konditions- och styrketräning visade på ökad maximal klivhöjd, ökad kondition och minskad risk hos kvinnliga patienter med ökad risk för hjärt-kärlsjukdom. Efter i genomsnitt 22 månader utan regelbunden gruppträning minskade åter den maximala klivhöjden, medan positiva effekter kvarstod för midjemått, VO_2-max, fysisk funktion och fysisk aktivitet. Regelbunden gruppträning med 2-3 pass med omväxlande konditions- och styrketräning var kopplat till bibehållen maximal klivhöjd. Enbart raska promenader om minst 150 minuter per vecka kunde inte bevara den maximala klivhöjden i en subgrupp av kvinnor.

LIST OF SCIENTIFIC PAPERS

I. Nyberg LA, Hellénius ML, Kowalski J, Wandell P, Andersson P, Sundberg CJ: Repeatability and validity of a standardised maximal step-up test for leg function-a diagnostic accuracy study. BMC Musculoskelet Disord 2011, 12:191.
DOI: http://dx.doi.org/10.1186/1471-2474-12-191

II. Nyberg LA, Hellénius ML, Wandell P, Kowalski J, Sundberg CJ: Maximal step-up height as a simple and relevant health indicator: a study of leg muscle strength and the associations to age, anthropometric variables, aerobic fitness and physical function. Br J Sports Med 2013, 47(15):992-997.
DOI: http://dx.doi.org/10.1136/bjsports-2013-092577

III. Nyberg LA, Sundberg CJ, Wändell P, Kowalski J, Hellénius ML: Long-term effects of group exercise intervention on maximal step-up height in female primary care patients with cardio-metabolic risk factors.
In manuscript.

PREFACE

My experiences of using physical activity and exercise as treatment in health care have been gathered during 35 years of medical work, of which 28 have been spent as a General Practitioner at Karolina Primary Health Care Centre in Karlskoga, a provincial Swedish town within Region Örebro County with around 30,000 inhabitants. Patients' aerobic fitness, strength and physical function have always been crucial to my clinical examination, choice of further investigation, assessment of diagnosis and suggested treatment. Over time, I have developed structured prescription of exercise and physical activity. My interest in exercise as a means of promoting well-being was established already in adolescence through formative experiences of a range of physical activities, outdoor recreation and competitive sport, in my case orienteering. This background influenced my interests at Medical School and stimulated my early subscription to membership of the Swedish Society for Physical Activity and Sports Medicine in 1980. It was also central to my decision to specialise in general medicine, an area where sports medicine could be brought to bear on everyday practice, a choice I have never regretted!

As a General Practitioner, I have always worked holistically with my patients, coaching them to set and reach individual goals for good health, not only to reduce cardio-metabolic risks, but also to help them reach optimal physical function for good health and quality of life. In this I drew substantially on my experiences from orienteering, both as an active competitor and as one of the doctors for the Swedish national team for twenty years. In these roles, I myself experienced that a person is 'no stronger than the weakest link', for example, physically, mentally or socially: everything needs to be optimised.

In my medical practice during the 1980s and 1990s, I prescribed recommendations for exercise for increased aerobic fitness, strength, health and quality of life at an evening health centre and also at an evening sports medicine centre, to which patients came on their own initiative. In my capacity as a medical doctor, I was able to answer questions and offer advice on how patients could plan and carry out exercise based on their needs and desires, while being mindful of former overuse or acute injuries and chronic diseases, other health risks and medication. The patients who came, either on the advice of medical staff or after their own researches, were already committed to exercise. They wanted to know their fitness level, how to initiate or restart exercise while suffering with, for instance, osteoarthritis, how to reduce the risk of overuse injuries or how to lose weight.

When medical practitioners tried to encourage suitable patients at my Primary Health Care Centre to visit the evening health centre instead, it was very difficult to persuade patients with a diagnosis or those who had no or reduced capacity to work to go there. The hardest group to motivate was those patients who described that they ‘did not feel well’. This group consisted primarily of women as two thirds of patients coming to primary health care are women. This situation gave me the idea and impetus to start the MABRA project – a new kind of group training programme in primary health care for both treatment and prevention of common diseases and disorders – focusing on precisely these kinds of patients in our daily clinical practice.

LIST OF ABBREVIATIONS

BMI	Body mass index
BOA	A supportive osteoarthritis self-management programme and register (Better management of patients with OsteoArthritis)
BP	Bodily pain (SF-36, subscale)
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
FaR®	Fysisk aktivitet på recept (PAP)
GH	General health (SF-36, subscale)
GP	General practitioner
HOOS	Hip disability and Osteoarthritis Outcome Score
ITT	Intention to treat
IKEPT	Isokinetic Knee Extension Peak Torque
KOOS	Knee injury and Osteoarthritis Outcome Score
LR	Likelihood ratio
MABRA	MÅ BRA project the name in the Swedish language
MH	Mental health (SF-36, subscale)
MET	Metabolic equivalent
MetS	Metabolic syndrome
MST	Maximal step-up test
MSH	Assessed maximal step-up height
eMSH	estimated MSH
aeMSH	advanced estimated MSH
n	number
OA	Osteoarthritis
OR	Odds ratio
PA	Physical activity
PAP	Physical Activity on Prescription (FaR®)
PE	Physical Education
PF	Physical function (SF-36, subscale)

PP	Per protocol
RE	Role limitation emotional (SF-36, subscale)
RP	Role limitation physical (SF-36, subscale)
SD	Standard deviation
SF-36	Short form (36) health survey
SF	Social function (SF-36, subscale)
T0	Measurements at baseline
T1	Measurements at 3-month follow-up
T2	Measurements at 14-30-month follow-up (mean of 22 months)
T2D	Type 2 diabetes
VO_2 max	Maximal oxygen consumption
VT	Vitality (SF-36, subscale)
WC	Waist circumference

1 BACKGROUND

1.1 INTRODUCTION – PRIMARY HEALTH CARE

In primary health care I have often encountered patients who, when asked, assess their level of aerobic fitness as low and who feel insufficiently strong. For these patients, this has often been their level of fitness and strength for many years. Research in the general field of physical activity and health is extensive. What is still missing, however, is research on how the new understanding brought by this research could be implemented in practice. Yet there is a lack of studies of established routine tests in clinical everyday practice of leg muscle strength and physical function. The need for assessment is much greater than a well-functioning physiotherapy service could reasonably manage. Because of the pressing need for large numbers of patients to be tested on leg muscle strength and leg function, and because the results from these tests – which are perishable goods – are needed at the very moment when a patient visits her or his GP or nurse, we need to find new and simple tests and routines.

Since primary health care has a central function when assessing, investigating and treating patients' health as a whole, it is of great significance that these studies of practical implementation and testing of physical function ought to start in primary health care. In Study I presented below, a novel test for assessing leg muscle strength and leg function – maximal step-up test (MST) – is introduced, that would be easy and quick to use by GPs, nurses and physiotherapists in everyday clinical practice [1].

General practice differs between national contexts. In Sweden today, it is common with an integrated form of practice where GPs, nurses, physiotherapists and other health professionals work as teams around a range of areas of expertise. Some examples of areas where prescription of physical activity as treatment and prevention (PAP, FaR®) are recommended according to the latest research (www.fyss.se/FYSS 2015) are cardiovascular disease/lifestyle, type 2 diabetes (T2D), chronic obstructive pulmonary disease (COPD) and symptomatic osteoarthritis (OA). One significant advantage of locating an intervention programme within primary health care – which was the case with the MABRA project described in this thesis in Studies II and III – is that it can be designed from the holistic perspective that the GP is afforded, knowing the full and varied history of each of her patients [2]. This understanding of the patient as a whole is also helpful when encouraging and supporting participation in such a project. In addition, GPs and teams of health care professionals in primary health care support their patients by offering continuity and coherence within a health care sector that is becoming increasingly specialised and fragmented.

1.2 WHY STUDIES ON WOMEN?

Stories of tiredness and a difficulty to cope with both work and looking after the home are common when we meet working-age women. A relevant question to ask in these cases is to what extent this experience may be due to low levels of aerobic fitness and low muscle strength. If the physical capacity is deemed to be low in one or both of these ways, the follow-up questions ought to be about what other potential consequences there may be of reduced fitness and strength, such as increased cardio-metabolic risk. These questions are especially important when a reduced capacity to work results in sick leave with cessation of transportation to work and reduced everyday activity: in sum, increased sedentary behaviour.

Studies have shown that women visit primary health care more often than men and it seems to be associated with their higher morbidity burden. The interaction between biology and socially constructed roles could also underlie this higher use by women, and is therefore an area that deserves further in-depth research [3]. There is also research to suggest that women still, on average, take greater responsibility for the practical running of the home and for childcare than men [4]. The majority of previous studies of physical function and health has most often been focused exclusively on men. For reasons of equality and democracy not least, there is thus an urgent need for studies of women’s physical function in relation to poor health, and of the most effective methods of treatment of low aerobic fitness and low muscle strength. These principles make up the background for the planning and implementation of the 3-month intervention programme from which data from a female population of patients aged between 22 and 83 have been gathered. Data collected at registration and at the end of the programme have been analysed in Study II, whereas data from the long-term follow-up at a median of 22 months form the basis of Study III.

1.3 KARLSKOGA MABRA PROJECT – A PRACTICAL TRAINING PROGRAMME FOR PATIENTS IN PRIMARY HEALTH CARE

The MABRA project was set up in the Swedish provincial town of Karlskoga to care for patients with a range of common diseases and illnesses for whom intervention with physical exercise was deemed beneficial for improved general health and well-being. As outlined in the Preface, the stimulus came from a felt need to support patients who required active intervention from health care professionals to start and maintain regular physical exercise at low, moderate or high intensity. The project consisted of a 3-month intervention programme in which patients committed to exercising in groups three times per week. Data from this project were used in Studies II and III. The principles and objectives for the MABRA project described below were discussed and agreed within the project team before the start of the project and then followed throughout.

Funding for the Karlskoga MABRA project came from Region Örebro County, the Swedish National Institute of Public Health (Folkhälsomyndigheten), Karlskoga Municipality, the Swedish Social Insurance Agency in Karlskoga (Försäkringskassan) and the Karlskoga Job Centre (Arbetsförmedlingen), all in Sweden.

1.3.1 Key objectives

One key objective for the project was to introduce patients to different forms of exercise by which to improve aerobic fitness and muscle strength, as treatment and for reducing cardio-metabolic risks. Another main objective was that the sum total of care throughout the intervention programme would improve patients' capacity to work.

1.3.2 Forms of exercise

A varied range of group activities was offered to maintain high engagement and participation. The forms of group exercise available mostly consisted of mixed aerobic fitness and strength training, such as circuit training, spinning, aqua aerobics and Nordic walking on forest tracks. Dance and movement therapy was chosen by patients with specific needs, most often psychiatric illnesses, in order to facilitate participation in group exercise. Qigong was chosen by patients suffering from stress or with chronic pain or fibromyalgia. Medical advice was available at every session. All patients were offered an individually tailored programme of self-selected group exercise, discussed with medical support at registration, which could be revised after tests and during the first two weeks of the programme if necessary.

Particular emphasis was placed on teaching patients to improve leg muscle strength in everyday life; for instance, by choosing the stairs rather than the lift or by using step-up boards at the gym with the same technique as used for the maximal step-up test.

1.3.3 Engagement and motivation

Great care was taken when selecting members of the project team to ensure that their attitude would engender increased confidence and well-being in patients. The members of the project team shared a keen awareness of the importance of the attitude communicated to patients and worked to create an environment in which exercise became enjoyable. For example, they used music to stimulate and engage patients and provided a positive atmosphere with plenty of encouragement and support. There was no discussion of illness or health care during the scheduled exercise.

Patients were asked to commit to exercising three times a week for three months in order to be admitted to the project. This requirement was included to ensure a sufficient level of motivation to carry out the intervention programme.

1.3.4 Accessibility and equality of care

Offering accessibility and equality of care was another core principle. The project was open to patients of both sexes, over the age of nineteen, with common diseases and illnesses. All exercise sessions during the 3-month intervention programme were free of charge for patients to ensure equal access. Accessibility was also promoted by organising group exercise in a large number of different locations across the town.

Short waiting times for taking up a place in an exercise group were guaranteed throughout. Flexible groups were created so that patients could begin group exercise straight at the point of inclusion in the project and new groups were started when needed. To make this possible, collaboration was initiated with local gyms and public health units. The optimal total number of patients within group activities at any one time was around 75 for the size of the project team in question, described in 1.3.5. At that level, each patient could be fully cared for. At its most extensive, there were around 130 patients participating in group exercise in parallel.

An intention within the project team right from the start was that the experience of regular physical exercise would encourage patients to maintain a sufficient level of physical activity long-term. At the end of the programme, patients were systematically referred to group exercise or individual exercise by a nurse. They were asked to report on their progress to their GP. These follow-on groups are today, after more than fifteen years since the start of the first groups, still on-going and led by instructors at local gyms or public health units who have been trained by the project team in supporting continuing exercise for these patients.

Due to a lack of resources for translation and interpretation it was not possible to include participants without a working knowledge of the Swedish language in the project.

1.3.5 Organisation of the project

The project team consisted of a project leader (GP) and four other members: a nurse as project coordinator; a nurse with a degree in Dance and Movement Therapy who took up the role as project coordinator later on in the project; and two certified exercise instructors who were also certified testers. The main tester had six years of experience from medical rehabilitation work. The project coordinator had over thirty years of experience as a nurse in clinical practice and primary health care and several years of experience of teaching nursing students at tertiary level. The members of the project team were carefully selected for their experience, skills and attitude. The practical organisation of the work within the project team was democratic and non-hierarchical.

The reason for hiring exercise instructors and testers as part of the project team was the high workload of physiotherapists employed at local primary health care centres, without room in their schedules for the level of involvement required by the project. However, physiotherapists at patients' local primary health care centres were consulted when support was needed on the level of an individual patient.

Medical care and consultation about sick leave were offered to patients by their ordinary GPs throughout the project.

1.3.6 The project team

<u>The project leader (GP)</u>

- offered medical advice and support at team meetings every week
- kept in touch with health care centres and units, local authorities and public agencies such as the Swedish Social Insurance Agency (Försäkringskassan) and the Job Centre (Arbetsförmedlingen)
- was responsible for producing material for collection of data
- continuously reported on findings to funding bodies
- had regular contact with doctoral supervisors at research centres and departments at Swedish and international universities
- contacted researchers for support with evaluation of results within health economic
- communicated with ethical committees
- applied for funding

The project coordinator (nurse)

- registered all patients at inclusion in the project
- acted as the patients' medical coordinator
- conducted a structured interview of one and a half to two hours at the start of the project which included
    - constructing a health profile based on patient questionnaire
    - discussion of potential interference of medical problems, social functionality and lifestyle with the exercise programme
    - measuring the patient's weight, height, BMI and waist circumference
- recorded self-assessed quality of life at start and follow-ups, especially with respect to physical function (SF-36)
- organised an obligatory talk by a nurse from the local public health unit to patients, giving them a basic understanding of the impact of diet on the effects of exercise

Testers and exercise instructors

- measured leg strength with maximal step-up test at start of project and at follow-up after the 3-month intervention programme and long-term;
- tested aerobic fitness with submaximal cycle test at start and follow-ups;
- planned and ran group exercise at appropriate levels;
- organised an obligatory talk by a physiotherapist on basic exercise physiology for patients with locomotor problems and prevention of acute and overuse injuries;
- arranged for physiotherapists to design appropriate programmes of strength training for patients with shoulder, neck/back, hip or knee problems;
- used the Borg RPE Scale for intensity control at each exercise session and taught patients to use it for themselves for the future;
- ensured that the pace of the music accompanying each exercise session set the level of intensity, low, moderate or high (Borg 9-11, 12-13 and 14-15).

The use of step-counting devices was discussed, but at time of the intervention programme this technology was comparatively premature and such measuring would have been logistically challenging to arrange at the time.

1.4 PHYSICAL ACTIVITY , AEROBIC FITNESS, MUSCLE STRENGTH AND HEALTH – CARDIO-METABOLIC RISKS

Numerous studies have shown a strong correlation between physical activity and health [5, 6] and both aerobic fitness and physical activity are independently associated with lower cardiovascular risk [7, 8]. Low aerobic fitness is an important predictor of mortality especially among women [9]. Notably, our study of female patients showed that VO_2 max at baseline was low compared to that of healthy women in other studies [10, 11]. Hakola *et al.* have shown that the number of chronic diseases was inversely associated with VO_2 max [11]. Furthermore, physical work capacity declines with age due to decreases in aerobic and musculoskeletal capacity.

A strong correlation has been shown between the degree of physical activity and premature death [9, 12-14], cardiovascular disease (CVD), type 2 diabetes (T2D) [15], colon and breast cancer, osteoporosis, symptomatic osteoarthritis (OA), asthma/COPD, depression and dementia. There is also a strong correlation between weak muscular strength and a high prevalence of obesity and metabolic syndrome (MetS) [16], premature death [17-19] and cancer [20]. Moreover, the assessment of the functional capability can help to determine the degree of physical decline in persons with MetS [16]. A large population-based study from 17 countries – which was run for four years with nearly 140 000 individuals (58% women) with median age 50 (42-58) years and with varying income and sociocultural background – showed that grip strength was a stronger predictor of cardiovascular and all-cause mortality than systolic blood pressure [21]. Knowledge about identified associations between psychological symptoms and common physical functions [22] – for example, reduced leg muscle strength – is important in prevention and treatment of our common diseases and disorders.

Assessment of physical activity, fitness, muscle strength and physical function is of great importance in clinical practice for diagnosis, treatment and follow-up of individuals at risk for, for instance, CVD and metabolic disease [7, 9, 23-25], symptomatic OA [26] the chronically ill [27] and patients with limited physical working capacity [28, 29]. Furthermore, objectively assessed physical performance – such as low maximal oxygen uptake [7, 9, 30] or low muscle strength [31, 32] – is a strong predictor of morbidity and premature death independently of physical activity and muscle mass. Interestingly, in men <60 years of age the rate of loss of strength has been shown to be more important than actual strength [33]. Muscle strength also provides a better estimate of mortality risk than does muscle quantity [34].

Recent evidence-based recommendations include endurance as well as resistance training [6] for health benefits. Loss of muscle mass and knee extensor strength correlates with an increased risk of falling and loss of functional independence, and has been identified as the most important factor limiting the ability to get up from a chair [35]. A primary risk factor for knee pain is quadriceps muscle weakness, disability and progression of joint damage in persons with OA of the knee [36], one of the most common medical conditions from middle age onwards [36, 37].

There is therefore a need in clinical practice for simple, robust and specific tests of leg strength and leg function to provide clinically relevant measures that reflect overall health. However, the tests recommended to date have several shortcomings. First, many tests – for example, walking tests – do not capture muscle strength *per se* but rather a combination of muscle strength and aerobic capacity. Second, robust standardisation of the performance test procedure is rare. Third, few tests allow discrimination between the two legs. Fourth, the vast majority of tests have been validated for elderly populations only. In a review of published studies that tested the validity and reliability of fall-risk assessment tools, few tools were tested more than once or in more than one setting [38] and the authors did not recommend a single tool for implementation.

1.5 OSTEOARTHRITIS – EXERCISE RECOMMENDED AS THE FIRST LINE OF TREATMENT

Early clinical diagnosis of chronic knee and hip osteoarthritis (OA) is important for prevention and treatment [26, 39]. A physiotherapist diagnoses clinical osteoarthritis using national guidelines in the context of patients' needs, providing information, supervised exercise, self-administered tests for strength and aerobic fitness, lifelong physical activity on prescription and a collaborative approach to dealing with weight loss [39].

It is important to treat risk factors for cardiovascular disease and premature death. Osteoarthritis in knee and hip reduces patients' physical activity, strength and fitness, and increases sedentary behaviour. A better understanding of sarcopenia helps practitioners identify implications for patients with OA [40]. Today one of the recommended assessments of leg function for OA patients is a 30-second sit to stand test [41]. Together with a test of controlled knee bending useful in clinical practice – for example, 'pick up a pencil from the floor using knee bending' – these tests could be used by all health care staff and also be suitable for self-testing.

From studies we know that patients with early symptomatic osteoarthritis showed worse functional capacity and self-reported health compared to healthy ageing workers. Patients with early symptomatic osteoarthritis of the hips and knees participated in the 3-month intervention programme in the Karlskoga MABRA project. In a study, a substantial proportion of female subjects with osteoarthritis reported worse mental health status in SF-36 than their male counterparts [42]. Also, when subjects with early symptomatic osteoarthritis of the hips and knees were studied, many female subjects did not meet physical job demands as was the case for many female patients with reduced leg muscle strength and function in Study II and III of this thesis [42].

In another study, information about a person's functional capacity to work was found to have complementary value for assessment of physical capacity to work [43], and also changed the judgments of the medical professional [44]. Testing of functional capacities together with self-reported physical function and health is widely used to discriminate potential patients from healthy persons, and to describe aspects where the patients do not meet physical job demands. In patients with hip and knee OA undergoing surgery, performance-based functional outcome tools give additional information to the patient's report in Hip disability and Osteoarthritis Outcome Score (HOOS) and Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaires. This will reduce difficulties in distinguishing between pain and function and will reduce floor and ceiling effects [45, 46]. Compared to preoperatively, a significant improvement in KOOS was still seen 5 years postoperatively, the best result was reported at 1 year, indicating a decline from 1 to 5 years after total knee surgery. To fully evaluate the results with regard to pain and PF, follow-ups after more than 2 years were recommended [47]. MST could be a useful test of leg strength and function as a complement to HOOS and KOOS questionnaires for patients undergoing OA joint replacement surgery and future research is recommended. Moreover, research on the usefulness of MST as a tool for prescription of physical activity for patients with OA in hip and knee and for long-term follow-ups is also recommended.

Exercise is recommended as first-line treatment of degenerative knee disease. Today in primary health care in Sweden, patients with OA in hip and knee are invited to a supportive osteoarthritis self-management programme called BOA (Better management of patients with OsteoArthritis). The self-management programme converts the scientific evidence on how best to train the arthritic hip and knee into clinical practice. The supportive osteoarthritis self-management programme is always led by a physiotherapist, often in collaboration with an occupational therapist and an osteoarthritis communicator. The knowledge transferred from scientific research to medical professionals and then onto patients enables patients to make decisions about personal health and changes in lifestyle for better health. The BOA register has existed as a National Quality Register for physiotherapists in Sweden since December 2010, www.boaregistret.se.

A supportive osteoarthritis self-management programme can reduce self-reported hip [48, 49] and knee pain and increase self-reported quality of life. OA patients ranging from mild to advanced symptomatic OA took part in the MABRA intervention programme studied in this thesis. They have been assessed with repeated MST and our experiences from these patients are good with no major side effects reported when assessing according to standardisation. MST addresses many components in neuromuscular exercise, targeting more closely the sensorimotor deficiencies and functional instability associated with the degenerative knee disease than traditionally used training methods [50].

Today's guidelines for clinical diagnosis of OA in knee and hip are shown in Figures 1 and 2.

Figure 1. Clinical diagnosis of osteoarthritis of the knee

- **Anamnesis (risk factors):** age, gender, overweight, previous joint injury, overuse at work or at home and heredity.
- **Symptoms:** pain at straining of the knee, reduced functionality and stiffness in the morning.
- **Clinical findings at examination of the joint:** crepitation, reduced mobility and widened joint.
- When three symptoms and only one or two clinical finds are present a less serious level of osteoarthritis is indicated.

Guidelines on osteoarthritis from the National Board of Health and Welfare, 2012

Reproduced with permission from Läkartidningen [39].

Figure 2. Clinical diagnosis of osteoarthritis of the hip

- **Anamnesis (risk factors):** age, gender, overweight, previous joint injury, overuse at work or at home and heredity.
- **Symptoms:** pain in the hip, stiffness after inactivity and reduced functionality.
- **Clinical findings at examination of the joint:** reduced flexion, inward rotation and pain at inward rotation.
- Several typical symptoms and clinical findings need to be present for a high diagnostic value.

Guidelines on osteoarthritis from the National Board of Health and Welfare, 2012

Reproduced with permission from Läkartidningen [39].

1.6 DEFINITIONS OF PHYSICAL ACTIVITY

The definitions of physical activity and related terms in this section have been translated and reworked from the 2015 edition of FYSS (Physical activity in the prevention and treatment of disease, www.fyss.se). FYSS has been written, and is continuously updated, on behalf of the Professional Associations for Physical Activity (YFA) in Sweden and funded by the The Public Health Agency of Sweden (Folkhälsomyndigheten). Reproduced with permission from YFA.

Physical activity is characterised by complex behaviour. It is defined, in physiological terms, as all movement of the body that increases the consumption of energy above and beyond the energy we consume at rest. Physical activity may occur at home, at work, during transportation from one place to another, in one's free time and in the form of organised exercise. Physical inactivity thus consists of an absence movement; that is to say, close to the consumption of energy we experience at rest. In some studies, physical inactivity is used as a classification to describe persons who do not fulfil the recommendations for level of physical activity. In FYSS, persons who do not fulfil these recommendations are described as 'inadequately physically active'. In Sweden, the concept of sedentary is also used to describe inactivity. A day consists of a mixture of types of inactive behaviour (lying down, sitting, standing) and different types and degrees of physical activity (bodily movement at low to very high intensity).

A person who is physically active at moderate intensity for 150 minutes per week is classified as ‘sufficiently physically active’. That phrase, however, does not say anything about the level of activity during the remaining waking hours. That means that it would be possible for a person to be described as, at once, ‘highly active’ and ‘sedentary’. Aerobic physical activity, the most common form of physical activity, is characterised by the need for energy, in the first instance, being covered by processes that expend oxygen. The intensity may be low, moderate or high. The general guidelines suggest that the recommended dosage of physical activity (at least 150 minutes per week) ought to be aerobic in character, and that the intensity ought to be at least at moderate level to lead to positive health effects. Aerobic fitness training is a form of aerobic physical activity with the purpose to maintain or improve fitness. The intensity could be at a moderate, high or very high level. Strength training is a form of physical activity where the intention, in the first instance, is to maintain or increase different forms of muscular strength (for instance, maximal power, explosiveness and/or muscular stamina) and to maintain or increase muscle mass.

1.6.1 Intensity – absolute and relative

Intensity describes the level of strenuousness at which physical activity is carried out. It is normally divided into several levels from very low to very high. Moderate intensity is characterised by an increase of pulse and frequency of breathing. High intensity means a marked increase in pulse and frequency of breathing, while very high intensity means maximal levels of pulse and frequency of breathing with anaerobic use of energy as a consequence, such as the formation of lactic acid. Intensity may be expressed as absolute or relative. The strenuousness at muscle-strengthening activities may be given as absolute intensity in relation to a person’s maximal ability (% 1RM=maximal strenuousness at repetition). Intensity can also be assessed as experienced exertion with the help of different scales, such as Borg’s RPE scale. Such self-assessed exertion is an expression of relative intensity [51].

An individual’s consumption of energy at rest is used to assess the energy use for a specific activity or for a day. The energy consumption of the specific activity or day is expressed as a multiple of the energy used at rest. The expression metabolic equivalent (MET) is used as shorthand. Energy consumption at rest is the equivalent of 1 MET. Energy consumption during a brisk walk, for instance, is assumed to be four times as high as at rest and is thus expressed as 4 METs. As an estimate, it is generally calculated that 1 MET is the equivalent of an oxygen consumption of 3.5 ml per kg of body weight and minute, or as an energy consumption of 1 kcal per kg of body weight and hour. These models for conversion are used when uptake of oxygen or energy consumption per unit of time are calculated based on METs. MET minutes or MET hours are concepts used to describe total energy consumption across time.

1.7 SELF-REPORTED HEALTH WITH FOCUS ON PHYSICAL FUNCTION

The Short Form (36) Health Survey, more commonly known as SF-36, is a patient-reported questionnaire for assessing patient health. It has been designed as a general indicator of patient health for use in population studies and evaluative studies of interventions for improving health. As a tool, it can also be used together with tests for specific diseases in clinical research. It is a self-instructing questionnaire which takes 5-10 minutes to fill out and presents eight dimensions of self-assessed health: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. The different dimensions cannot be summarised as one. Instead results are reported in the form of health profiles consisting of eight different scores.

When used on persons of good health who increase their level of physical activity, the SF-36 scores on physical functioning and mental health may be too low for recorded improvements of health to be significant. The highest score for physical functioning corresponds to the most basic capacity for participating in any form of strenuous activity such as running or lifting something heavy. It is common for the SF-36 questionnaire to be used at rehabilitation of particular groups and when studying physical activity in elderly populations. The questionnaire is one of the most frequently used tests in Sweden today and there is a Swedish translation which is commonly used [52].

Two thirds of the patients in the project were on temporary part-time or full disability pension or sick leave at the time of referral. They had low scores on the SF-36 physical scales and also low scores for mental health. In the Swedish norming population [53], low scores in SF-36 were associated with women, social risk factors such as disability pension and unemployment, reduced physical functioning and increased bodily pain. Physical function scores were strongly associated with age, whereas there were only small differences in the mental health scales across age groups [53].

2 AIMS

The aims of this thesis were to study the repeatability and validity of MST (Study I) and to study the associations to age, anthropometric variables, maximal oxygen uptake (VO_2 max), and self-reported physical function before and after a 3-month group training intervention programme (Study II). Furthermore, the aim was to study the long-term effects of the intervention programme on MSH after a mean of 22 months (Study III).

2.1 STUDY I

The aims were to evaluate a novel method for measurement of lower-extremity function, the standardised maximal step-up test (MST), by assessing maximal step-up height (MSH) repeatability and MSH relation to leg muscle strength assessed as isokinetic knee extension peak torque (IKEPT), in relation to health-related quality of life (SF-36, subscales for physical function (PF), bodily pain (BP) and general health (GH)), individual characteristics and self-reported physical activity (the International Physical Activity Questionnaires, IPAQ, short form) and MSH cut-off for any limitations in physical function (SF-36, PF score and summary of selected item responses).

2.2 STUDY II

The aims were to investigate – in a female patient population with common diseases, elevated cardio-metabolic risk, musculoskeletal pain and reduced capacity to work – the associations between maximal step-up height (MSH) and age, anthropometric variables, maximal oxygen uptake (VO_2 max) and physical function as well as the effects of a 3-month group exercise intervention on MSH.

2.3 STUDY III

The aim was to investigate – in a female patient population with common diseases, elevated cardio-metabolic risk, musculoskeletal pain and reduced capacity to work – the long-term effects of a 3-month group exercise intervention on MSH, cardio-metabolic risk factors and physical function. Furthermore, we studied factors associated with long-term effects on MSH in the whole study population, in subgroups of patients of different ages, as well as in subgroups with high, moderate or low maintenance of MSH.

3 MATERIALS AND METHODS

3.1 DESIGN

3.1.1 Study I

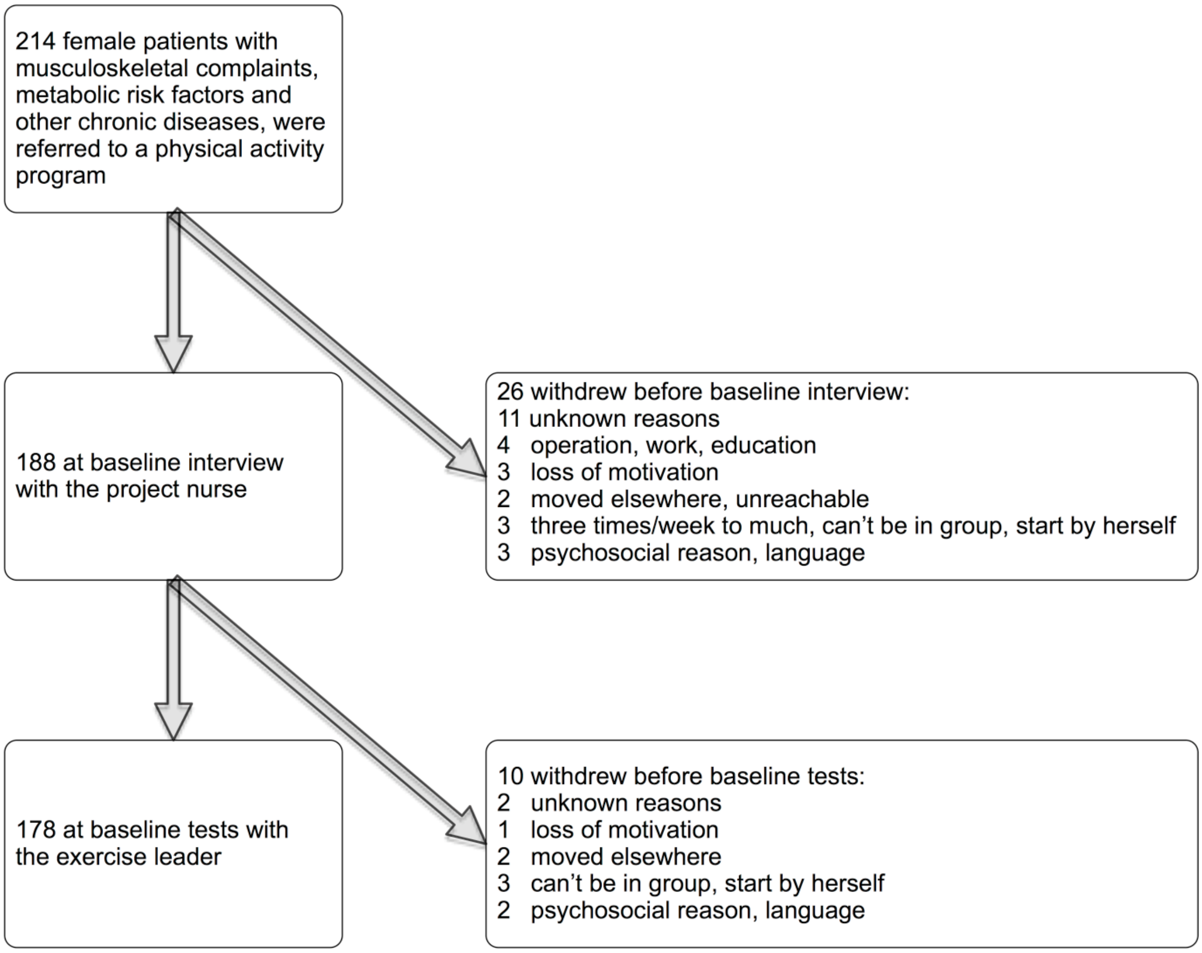
Subjects were invited in groups of ten to two test occasions (occ 1 and occ 2), one week apart, for intra-tester assessment of MSH test-retest repeatability. Four weeks after occ 1, the participants came individually to the third test occasion (occ 3) for assessment of IKEPT and MSH test-retest repeatability (comparing occ 1 and occ 3). At occ 1 and occ 2, MSH was assessed twice at least 30 minutes apart by two testers – the first author and a tester accustomed to the MST – in random order for assessment of inter-tester test-retest repeatability. MSH of both legs was assessed with the MST on all three occasions.

The MST values remained secret between testers and occasions, and the subjects agreed not to inform the tester of earlier results. Weight and height were measured at occ 1, and weight at occ 3. The SF-36 was assessed at occ 1. Physical activity levels during the week between occ 1 and occ 2 and the week before occ 3 were assessed. The subjects were instructed to maintain their ordinary physical activity habits during the study. At occ 3 all subjects began with an MST conducted by the first author. 30 minutes after the test, IKEPT was measured by a physiotherapist well acquainted with the procedure.

3.1.2 Studies II and III

214 female patients were recruited consecutively over an 18-month period, through referrals from primary health care, to an on-going 3-month intervention programme with group exercise three times per week (Karlskoga MABRA project). The patients' ability and willingness to take part in the project were documented. Data were collected at baseline and immediately after the 3-month intervention. Out of the 214 female patients, 178 attended the test at baseline (T0) and 156 of those participated in the 3-month intervention programme and took part in a second assessment (T1) [2]. Out of these 156 patients, 114 were randomly invited for a third assessment (T2), out of whom 101 agreed to participate (89% response rate). The reasons not to attend the long-term follow-up were diverse, see Figure 3.

Figure 3. Flowchart describing the inclusion, sample sizes and drop-out numbers



178 patients (83% response rate) were included out of 214 female patients referred to the 3-month intervention programme. The reasons for not attending were diverse.

3.2 STUDY POPULATIONS

3.2.1 Study I

The inclusion criteria were: 1) female or male, 2) 30-65 years old, 3) no self-reported complaints associated with legs or hips leading to a visit to a health care unit within the previous six months, 4) no major health problems that interfered with climbing stairs, 5) from inactive to regularly physically active, 6) never before having been tested with a step-up test, climbing test or on an isokinetic device, 7) well motivated, and 8) have working knowledge of the Swedish language. Invitations were distributed to a number of workplaces, a men's running group and their partners. 30 women and 30 men with a median (range) age of 53 (34-63) and 55 (36-64) years respectively were enrolled. All female and male subjects were in employment and came from about 20 different workplaces respectively. They represented a wide variety of professions and educational backgrounds.

3.2.2 Studies II and III

The inclusion criteria were: 1) voluntarily seeking primary care for a common complaint or disease related to the musculoskeletal system, obesity, cardiovascular disease, diabetes, asthma/chronic obstructive pulmonary disease (COPD), mental disorders (that is, depression, anxiety, stress related symptoms, sleep disturbances, burn-out syndrome and fibromyalgia), and/or other chronic diseases against which increased physical activity was deemed likely to be beneficial, 2) aged 19 years or over, 3) sufficiently motivated and willing to accept group training three times per week for three months, 4) able to take part in group training without personal assistance, 5) able to transport herself independently to and from the exercise activities, and 6) have working knowledge of the Swedish language.

Half of the 178 female patients included had upper secondary school as their highest level of education; one third had been to university or college. Most of the patients (72%) were married or co-habiting. A majority (66%) was on sick leave or had part-time or full temporary disability pension. 16% were working despite medical problems. 5% were working and were allowed two hours three times per week of exercise as illness-prevention or rehabilitation with financial support from the Swedish Social Insurance Agency (Försäkringskassan). 10% had old-age pension and 3% were looking for a new job and receiving job seekers' allowance.

The main chronic diseases, psychosocial conditions, illnesses and complaints in the musculoskeletal system (symptomatic osteoarthritis was common), were diagnosed and documented by the referring GP on the standardised referral documents. Medications were reported by the referring GP and confirmed by the patient at inclusion. Over two thirds (71%) of all 178 patients were taking analgesics. 88 (49%) of the patients had at least one of the psychosocial conditions diagnosed in primary health care – depression, anxiety, stress-related problems, sleep disturbance, burn-out syndrome or fibromyalgia – and 49 (56%) of these 88 patients were taking medication for these indications. Daily smoking was reported by 26%. No significant difference in baseline measurements between the 101 participating patients and the remaining 77 were found regarding anthropometry, education, sick leave, self-reported pain and/or reduced physical function. However, age differed significantly, with a higher mean age in the 101 participants compared to the 77 who did not participate in T2 (mean 52 years versus 47 years, p=0.003).

3.3 ETHICAL APPROVAL

Written informed consent was obtained from all participants after oral and written information about the studies had been provided. The local ethics committee at Örebro County Council approved all procedures for all three studies.

3.4 MEASUREMENTS

3.4.1 Patient characteristics

Height was measured without shoes to the nearest 0.5 cm using a scale fixed to the wall. Body weight was measured in light clothing without shoes to the nearest 0.1 kg using electronic scales (Seca Delta model 707). Body mass index (BMI) was calculated according to the standard formula ($kg \cdot m^{-2}$). In Studies II and III waist circumference (cm) was assessed at the level of the umbilicus according to standard practice.

3.4.2 Isokinetic knee extensor peak torque

IKEPT ($N \cdot m$, $60° \cdot sec^{-1}$), essentially reflecting maximal concentric quadriceps strength, was assessed in an isokinetic dynamometer (Biodex System III PRO, Biodex Medical System, New York, NY, USA) due to standard praxis (Study I).

3.4.3 Aerobic fitness – Åstrand's submaximal test on oxygen consumption

In Studies II and III the VO_2 max was estimated as described by Åstrand [54] from each participant's individual heart rate response to a given sub maximal workload (that is, 50-150 W, depending on the participant's weight and self-reported physical activity) using a bicycle ergometer (Monark, Varberg, Sweden) recorded at a steady state of heart rate (120-150 $beats \cdot min^{-1}$), and quantified as peak absolute oxygen consumption per minute ($L \cdot min^{-1}$) and per kg body weight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$).

3.4.4 SF-36 physical function score

To assess self-reported health-related quality of life, the Swedish version of the SF-36 was used [52]. Patients filled out the forms in advance and at the visit assistance was given when needed as directed in the manual. All raw scores were transposed onto scores on a weighted 0-100 scale, higher scores representing better health status [55]. The subscales physical function (PF), bodily pain (BP) and general health (GH), all with a strong correlation to age [53], were used to describe subjects in Study I. All eight subscales were used in Studies II and

III, and compared with the general Swedish population. The subscale PF was extracted for further item analyses. A selection of items 3a, 3b, 3d, 3f and 3g, assumed by the authors in this study to be suitable for assessment of subjects with capacity to work, were used for comparison with the first assessment of MSH (mean of right and left leg) at occ 1 in Study I. A selection of items 3b, 3d, 3f and 3g, assumed suitable for assessment of patients, were used for comparison with all assessments of MSH (mean of right and left leg) in Studies II and III.

This scale was also used to investigate whether any MSH score cut-off level identified subjects in Study I with any limitation (score <100), and in Study II with severe limitation in physical function.

3.4.5 Physical activity

A locally adapted version of the self-administered International Physical Activity Questionnaire (IPAQ), 'the last 7 days short form questionnaire' [56], was used for assessing self-reported physical activity ($min \cdot wk^{-1}$) in Study I. Energy expenditure ($kcal \cdot wk^{-1}$) was calculated according to MET (Metabolic Equivalent) estimates [57]. Mean energy expenditure from reported vigorous and moderate activity and strength training time over a two-week period were used.

3.4.6 Self-reported exercise and physical activity levels

Exercise and other physical activity were assessed at baseline (Studies II and III) and at the third assessment (Study III) with a validated questionnaire used in occupational health care in Sweden [58]. The physical activity question included a definition of exercise, that is, to allocates time for exercise in order to maintain or improve fitness, health and wellness [58].

3.4.7 Exercise and physical activity measurements

In Studies II and III leisure-time physical activity was not registered during the 3-month group exercise intervention. The patients filled in an exercise diary at each training session and the coaches checked and signed the diary. The self-selected workouts were evaluated in groups of i) mixed aerobic fitness and strength training, ii) aerobic fitness training, and iii) strength training. The number of exercise sessions per week (t.p.w), the number of minutes of exercise per week (m.p.w) and the intensity during each session (6-20 Borg RPE Scale) were recorded. The number of dance therapy and Qigong sessions (replacing other types of exercise) – often chosen because of fear of movement or to improve balance and coordination – were registered and included in the sum total of exercise. An effort equivalent of at least 30 minutes of brisk walking corresponding to 11-13 Borg RPE Scale level was required for registration as an exercise session.

3.4.8 Diagnosis

A standardised and structured protocol was used by GPs to refer patients to the intervention programme. It included information on common diseases, joint pain or discomfort (14 localisations), and medication, if any.

3.4.9 Capacity to work

The capacity to work, prevalence of sick leave, disability pension and/or job seekers' allowance were also recorded in the protocol used by GPs when referring patients to the intervention programme. The length of time when a patient did not have capacity to work – that is, when no time was spent at work or on transportation in connection with work – was deemed to influence the total amount of patients' physical activity and sitting-time. The variance in time to long-term follow-up in Study III could be influenced by this.

3.5 MAXIMAL STEP-UP HEIGHT – A NOVEL ASSESSMENT OF LEG STRENGTH AND FUNCTION

Stepping up onto something is a movement that is natural to most people. This was the basic idea behind developing a standardised test for measuring leg strength and function over time. A key criterion for the test at the stage of development was that it must be simple and realistic to use in ordinary clinical practice within primary health care for measuring step-up ability. The test also had to be easy to perform and repeat relatively frequently as leg strength and function are perishable. When patients were familiar with the test, it was performed within a few minutes. The clinical assessment of the patient in movement generated a great deal of important information.

We have found no other studies in which a patient's maximal step-up height has been tested at small intervals in a standardised way. In our study, the standardised intervals were 3 cm on a step-up box built by the author (Figure 4). In previous studies, subjects have been required to climb up to certain predetermined levels, or climb up and down with or without the help of handrails [59-62]. For instance, leg function was tested in a non-standardised way by having the patient mount an ordinary platform with five levels and step height correlated to muscle strength in older people [59, 61] and patients with knee and hip OA [62]. Elsewhere, assessment of middle-aged meniscectomised patients based on a footstool climbing test with few levels did not provide acceptable results when test-retest and floor/ceiling effects were taken into account [60]. Although there are several tests assessing leg function with both multifactor and functional ability assessment tools [63-64], a systematic review concluded that no single tool can be recommended for implementation in all settings or for all subpopulations within each setting [65]. A consensus-derived set of performance-based tests of physical function for use in people diagnosed with hip or knee OA or following joint replacement have recently been presented [41] with comments [66] and a reply by the authors [67].

Many tools for the assessment of fall-risk prevention among older adults have also been studied. We sought to evaluate an assessment tool suitable for all ages by being differentiating and difficult enough to perform also for young and middle-aged persons. The test for leg strength and leg function in this thesis was developed in order to be a standardised procedure suitable for daily clinical use. Standardisation, carried out in the author's clinical practice, started with assessing patients' ability to step up on one or two ordinary stairway steps. This only discriminated for 18 and 36 cm. Therefore a maximal step-up test (MST) with 3-cm intervals between step heights was developed for assessment of maximal step-up height (MSH). The rationale for choosing 3-cm intervals was

1. to have enough levels for discrimination between subjects/patients and test occasions,
2. to have sufficiently few levels not to exhaust subjects/patients and
3. to be able to come as close as possible to the highest theoretical individual MSH due to standardisation while taking 1. and 2. into consideration.

In our study, the highest step-up height reached with the standardised MST at a specific test occasion is denoted as 'maximal step-up height' (MSH). The individual goal suggested was to manage MSH with 90 degrees in hip and knee in the start position. Experience from the standardisation process suggests that it is possible to reach that level even at a high age provided strength fitness is high.

The standardised maximal step-up test (MST) method includes instructions for the tester on how to instruct and encourage the patient during the MST. The new standardised MST [1] determines the greatest height to which a subject/patient can step at that moment (MSH). We study if it can be an easily available and robust assessment of leg strength and leg function in clinical practice, for diagnoses, treatment and follow-up of individuals at risk and for patients with chronic diseases and limitations in capacity to work.

3.6 MAXIMAL STEP-UP TEST – STANDARDISED INSTRUCTIONS

The maximal step-up test (MST) assesses maximal step-up height (MSH) at a particular moment as seen in the images below (Figure 4). What follows are detailed instructions to be used by the tester and subject.

I. Begin your demonstration of the MST with the height set at a relatively low level; that is, to correspond to the height of a step of an ordinary flight of stairs. The step-up test is carried out in ordinary cloths and in bare feet or socks. To avoid any undesirable side effects an incremental increase of height is recommended.

II. During the step-up demonstration, carefully explain the rules for the approved MST:

i. the foot of the step-up leg should be put in a place where good balance can be established
ii. the arms should hang vertically at the sides
iii. stand in an upright position
iv. move slowly while performing the step-up
v. the pelvis should remain in a central position during the step-up
vi. avoid kicking off from the floor with the foot still on the floor
vii. tilting backward or forward, or bending forward with the face passing the vertical line from patella, is not allowed.

III. After the demonstration ask the subject if there are any current or previous problems with leg function, joint pain or muscle weakness. Select a level at a low step-up height for training purposes, and start with what the subject considers the strongest or dominant leg, to obtain familiarity with the test procedure. Then choose an MST start level at which the subject feels certain of being able to perform the test procedure in full compliance with the instructions. Then ask the subject to start the MSH assessment with the leg suspected to be the weakest. If an approved MST is not carried out, try a lower level as the starting level.

IV. Testers' instructions to subjects during the MST (see legend to Figure 4)

V. The tester supervises and approves the MST on one or both legs and the subject is then told to try a higher level. Three attempts at the highest level for each leg are allowed. The subjects are given verbal encouragement to perform at their best. The highest approved level is the maximal step-up height for each leg.

Figure 4. The standardised maximal step-up test (MST) – instructions to subject

First image. At starting position put the floor foot 5-10 cm in front of the step-up box, and put the step-up foot onto the board. Finish starting position by getting up as high as possible on the toes of the floor foot. Stand still and find your balance.

Second image. Look straight ahead and straighten your back while moving your body weight over to the step-up leg on the board of the step-up box. Stand still and again find your balance.

Third image. Start the step-up by pressing the step-up foot into the board. During a slight forward bend, and without kicking with the floor foot, slowly step up onto the board while extending your knee and hip.

Fourth step. Slowly put the floor foot onto the board of the step-up box and the MST is completed.

3.7 STATISTICS

The statistical methods used in the three studies are summarised and presented in Table 1. Analyses were done both as intention to treat (ITT) and as per protocol (PP) and there were no significant differences. Results from the ITT analyses are presented in Studies II and III.

Table 1. Summary of statistical methods used

Statistical methods in study	I	II	III	The primary outcome variable for the statistical analyses of this thesis was the maximal step-up height (MSH), where the mean and standard deviation (SD) of right and left leg was used for all MSH analyses.
Descriptive statistics				All data were analysed with descriptive statistics, at baseline and follow-ups.
Mean (SD)	▪	▪	▪	Mean and standard deviation, for all continuous variables at baseline and follow-ups
Frequencies (%)	▪	▪	▪	Frequency for all continuous variables
Relative frequencies (%)	▪	▪	▪	Relative frequency for all categorical variables
SF-36	▪	▪	▪	Scoring according to the first Swedish version was used. All raw scores were transposed onto scores on a weighted 0-100 scale, higher scores representing better health status. The subscale PF was extracted for further item analyses of the limitation level in the PF items ranging from 1-3 (1=severely limited, 2=somewhat limited, 3=no limitation), and the summary of item responses: **I.** 3a, 3b, 3d, 3f and 3g ; **II and III**: 3b, 3d, 3f and 3g.

Analytical statistics				The three studies were exploratory, had a wide focus with several objectives with unknown baseline values, effects, and distribution of the outcomes, therefore no power analysis was performed.
Mean Differences (SD)		▪	▪	Mean difference for all categorical and continuous variables after intervention up to both follow-ups were computed.
ANOVA	▪		▪	Estimating the within-subject standard deviation for further calculation of MSH – the test-retest repeatability was analysed, 95% of differences between paired observations was expected, to be less than this definition of a repeatability adopted: **I.** – between paired observations, *i.e.* test leaders and subjects repeated assessments, respectively in a working population both women and men. **III.** – between paired observations, *i.e.* test leaders, in a female patient population with common diseases and reduced fitness, physical function and capacity to work.
Logistic Regression Analysis	▪	▪	▪	**I.** To determine whether MSH at occasion 1, the mean MSH between the first and second assessment was: i. Tested for discrimination of a cut-off score (cm) for any limitation (numerically <100) or no limitation (=100) in SF-36, PF score (item 3a-3j) ii. tested for discrimination of a cut-off score (cm) for presence of any limitation dichotomized (1 and 2) versus no limitation (3) in SF-36, PF item response 3a, 3b, 3d, 3f and 3g. **II.** To estimate the odds ratio (OR) and the corresponding 95% confidence interval (CI) for presence of severe limitation (item response 1) versus little or no limitation

				(item response 2 and 3) in SF-36, PF items summary 3b, 3d, 3f and 3g. MSH was included as the independent factor in the model, a cut-off level (cm) was estimated for severe limitation versus other. **III.** Logistic regression analysis was performed to explore subjects with maintained MSH as outcome (maintained or increased MSH versus decreased MSH). Mixed aerobic fitness and strength training sessions were dichotomized into high (>21 sessions during the 3-month training period) or low (≤21 sessions). Age (years), time to follow-up (months) and MSH (cm) at baseline were included as covariates, as these were found to be significant in univariate regression analyses.
Odds Ratio (OR)	▪	▪	▪	**I and II.** A cut-off level (cm) was estimated where the odds ratio (OR) for any limitation was set to 1.0, discriminating between those who have a limitation of the SF-36 PF items specified in the analyses and those who did not have that limit. **III.** Logistic regression analysis was performed and results are presented as odds ratio (OR) with 95% confidence interval (95% CI). Model specification was tested by Pearson's and Hosmer-Lemeshow's tests.
Sensitivity, Specificity and Likelihood Ratio (LR)	▪	▪		The cut-off level observed was used to compare predicted values against observed values. The measures of sensitivity, specificity and likelihood ratio (LR) were calculated to address the potential for MSH to discriminate subjects with: **I.** Any limitations (item response 1+2) in SF-36, PF in items summary of 3a, 3b, 3d, 3f and 3g. **II.** Severe limitation (item response 1) in SF-36, PF in items summary of 3b, 3d, 3f and 3g.
Pearson Correlation	▪	▪	▪	**I.** Validity of MSH was investigated by analysing the

Coefficient				relation between: i. MSH at occasion 3 and mean isokinetic knee extension peak torque (IKEPT) of the right and left leg, ii. MSH at occasion 1 and SF-36 subscales PF, BP and GH scores (0-100) and PF the items response summary of 3a, 3b, 3d, 3f and 3g. **II and III.** Mean difference for all categorical and continuous variables after intervention at 3-months and 14-30 months follow-up, respectively, was computed and correlations, explorative univariate relation between all variables and MSH, were calculated.
T-test		▪	▪	**II and III.** Main variables and their changes from baseline to 14-30-month follow-up and changes to after the 3-month intervention programme were analysed using the students T-test. All tests were two-sided and P<0.05 was regarded as statistically significant. No adjustments for multiplicity were done as this is an exploratory study. Overall, we can expect 1/20 statistical significant results to be caused by random for analysis in independent variables.
Mann-Whitney U-test (non-parametric)			▪	**III.** To describe differences (rank order) in MSH correlations to subjects main variables between the two subgroups with the highest MSH maintenance (increased or maintained) and the subgroup with the lowest MSH maintenance (decreased), the Mann-Whitney U-test, 2*1-sided exact *p*-test was used. The same when analysing differences between age tertiles.
Multivariate Linear Regression (Analysis of Variance)	▪	▪		**I.** MSH at occasion 3 was used to assess the relation to demographic factors such as sex, age, weight, body height, BMI and mean energy expenditure using multiple linear regression.The multivariate analyses were performed in two models. **II.** The multivariate correlations between MSH and age,

				aerobic fitness, self-estimated physical functions and physical activity, anthropometric variables, diseases and complaints as well as characteristics of the physical activity intervention programme were analysed. The multivariate analyses were performed in three models, for correlation to MSH at baseline, at 3-month follow-up and to change in MSH from baseline to three months.
Univariate Regression Analysis	▪	▪	▪	**I, II and III.** Correlations were calculated using the Pearson Correlation Coefficient to explore univariate relation between all variables and MSH. For exploratory use as separate univariate tests of significance may not be appropriate for correlated dependent variables as they are not independent.

4 RESULTS

4.1 STUDY I

4.1.1 Characteristics of the study population

The characteristics of the subjects and scores on the SF-36 subscales are presented in table 1 in Study I. The mean BMI indicates that both women and men were overweight. Energy expenditure data indicate moderate physical activity among men and less among women. Subjects from both sexes ranged from inactive to moderately active, and were representative of patients in primary health care most commonly referred to physical activity on prescription today [68-70]. Assessment of SF-36 showed that our subjects had marginally better PF and BP than, and about the same GH as, the general Swedish population [53]. In our study 58.3% (34-64 years) had at least one limitation in PF, compared with 60.6% (35-64 years) in the general Swedish population [53]. Our subjects thus appear representative for the middle-aged general population in Sweden. Nearly all limitations reported by our subjects were found in items 3a, b, d, f and g. Older subjects and women reported a greater number of limitations. The MSH range was 12-45 cm for women and 18-45 cm for men. The mean (SD) maximal step-up height (cm) for each leg for all assessments at occasions 1, 2 and 3 are presented in Table 2. The differences between legs and assessments were minor.

Table 2. Maximal step-up height mean values right and left leg

Occasion	Leg	Right	Left
(n=60)		Mean (SD)	Mean (SD)
T1	First assement	31.3 (5.8)	31.2 (4.9)
	Second assement	31.7 (5.7)	31.5 (5.0)
T2	First assement	32.2 (5.3)	31.8 (4.9)
	Second assement	31.7 (5.9)	31.3 (5.3)
T3	First assement	32.1 (5.4)	32.1 (4.8)

4.1.2 Repeatability

The intra-tester test-retest (one week between occasions) showed MSH repeatability of 6.9 and 5.9 cm for right and left leg, respectively. When four weeks passed between the first and third occasion the corresponding figures were 5.0 and 4.9 cm. The inter-tester (minimum 30 minutes) repeatability was 9.6 and 8.5 cm (occ 1), and 6.6 and 5.6 cm (occ 2), for the right and the left leg respectively.

4.1.3 Correlations

Mean MSH – that is, the mean of right and left leg – at test occasion 3 (T3) was correlated to age and gender (Figure 5) and to BMI and gender (Figure 6). MSH was correlated to isokinetic knee extension peak torque (IKEPT) (r=0.68, P<0.001) (Figure 7), to SF-36, PF score (r=0.29, P=0.03) and to limitations in the selected items in PF (3a, b, d, f, g) (r=-0.30, P=0.02). MSH was not correlated to the BP (r=0.08, P=0.53) or GH (r=0.02, P=0.88) scores of the SF-36.

Figure 5. Maximal step-up height in relation to age and gender

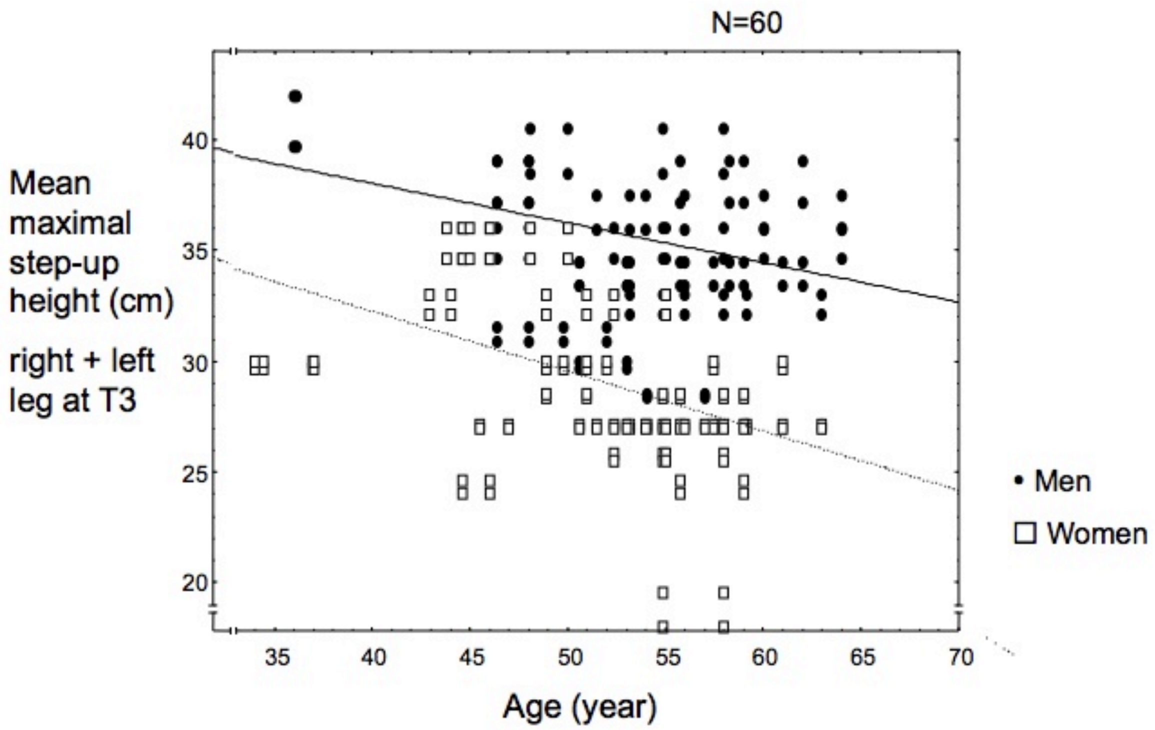


Figure 6. Maximal step-up height in relation to BMI and gender

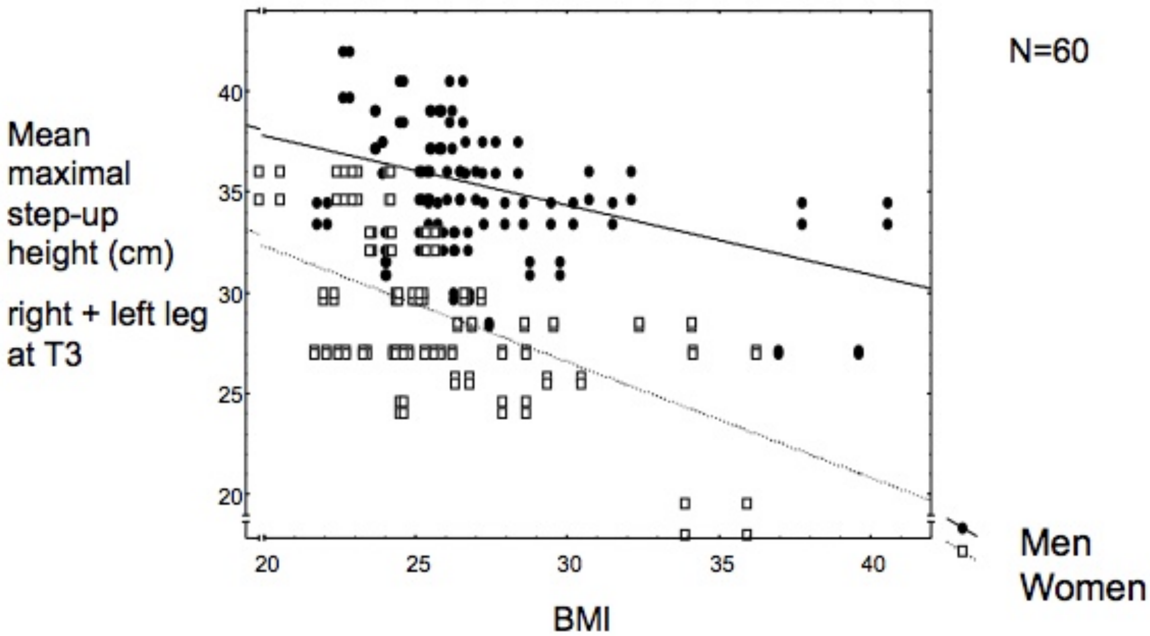
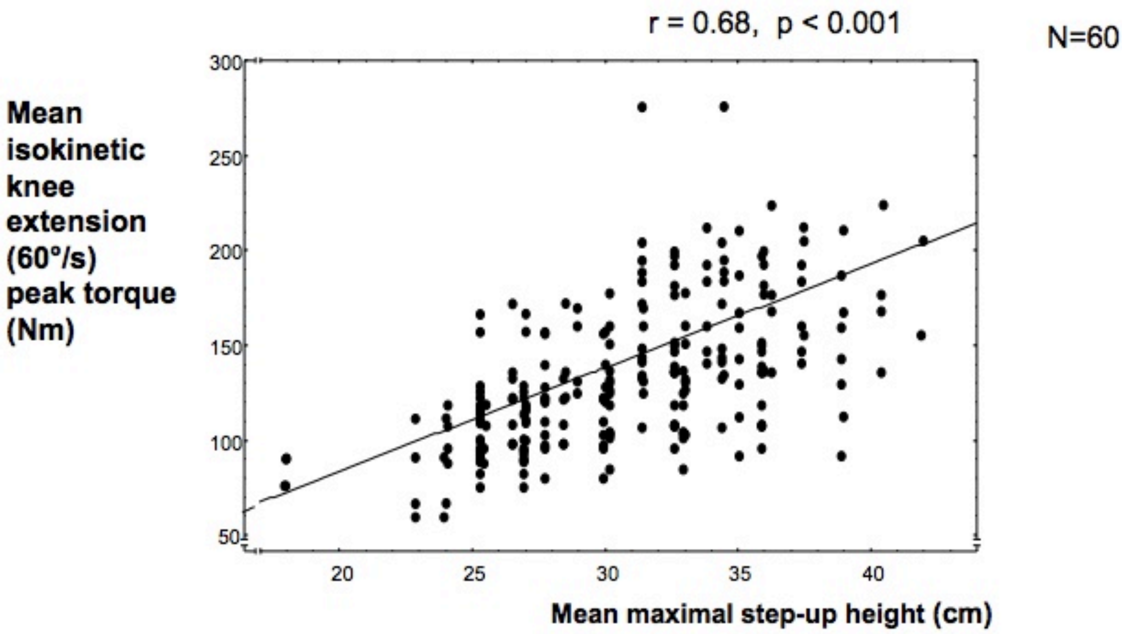


Figure 7. Maximal step-up height and quadriceps strength



4.1.4 Regression analysis

The correlation of MSH to subject characteristics and self-reported physical activity is presented in Table 3. Both models revealed significant inverse correlations. The first model revealed significantly lower MSH among women, and lower MSH with increasing age and BMI. The second model showed significantly lower MSH among women, and with increasing age and higher weight. Body height and self-reported physical activity did not significantly correlate to MSH. Results from the logistic regression modelling showed that MSH at the first test occasion could discriminate limitations in physical functioning, OR=1.13, P=0.037, and a corresponding cut-off level at 34 cm. The model had a sensitivity of 71% and a specificity of 58%. Subgroup calculations showed a cut-off level of 32 cm for women and 35 cm for men, which discriminated those reporting any limitation in SF-36, PF. There were 7 out of 30 women and 14 out of 30 men having MSH >32 cm and >35 cm, respectively, on both legs.

Leg problems and injuries (>6 months before study) reported by the subjects could explain lower MSH and IKEPT values as well as low values in PF scores. The subjects did not report any adverse effects of the study and there were no drop-outs. Performing the MST took 5-15 minutes and IKEPT took 25-30 minutes.

Table 3. Linear regression: mean maximal step-up height at test occasion T3, n=60

	Estimate (B)	SE of B	p-level	R^2
Model 1				**0,598**
Intercept	54,46	4,07	<0.001	
Gender (Female=1, Male=0)	-7,34	0,86	<0.001	
Age (years)	-0,16	0,07	0,020	
Body mass index (BMI)	-0,38	0,11	0,001	
Model 2				**0,594**
Intercept	40,77	16,35	0,016	
Gender (Female=1, Male=0)	-7,76	1,41	<0.001	
Age (years)	-0,17	0,07	0,020	
Height	0,08	0,09	0,341	
Weight	-0,13	0,04	0,002	
Kcal/wk mean	0,00	0,00	0,967	

4.2 STUDY II

4.2.1 Response rate

178 patients (83% response rate) were included. The reasons not to attend the intervention project were diverse (Figure 3). The reasons for not coming to 3-month follow-up (22

patients, 12%) were: premature ending of supervised training without explanation, starting a new job or education, psychosocial reasons or moving away.

4.2.2 Patients' characteristics

At registration, nearly three in four of the patients (72%) reported exercising either never, occasionally or at most one to two times per week. One quarter (24%) reported that they participated in leisure-time activity/structured exercise lasting at least 30 minutes either three to five times per week or more than five times per week. Of the 178 female patients included, 97% had musculoskeletal complaints. Three quarters (75%) of those with musculoskeletal complaints had pain or dysfunction in two to five out of 14 possible localisations reported in the standardised referral document by the patient's GP. Altogether, 49% (88 out of 178 patients) also had at least one of the psychosocial conditions diagnosed as common practice in primary care: depression, anxiety, stress-related problems, sleep disturbance, burn-out syndrome or fibromyalgia. One fourth (26%) had been diagnosed by their GP with cardiovascular disease, 12% with type 2 diabetes and 12% with asthma/COPD. A majority (66%) was on part-time or full-time temporary disability pension or on sick leave as reported by GPs.

4.2.3 Descriptive statistics and intervention effects

Descriptive statistics for age, anthropometric variables, cardio-respiratory fitness, self-reported physical and mental function, at baseline and after 3-month intervention, are presented in Table 4. Body weight and aerobic fitness improved after the intervention period. Physical and mental functions also improved. Four different dimensions of physical limitations, as measured by SF-36, improved: these were the items describing doing moderate activities (3b), climbing several flights of stairs (3d), bending, kneeling or stooping (3f) and walking more than 2 km (3g).

Table 4. Mean (SD) for age, anthropometric variables, cardio-respiratory fitness, self-reported physical and mental function, at baseline and after 3-month intervention with group training

Age, anthropometric variables and aerobic fitness	n	Baseline Mean (SD)	Change baseline to 3-month follow-up, Mean (SD)	
age (years)	156	49.9 (12.0)	0.4 (0.5)	**p<0.001**
height (cm)	156	163.9 (6.6)	NA	

weight (kg)	155	79.5 (18.0)	-0.8 (3.2)	**p=0.002**
BMI	155	29.6 (6.5)	-0.3 (1.1)	**p=0.001**
waist (cm)	151	95.2 (14.8)	0.3 (3.7)	p=0.307
VO_2 max ($mL \cdot kg^{-1} \cdot min^{-1}$)	121	27.8 (8.0)	5.0 (5.4)	**p<0.001**
[1]SF-36 score (0-100)	n=156	Baseline Mean (SD)	Change baseline to 3-month follow-up, Mean (SD)	
Physical				
PF-Physical function		64.7 (20.4)	6.4 (15.7)	**p<0.001**
RP-Role limitation physical		34.3 (38.9)	9.0 (37.8)	**p=0.004**
BP-Bodily pain		39.5 (21.0)	8.7 (18.4)	**p<0.001**
GH-General health		44.9 (18.4)	8.0 (16.1)	**p<0.001**
Mental				
VT-Vitality		34.9 (21.5)	13.3 (21.7)	**p<0.001**
SF-Social function		64.9 (27.4)	7.8 (25.4)	**p<0.001**
RE-Role limitation emotional		53.4 (45.2)	6.2 (43.3)	p=0.076
MH-Mental health		62.7 (23.1)	6.4 (18.9)	**p<0.001**

NA=Not applicable

[1]SF-36, the Swedish version of a generic health-related quality of life survey, consists of 36 items that cover eight domains of health status. All raw scores were transformed into scores in a range between 0 and 100, and higher scores represented a better health-status score.

Mean maximal step-up height (MSH) in the total group increased by 1.6 cm from baseline to follow-up after 3-month intervention (Table 5). When the data was analysed for different subgroups we noted 7.8 cm higher mean MSH (mean right and left leg) in the youngest compared to the oldest age group and 5.7 higher mean MSH (mean right and left leg) in the group with VO_2 max ≥40 ml compared to the subgroup with <25 ml.

No adverse effects of the MSH assessments and no adverse effects from group training leading to interruption were reported. Performing the MST took between 5 and 15 minutes depending on the patient's physical condition and whether it was the MST at baseline or at follow-up.

Table 5. Mean (SD) of maximal step-up height (MSH) at baseline and changes from baseline to after 3-month intervention. Significant difference analysed, two-sided at $p<0.05$, is marked in bold.

MSH at baseline and changes to 3-month follow-up (n=140)	Baseline Mean (SD)	Change baseline to 3-month Mean (SD)	
Left leg (cm)	27.1 (6.3)	1.4 (2.6)	p=0.069
Right leg (cm)	26.9 (6.0)	1.7 (3.2)	**p=0.021**
Mean of right and left leg (cm)	27.0 (5.9)	1.6 (2.5)	**p=0.033**

4.2.4 Pair wise correlation analysis

Maximal step-up height – that is, maximal step-up height the mean of right and left leg (cm) – had significant negative correlations to age, weight, BMI and waist circumference. It correlated positively to SF-36 physical function score (the ten items 3a-j), VO_2 max, height and musculoskeletal pain and disorder(s) from lumbar spine to foot. Some correlations at baseline between MSH and other main variables are presented in Figures 8-13. However, maximal step-up height was not correlated to physical activity >30 minutes per day with the intention of maintaining or improving aerobic fitness, health or wellbeing before the intervention. At 3-month follow-up MSH correlated significantly to the same variables, and also to training intensity, but not to total number of training sessions (101, 47 and 8 patients with ≥25, 13-24 and ≤12 sessions, respectively), and not to ‘doing moderate activities’ (PF item 3b) or to pain from lumbar spine to foot reported at baseline.

Figure 8. Maximal step-up height correlated to age (baseline, n=178)

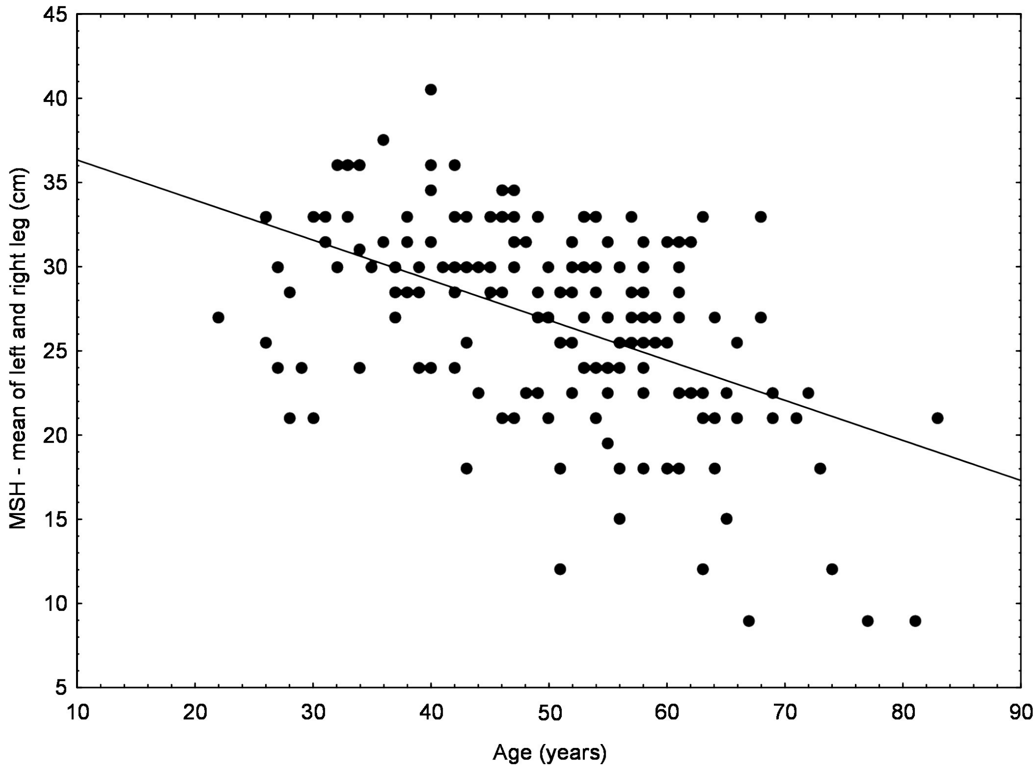


Figure 9. Maximal step-up height correlated to BMI (baseline, n=178)

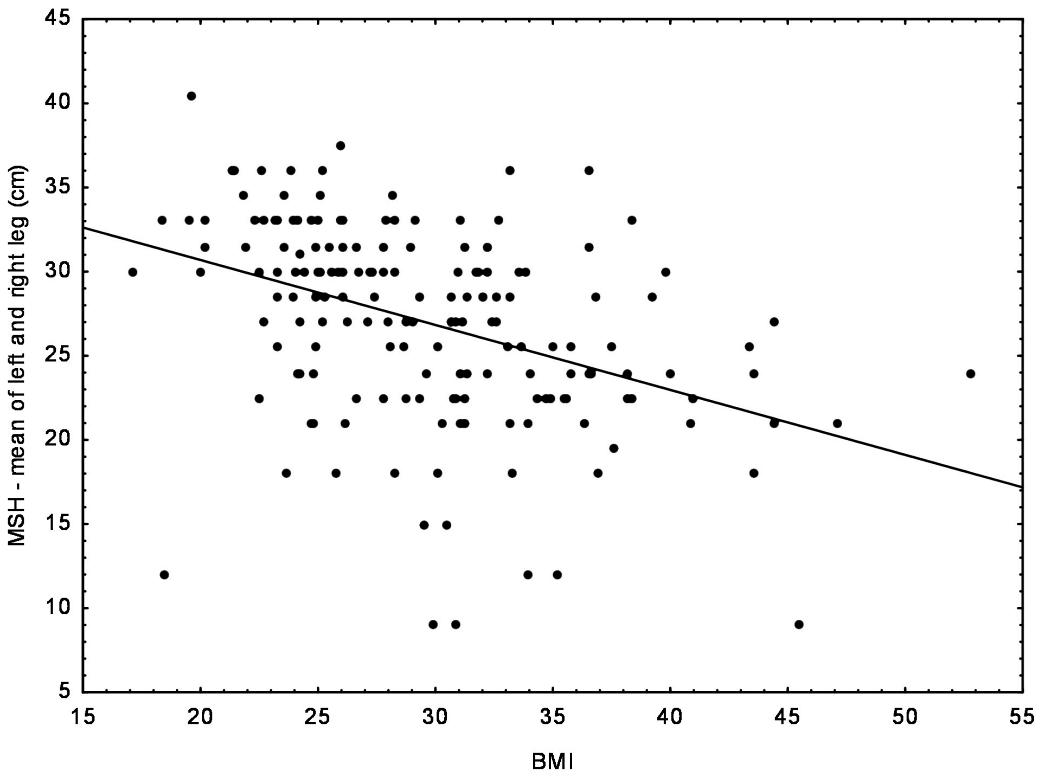


Figure 10. Maximal step-up height correlated to waist circumference (baseline, n=178)

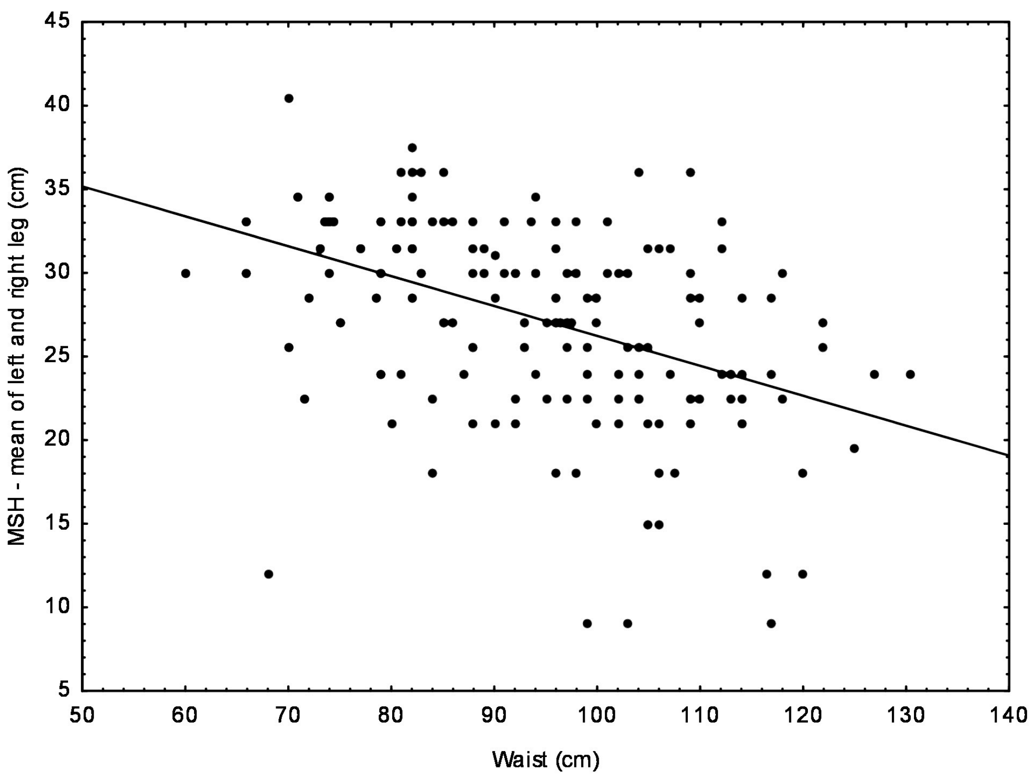


Figure 11. Maximal step-up height correlated to SF-36 physical function (baseline, n=178)

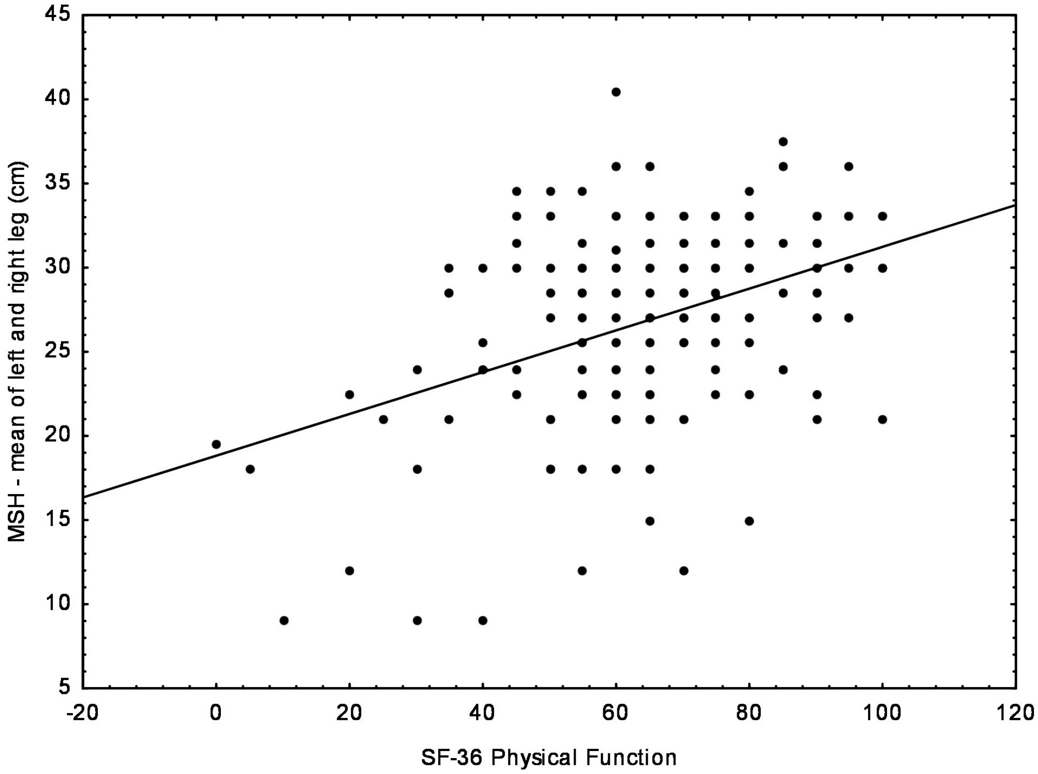


Figure 12. Maximal step-up height correlated to VO_2 max (baseline, n=178)

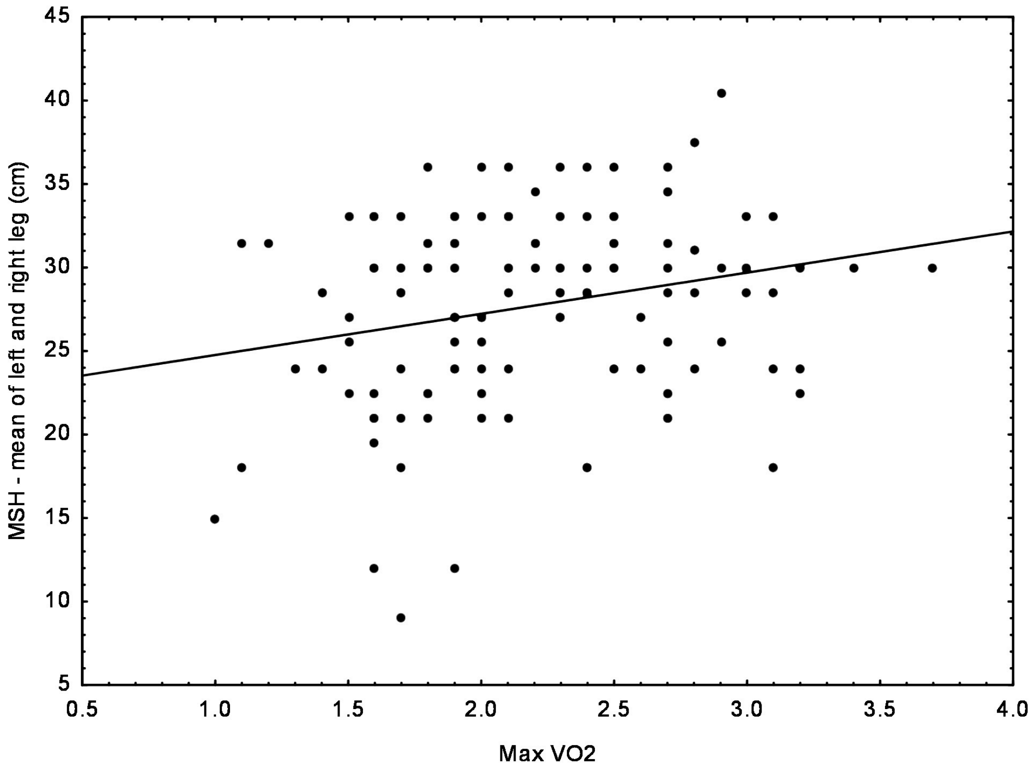
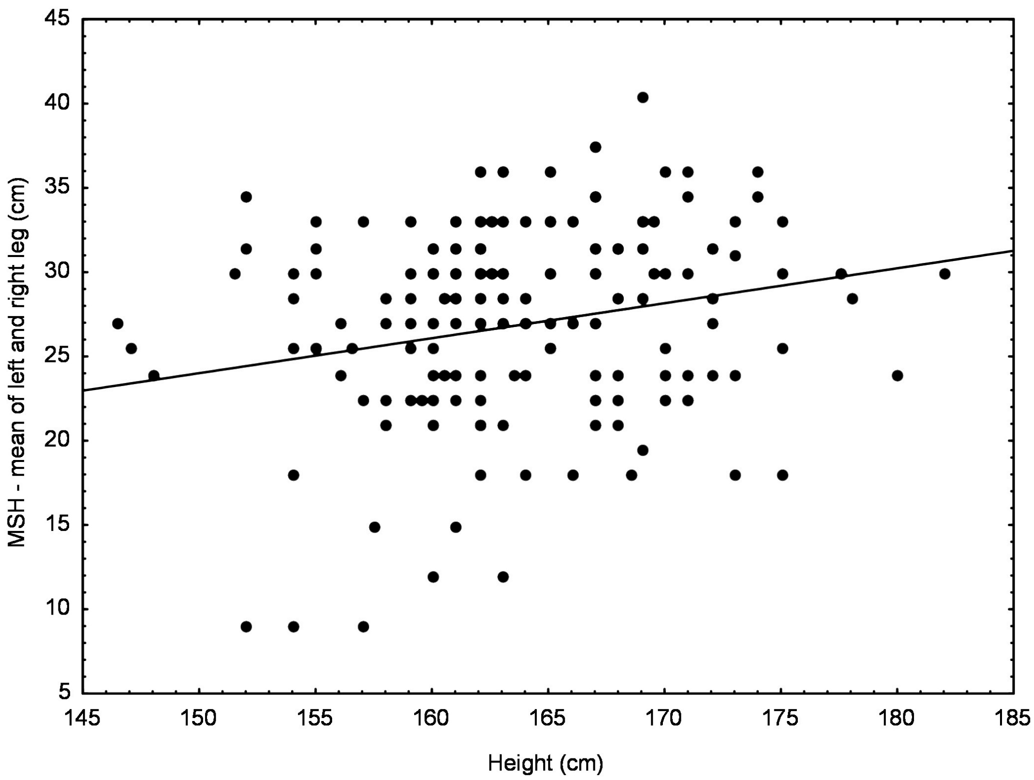


Figure 13. Maximal step-up height correlated to height (baseline, n=178)



MSH changes from baseline to three months correlated with changes in weight, BMI, waist circumference, physical limitations and physical function, but not with changes in VO_2 max (Table 6). Analyses were done both as intention to treat (ITT) and as per protocol (PP) and there were no significant differences.

Table 6. Correlation in pairs of mean maximal step-up height [1](MSH) changes and changes in other variables from baseline to 3-month follow-up after group training analysed with intention to treat (ITT). Significant correlation, two-sided at $p<0.05$, is marked in bold.

Var	[2]weight	[3]BMI	[4]waist	[5]VO_2 max	[6]3bdfg	[7]PF
[1]MSH	-0.20	-0.19	-0.20	0.08	0.24	0.23
	p=0.017	**p=0.027**	**p=0.017**	p=0.456	**p=0.004**	**p=0.006**
[2]weigh		1.00	0.51	-0.34	-0.21	-0.13
		p<0.01	**p<0.001**	**p<0.001**	**p=0.010**	p=0.114
[3]BMI			0.51	-0.34	-0.21	-0.14
			p<0.001	**p=0.001**	**p=0.008**	p=0.092
[4]waist				-0.21	-0.16	-0.12
				p=0.036	**p=0.053**	p=0.151
[5]VO_2 max					0.12	0.02
					p=0.246	p=0.830
[6]3bdfg						0.90
						p<0.01

1) MSH *i.e.* the mean of right and left leg (cm) (n=140), 2) weight (kg) (n=155), 3) BMI *i.e.* body mass index (n=155), 4) waist circumference (cm) (n=151), 5) VO_2 max *i.e*. maximal oxygen uptake ($mL·kg^{-1}·min^{-1}$) (n=104), 6) sum3bdfg, PF, SF-36, *i.e*. summary of item 3b, 3d, 3f, 3g any limitations score (1=severe, 2=somewhat, 3=no limitation) (n=156), 7) PF *i.e*. physical function, SF-36 (score 0-100) (n=156).

4.2.5 Regression analysis

Multiple regression analyses showed that the change in maximal step-up height (MSH) from baseline to three months correlated negatively with change in waist circumference and positively with change in the sum of physical limitations in items 3b, 3d, 3f and 3g, where high scores indicate no limitation (Table 7). No correlation was found between change in MSH (mean of right and left leg) from baseline to 3-month follow-up and change in VO_2 max or patients' age. We noticed linearity between patients' age and changes in mean VO_2 max and changes in physical limitations at 3-month follow-up when added together to Model 3.

Nearly all the patients (n=172 out of 178, 97%) were assessed with the maximal step-up test at baseline. Only 137 women (75%) could perform the VO_2 max test on the bicycle, mostly because of medications that interfered with the test (n=27). Others who were not tested with the cycle ergometer had stress-related problems with a heart rate too high for an appropriate calculation of VO_2 max from the sub maximal exercise test.

Using logistic regression, we estimated a maximum of MSH of 24 cm as a cut-off to discriminate those who self-reported severe limitation in at least one of the PF items 3b, 3d, 3f and 3g. Comparison of observed versus predicted values based on the cut-off level of 24 cm showed 64% agreement. The model had a sensitivity of 83% and a specificity of 39% explained by age and BMI.

Table 7. Regression summary for dependent variable mean maximal step-up height [1](MSH) assessments of 156 female patients at baseline and at follow-up after 3-month intervention with group training. The regression summary for dependent variable changes of mean MSH and changes of variables after 3-month intervention. Changes analysed as ITT. Significant difference, two-sided at p<0.05, is marked in bold.

	Model 1 – baseline			Model 2 – at 3 months			Model 3 – changes to 3 months		
Variables	B (n=114)	SE(B)	p-value	B (n=98)	SE(B)	p-value	B (n=98)	SE(B)	p-value
[2]age	-0.15	0.04	**<0.001**	-0.11	0.04	**0.008**	0.03	0.02	0.220
[3]waist	-0.13	0.04	**<0.001**	-0.14	0.03	**<0.001**	-0.17	0.07	**0.014**
[4]VO_2 max	0.11	0.06	0.070	0.03	0.05	0.639	0.02	0.05	0.697
[5]sum3bdfg	0.42	0.20	**0.037**	0.54	0.23	**0.023**	0.39	0.17	**0.022**
[6]intensity				2.17	0.71	**0.003**			

Model 1 – R^2=0.461; **Model 2** – R^2=0.565; and **Model 3** – R^2=0.138.

1) MSH *i.e.* maximal step-up height the mean of right and left leg (cm), n=140, 2) age at baseline used in analysis in Model 3, age changes about three months for all, 3) waist circumference (cm), co linearity to BMI and weight, 4) VO_2 max *i.e.* maximal oxygen uptake ($mL{\cdot}kg^{-1}{\cdot}min^{-1}$), 5) sum3bdfg *i.e.* any limitations in SF-36, physical function, items 3b, 3d, 3f, 3g, 6) intensity *i.e.* group training intensity from level one to three, light-light, light, ordinary level according to the music pace, the patients' lowest was registered.

4.3 STUDY III

All tables and figures for this section are included in Study III at the back of the thesis.

4.3.1 Repeatability test at long-term follow-up

The inter-examiner (minimum 30 minutes) repeatability was 3.94, *i.e.* in 95 % of the mean MSH right and left leg assessments. A variation of up to 4 cm can be expected between testers.

4.3.2 Characteristics of the study population at baseline

Some characteristics of the study population are presented in tables 1a and 1b. The mean BMI and mean waist circumference at baseline described that a majority of the study population was overweight and abdominal obesity was common. Mean (SD) VO_2 max was rather low 27.5 (7.3) $mL \cdot kg^{-1} \cdot min^{-1}$ and MSH was 27.2 (5.7) cm.

Furthermore, 74% were co-habiting and 20% were smokers. 18% of participants reported having completed elementary school as their highest educational qualification, 46% upper secondary school and 37% degree level at university or college. The exercise habits before the age of twenty varied considerably: 2% reported being exempt from physical education (PE) class at school, 38% reported no training other than PE, 36% reported exercising through non-competitive participation in a ball sport, 19% did participate in both exercise and competitions and 5% were serious participants in athletic competitions.

4.3.3 Changes in exercise and physical activity, SF-36, capacity to work and sick leave

As the long-term follow-up (the third assessment, T2) was conducted across three months, whereas participants had been referred to the study consecutively over a longer period of time, we obtained a time range between T0 and T2 of 14-30 months (mean 22 months).

Significant increases in self-reported exercise/PA five levels onto mean 22-month follow-up were analysed, see table 1a. The main activity reported from patients' diaries at T2 was brisk walking consisting of ≥30 minutes per day on an average of five days of the week. A substantial decline in group exercise was reported three months before T2 compared to T1, see additional file 1.

Significant improvements in SF-36 scores were seen in all scales at both follow-ups as seen in table 1b. From SF-36 the items 3b, 3d, 3f and 3g were evaluated separately and increased ability were seen in three of four of these physical functions, the limitations for knee bending (3f) did not significantly change by the two follow-ups. Compared to baseline there were some improvements concerning great limitations for 'bending knees' at the 3-month follow-up for 6 out of 19 patients, but this change did not persist at long-term follow-up, see table 1b.

The proportion of patients with capacity to work – including workers, job seekers and students – had increased from 33% to 58% by T2. The mean degree of sick leave – as a share of 1.0 (SD) – at T0 and T2 for the subgroup with highest maintenance of MSH (n=27) were 0.45 (0.46) and 0.21 (0.41) (p=0.002) respectively. These degrees were compared to the non-significant change in degree of sick leave from T0 to T2, 0.48 (0.46) and 0.28 (0.44) (p=0.121) respectively for the group with lowest MSH maintenance (n=22).

4.3.4 Changes in MSH and metabolic risk factors after group exercise intervention

MSH values from all three test occasions were plotted along a time axis and a large distribution of MSH values could be seen at baseline as seen in figure 1a. When we placed three measurements at three places along a time axis, the positive change in MSH during the 3-month group exercise intervention programme was more clearly visualised, as was the – often parallel – decreases in MSH up until the long-term follow-up as shown in figure 1b.

Significantly lower weight and BMI were seen at the 3-month follow-up, but there were no changes in these variables at the long-term follow-up as seen in table 1a. Waist circumference was not changed at 3 months but was significantly lower, -2.4 cm, compared to baseline at the long-term follow-up, tables 1a and 2. Significantly increased VO_2 max at both follow-ups and increased MSH at 3-month follow-up and decreased MSH at long-term follow-up were noted (table 2).

We found no significant seasonal differences in mean MSH at T0 and T1 or MSH changes from T0 to T1 assessments between seasons.

4.3.5 Other subgroup analyses of MSH and changes of MSH at follow-ups

When the whole group was divided into tertiles by age at T0 there were differences in MSH, waist circumference and VO_2 max between groups. The middle age group had measurements closer to the oldest group as seen in table 2. Furthermore, other subgroup analyses presented in additional file 2 show that obese patients with type 2 diabetes had a steeper MSH decline than obese patients without diabetes after the 3-month intervention programme. A steeper decline in MSH was also found for patients with only hip pain compared to those with combined hip/knee or only knee pain. Additional file 2 also presents supervised group exercise intensity, neck and shoulder pain and mental diseases. The subgroup explorative analysis of mean MSH and MSH changes between T0 and T1, and T0 and T2, respectively.

4.3.6 MSH correlations and regression analysis

Univariate correlations between main variables and the changes from baseline to follow-up after 14-30 months are shown in table 3. The decline in MSH correlated to follow-up time and changes in weight, BMI and waist circumference. Reduction in waist circumference was significantly correlated with the total number of registered exercise sessions before long-term follow-up (table 3).

Two models for multivariate regression analysis were performed: the first model is recorded in table 4a (R^2=0.620) with MSH at 14-30 months as dependent variable; and the second model is recorded in table 4b (R^2=0.426) with the change in MSH from baseline to long-term follow-up as dependent variable. The cardio-metabolic risk variables and the follow-up time are included in the models.

As demonstrated in table 4a, MSH is affected by age and metabolic factors, but not by length of time to follow-up. This result contrasts with the change in MSH (table 4b) where the length of time to follow-up has the largest correlation to MSH maintenance, together with the change in BMI.

Logistic regression was performed with maintained MSH as outcome, and in a univariate model the number of mixed aerobic and strength sessions was significant, OR 3.33 (95% CI 1.25-8.89). In the final multivariate model (n=98) this factor was no longer significant, OR 1.95 (95% CI 0.58-6.61). Covariates were the length of time between the first follow-up (T1) and long-term follow-up (T2) OR 0.78 (95% CI 0.68-0.90), MSH at baseline OR 0.88 (95% CI 0.78-1.00, p=0.043), and age at baseline OR 0.92 (95% CI 0.87-0.99). Goodness-of-fit by Pearson’s test was 0.20, and by Hosmer-Lemeshow’s test was 0.13.

4.4 ANALYSIS OF FACTORS BEHIND DROP-OUTS

Table 8. Age, anthropometric variables and aerobic fitness, at baseline and at 3-month follow-up

Variables at baseline N=178	Attending 3-month follow-up n=156 (SD)	Missing at 3-month follow-up n=22 (SD)
age (years)	49.9 (12.0)	48.0 (10.8)
height (cm)	163.9 (6.6)	163.4 (5.8)
weight (kg)	79.5 (18.0)	79.4 (17.3)
BMI	29.6 (6.5)	29.8 (6.6)
waist (cm)	95.2 (14.8)	95.1 (14.2)
VO_2 max ($mL \cdot kg^{-1} \cdot min^{-1}$)	27.8 (8.0)	28.3 (8.3)
Variables at 3-month follow-up, n=156	Assessed MST both at baseline and at 3-month follow-up n=140 (SD)	Missing MSH at 3-month follow-up n=16 (SD)
age (years)	50.2 (12.1)	51.6 (9.7)
height (cm)	163.9 (6.4)	163.3 (8.1)
weight (kg)	78.9 (17.3)	76.8 (17.5)
BMI	29.4 (6.4)	28.7 (6.0)
waist (cm)	95.7 (14.5)	94.2 (14.6)
VO_2 max ($mL \cdot kg^{-1} \cdot min^{-1}$)	32.9 (9.7)	31.3 (13.0)

5 DISCUSSION

The main findings from this thesis were that the novel maximal step-up test assessing maximal step-up height is considered to be a useful and reliable test for leg muscle strength and leg function in clinical practice. Furthermore, it may also function as an indicator of metabolic health.

The results of a 3-month group training intervention programme with 2-3 sessions per week of mixed aerobic fitness and strength training demonstrated increased maximal step-up height, improved fitness and self-reported health, and decreased risk in female patients with reduced capacity to work and an elevated cardio-metabolic risk. After an average of 22 months without regular group training, maximal step-up height was reduced again, while positive effects remained for waist circumference, VO_2 max, physical function and physical activity. However, regular group exercise 2-3 times per week with mixed aerobic fitness and strength training was associated with maintenance of maximal step-up height, whereas brisk walking for at least 150 minutes per week was not sufficient to maintain maximal step-up height in a subgroup of women.

In clinical care, it is essential to assess broad as well as specific aspects of physical function. Many earlier performance tests that measure a combination of muscle strength, leg function and aerobic capacity do not have a robust test standardisation procedure and do not discriminate between legs. Also, many earlier studies were performed on elderly populations older than 65 years of age, while in our study mean (range) age was 50 (22-83) years.

The advantages of this new maximal step-up test include a focus on leg strength and function, the possibility to discriminate between the two legs and a standardised test procedure. The theoretical highest possible step-up height in accordance to standardisation (approximately 90 degrees in the knee and hip joints in the step-up leg at the starting position) is individual, leading to reduced probability of ceiling effects irrespective of age.

The maximal step-up test was found to be an easy-to-use and relevant assessment of leg strength and function for evaluating the effects of exercise – perishable goods, of course – and for planning individual patients' exercise programmes during intervention. No adverse effects were reported from the MSH assessments. The maximal step-up test is regarded as a safe physical performance test in our standardisation.

5.1 STUDY I

5.1.1 Main findings and reflections

Study I shows that the maximal step-up test is a simple, robust, safe and relevant test for leg strength and leg function in both women and men in middle-age. Compared to IKEPT we rated MST as a fast test. The subjects' limitations in physical function, their low to moderate energy expenditure and mean BMI>25 indicated that many of the subjects in our study would be suitable candidates for a physical activity prescription when they present themselves in primary health care. The measure of repeatability for this standardised MST indicates that 95% of all differences between occasions should be less than 6 cm on group level. Larger differences are to be considered as 'true', reliable individual changes. Further, systematic changes on a group level – that is, differences between or within groups – may be detected at lower levels.

The lower inter-tester difference between MSH at occasion 2 compared to occasion 1 could reflect a tester and/or subject learning effect. The threshold for maximum expected intra- and inter-tester differences in MSH in our study was 6 cm, which is less than the 10-cm interval used by other researchers when correlating step height to significant changes in leg strength and leg function, where subjects also had the possibility to kick off with the floor foot and to use handrails [61, 62, 71]. Future studies are needed to further investigate the clinical significance of the 6 cm repeatability.

While not intending to predict knee-extension peak torque from MSH values, this study showed a significant correlation between MSH and IKEPT. This study indicates that MST is a valid test for knee extension function and less time-consuming. IKEPT values, used in our study as the gold standard, are highly reliable, and no learning effect has been observed [72]. Earlier results in two studies investigating the correlation between the maximum rising strength from sitting and isometric knee extension strength show correlations comparable to those in the present study [73, 74]. Furthermore, MST assesses leg strength and performance in functional positions and movements and does not require expensive equipment as does IKEPT measurements.

We also found a significant correlation between MSH and SF-36, PF score and the sum of selected items 3a, 3b, 3d, 3f and 3g. Therefore, the standardised MST could be useful both to identify consequences of sarcopenia [75] for early diagnosis and to support follow-up of treatment.

Further studies are needed to investigate the effects of prescribed physical activity [69] on an individual's MSH, most likely corresponding to changes in knee extension function and self-reported physical function. In studies with older community dwelling populations objective measures of physical capability are predictors of all-cause mortality [76].

On speculation, we explored whether an MSH cut-off value could identify perceived limitation of physical function and found cut-off values of >32 cm (women) and >35 cm (men) on a group level. This might be of use for clinical assessment of the risk of falling or loss of functional independence in the future. Studies on larger groups of patients and comparisons with healthy subjects are needed before any further conclusions can be made.

We present MSH correlations to sex, age and demographics in two models with multiple linear regressions in Table 3 indicating that the MST can be a useful tool for lifestyle interventions. In Model 1, where BMI was used in the model alongside weight and height as separately included, a certain correlation was found to weight whereas no correlations could be detected to height. The lack of correlation between MSH and body height in Model 2, also found by other researchers investigating step height [59], could be due to the relatively small size of the study. The MSH did not correlate to self-reported physical activity. Objective estimates of physical activity [77] might have yielded lower values and a different activity pattern, possibly with lower variability. If so, a correlation between MSH and physical activity might have been identified.

5.2 STUDY II

5.2.1 Main findings and reflections

Maximal step-up height in Study II was correlated to self-reported physical function and limitations when performing common daily activities. Those patients who had an MSH of less than 24 cm had severe limitations when carrying out activities such as climbing several flights of stairs, kneeling or walking more than 2 km. It has been suggested that early assessment of and intervention to improve muscle strength are important for prevention of future functional limitations [78]. Thus MSH, when assessed at an early stage, could possibly be a useful measure to optimise a risk reduction prevention strategy. Assessing maximal step-up height could also be a useful complement to ordinary leg examination in clinical practice, not least as a measurement of physical function and loss of function, and as a means for investigating if there are any differences between legs.

Increases in maximal step-up height (MSH) after a 3-month group training intervention programme correlated to reductions in waist circumference and weight, and to improvements to self-reported physical function scores and physical limitation. This is in accordance with other studies on associations between muscle strength and cardiovascular risk factors for both women and men, and for adolescents [79, 80]. Significant correlation of MSH to intensity of exercise reflects the results reported in recent studies [81-83]. On the one hand, we already know that increased abdominal fat is associated with all common endemic chronic diseases like cardiovascular disease, type 2 diabetes, dementia [84-87], cancers [88] and symptomatic osteoarthritis [89]; and, on the other hand, we know that low muscle strength is an indication of risk factors for the same chronic diseases [19, 79, 84]. Therefore, we found it very interesting that leg muscle strength and leg function assessed with maximal step-up test was associated to cardiovascular risk factors such as waist circumference and VO_2 max in a subgroup of female patient population.

Sedentary behaviour, physical inactivity and low muscle strength are major causes of dysfunction, common diseases as well as premature deaths in modern societies. For as long as we lack valid and simple measurements in clinical practice, the promotion of physical activity and strength training will not get the attention it deserves in health care [90]. In this study on female primary health care patients, of which a majority (2/3) was on registered sick leave or had part-time or full temporary disability pension, we could show that the standardised maximal step-up test was a simple, robust, safe and relevant test. We found that the test was also useful for exercise instructors when coaching patients. Patients themselves also became aware of low leg muscle strength, limitations in step-up function and any differences between the two legs.

The relatively low use of functional tests – for example, a 30-second ‘sit-to-stand test’ – when examining patients in clinical practice risks leaving GPs with an insufficient understanding of patients’ muscle strength and function, and may serve as an obstacle to prescribing physical activity as treatment. Reasons for this low use of functional tests may include 1) a lack of awareness of the importance or existence of such tests, 2) a lack of knowledge and training, leading to a general uneasiness about their use, 3) a perception that tests are not sufficiently clinically useful, 4) an assumption that tests may be too cumbersome to perform and 5) a lack of reimbursement mechanisms for diagnostic and follow-up tests. It may also be the case that functional tests are indeed used by physiotherapists, but that the assessment outcomes are not communicated to GPs and nurses. In this study, MST was explored in female patients with musculoskeletal complaints, metabolic risk factors and other chronic diseases common in primary health care [91]. The patients demonstrated a high level of compliance with the exercise programme they had chosen, suggesting that a high level of adherence can be achieved in a self-selected exercise activity. The intervention programme with enjoyable group training and individual support from medically educated trainers could also have been of importance for compliance.

5.2.2 MSH and correlates

We found univariate correlation between maximal step-up height (MSH) and VO_2 max at baseline, but not when tested multivariate with physical limitations (SF-36, PF the sum of reported limitations in items 3b, 3d, 3f and 3g) and age in the same model. Most likely, this was owing to co-linearity; that is, outcome measures assessing the same outcome variable. The MSH cut-off value 24 cm (below) had 64% sensitivity for identifying female patients (mean age 50 years) with at least one severe self-reported limitation in PF. For comparison, in Study I the upper cut-off values 32 cm (for women, mean age 53 years) and 35 cm (for men, mean age 55 years) had a sensitivity of 71% to identify those without any limitations recorded in SF-36. In light of the fact that physical activity is a complex set of behaviours, we need better diagnostic tools to identify relevant problems in individual patients. Therefore we find the information provided by the assessed maximal step-up height, measuring leg strength and function and differences between legs, useful when prescribing physical activity and exercise [69, 70], for lifestyle interventions [92], as well as for selecting patient characteristics in future research.

5.2.3 Strengths and limitations of Study II

One strength of our study was that it took place in ordinary clinical practice, was pragmatic, and we regard the clinical relevance as high. There is, in fact, a shortage of studies of leg strength and function performed on women. Our study population consisted of female patients recruited consecutively in routine primary health care. Another strength of the study was that the standardised maximal step-up test was validated on a patient population with overweight, obesity, reduced physical function or reduced aerobic fitness. These are known risk factors for low capacity to work and also for symptomatic osteoarthritis (that is, pain and reduced knee function) [93].

Study II has some limitations. We decided to include only women in our study as two thirds of patients coming to primary health care are women, and also because only a small number of men were referred to the supervised physical activity programme. The data/results can therefore not be generalised for men, and neither for adolescents nor the oldest age groups. Another limitation is that the assessment of physical activity, at baseline and during the supervised training period, was not supported by step counting for a more accurate assessment of total daily physical activity. Furthermore, we had some missing data and one reason for this was that it was a clinical study. The individual maximal possible change in MSH after intervention is affected by the difference between a patient's theoretical highest MSH [1] and her or his MSH level as assessed at baseline. Patients' theoretical highest MSH was not measured and thus we could not take that variable into account when analysing our data.

5.3 STUDY III

All tables and figures for this section, written out in lower case, are included in Study III and referenced below.

5.3.1 Main findings and reflections

Our main findings were that a primary care-based 3-month group exercise intervention increased leg muscle strength and leg function assessed as maximal step-up height (MSH). Furthermore, we found that MSH was declining to below baseline level at 14-30 months follow-up. By that time, our female patients had stopped with their regular group training 2-3 times per week, but reported brisk walking most days of the week as their main exercise. Furthermore, at the long-term follow-up, at a mean of 22 months, the patients still had remaining positive effects on waist circumference, VO_2 max, self-reported health, physical function, exercise and physical activity. Moreover, at the first follow-up directly after the 3-month period of group exercise as part of the intervention programme, patients had a significant decline in weight and BMI. Weight stability compared to baseline remained at the long-term follow-up. Clinically acceptable inter-rater variation is a minor concern compared to test-retest variation, which measures at 6 cm [17]. This means that to achieve high validity of MSH results within a study, it is more important that raters are robust in their testing methods than that we use several different raters.

Group exercise included different workouts, mostly mixed aerobic fitness and strength training with a moderate to high intensity 13-15 on 6-20 Borg RPE scale, which the patients were trained to use for intensity control. However, also sessions with merely strength, balance and coordination training were offered, see additional file 1.

Analysing MSH subgroups according to level of maintenance of MSH at long-term follow-up, we found that even the subgroup with the lowest maintenance of MSH maintained their MSH at the follow-up directly after the 3-month group-training period. Thereafter their MSH declined from different MSH baseline levels, figures 1a and 1b, and did so more steeply than for participants in the other subgroups. Most important for MSH decline – in a logistic regression multivariate analysis with maintenance of MSH as outcome – was the length of time before long-term follow-up, indicating a continuous decline of leg muscle strength and function detectable within a mean period of 22 months. Secondly, an increase in BMI and thereafter higher age (increased sarcopenia) and higher MSH levels at baseline were important for MSH decline.

In the subgroup with the lowest maintenance of MSH, 44% of the female patients were assigned sick leave by the long-term follow-up compared to 27% of the patients with the highest maintenance of MSH. One reason for the decline in MSH may be extended absence from work where, without transportation to work and when not participating in any mixed aerobic fitness and strength training or just one session per week, patients were unable to maintain MSH. Also, many participants in the total group were overweight or obese at the start of intervention. Notable was that the obese patients in this subgroup of female patients had the highest MSH at baseline, but at long-term follow-up without regular group exercise, muscle strength to maintain the ability to move the body vertically was not enough and it was hardest for the obese patients to maintain MSH. If there had been significant statistical power when doing logistic regression analysis, mixed aerobic fitness and strength training would probably have had significant positive association with maintenance of MSH.

Sickness and obesity, together with reduced capacity to work and insufficient daily physical activity, appear in our study to create this MSH decline earlier than muscle weakness due to age would have resulted in [40, 94], and with an increased cardio-metabolic risk. Higher BMI as determinant of decreased activity has previously been reported [95]. Furthermore, the role of increased sedentary behaviour (SB) – due to reduced working capacity and cessation of transportation to work – could be one reason for steeper MSH decline in our study, though SB was not assessed. Moreover, evidence presented in a recent meta-analysis shows lifestyle interventions as having the potential to reduce sedentary behaviour in adults [96]. As our participants reported significant positive change in exercise and physical activity at long-term follow-up, the results from our study are in accordance with earlier studies. Our results are indicating that our female patients – who had a high metabolic risk at baseline – had moved from a low level of exercise/physical activity to a higher level with reduced cardio-metabolic risk.

Thus those who could find regular group exercise with mixed aerobic fitness and strength training during holiday season – that is, the three summer months during which long-time follow-up assessments were carried out – increased their ability to maintain leg muscle strength and function assessed as MSH. Brisk walking most days of the week was not enough to maintain these individuals' leg strength and function. Also, lower levels of support from primary health care professionals to encourage patients to prioritise regular group exercise – with mixed aerobic fitness and strength training 2-3 times per week with the subjective intensity of 13-15 on the 6-20 Borg scale – could be a reason for the steeper MSH decline beyond what would be expected due to age.

5.3.2 MSH along a time axis visualises changes in muscle strength

Patients with high baseline MSH appeared more frequently than others early on the time axis in the on-going intervention project, see figure 1a. One important reason for this was that patients with several diseases and consequently lower MSH were deemed not to manage the training intervention by their GP, for both physical and mental reasons. The opinions of GPs, however, changed over time after positive reports from patients. Analysing MSH change over time shows that a new functional status can appear quite rapidly, and this is related to decreased muscle strength. When changing to a more inactive lifestyle – for example, when being assigned sick leave, getting sickness benefit or being unemployed – with a rapid decline in muscle strength and function as a result, the metabolic and cardiovascular risks are markedly enhanced [97]. In occupational health, when preventing obesity and weight gain, early support measures have been recommended for obese employees in the form of a focus on enhanced physical functioning and treatment of obesity and its co-morbidities [98]. According to a recent European multicentre study, the greatest difference in mortality risk was observed between the two lowest activity groups for a population with abdominal and general adiposity, as in our female patient population [99].

5.3.3 Mixed aerobic fitness and strength training with higher intensity important for MSH

In a meta-analysis, combined aerobic and resistance training – the most effective training modality to reduce anthropometric outcomes – have been recommended in the prevention and treatment of overweight and obesity whenever possible [100]. Mixed aerobic fitness and strength training 2-3 times per week in our study (see additional file 1) significantly improved MSH and VO_2 max at both follow-ups and also reduced waist circumference at long-term follow-up. Brisk walking – as reported in our female patient population as the main exercise at long-term follow-up with the mean of 22 months – was at the level of the recommended 150 minutes per week with moderate activity [6], but this was not enough for maintenance of their MSH. In a systematic review, interventions increased regular walking among targeted participants by 30-60 minutes per week on average, at least in the short term. Important for a successful increase was when intervention was tailored to participants' needs and targeted at those with low physical activity [101]. The Karlskoga MABRA project intervention was designed on such principles. Furthermore, a recent study shows that walking groups are effective and safe with good adherence and wide-ranging health benefits. It was concluded that walking could be a promising intervention as an adjunct to other health care or as a proactive health-promoting activity [102]. Our patients' experiences from the MABRA project intervention were probably important for long-term effects on achieving and maintaining the 150 minutes of PA deemed sufficient for good health in this subgroup of female patients. They were offered an individually tailored programme of exercise and regular medical support during intervention, as well as motivational interviews and physical activity on prescription at the end of the period of supervised group exercise.

5.3.4 Health-economics and importance of tailoring exercise to participants' needs

A thesis from 2014 that assessed health-economic consequences of physical activity on prescription (PAP; FaR®), and that also identified the target groups benefiting most from this type of treatment of inactivity, showed that the resulting increased physical activity from PAP reduced costs to society by 22% due to reduced costs for health care and loss of production. It also demonstrated that if we target patients appropriately with the right dosage of physical activity, PAP for inactivity will be cost effective. Moreover, the analyses revealed the importance of increasing access to forms of physical activity and exercise to make it easier and cheaper for inactive individuals to be physically active, noting that weak socioeconomic groups value the health benefits of exercise lower than stronger socioeconomic groups. Two thirds of patients within the study did not complete the intervention programme of physical activity that had been set. They were deemed to need a higher level of help and support to achieve the goals set, such as directed efforts by health care professionals [103]. The treatment of patients with physical activity studied in the MABRA project shows similar results for comparable groups. The results also show that the amount of time spent on exercise was associated with enjoyment of exercise [104, 105]. In the studies referred to in this section, a successful increase in physical activity has been shown when the exercise intervention has been tailored to participants' needs and targeted at individuals with low physical activity. The group exercise intervention in the MABRA project was designed with the same intentions, showed sustainable clinical benefits and reported improvements of exercise and physical activity. Therefore this intervention could be recommended to women with common diseases and with low capacity to work as well as to patients with cardio-metabolic risks.

5.3.5 Women in their 50s and cardio-metabolic risk

When divided in tertiles by age, unexpectedly the women in their 50s (tables 2 and 3c) had lower aerobic fitness levels than the oldest age group. Also, their MSH level and waist circumference were in between the levels within the other groups, but closer to the lower level of the oldest age group than to that of the youngest group. It is known that cardiorespiratory fitness in general declines at a nonlinear rate which accelerates after 45 years of age [106], and possibly the situation is the same for MSH. Furthermore, it has been shown that elderly women with metabolic syndrome have lower functional capacity, muscle strength, lower limb power and flexibility when compared to women without metabolic syndrome [16]. With high waist circumference, low aerobic fitness and relatively low leg muscle strength within our female patients, metabolic syndrome is a probable diagnosis.

5.3.6 Changes in MSH and metabolic risk

The subgroup with the highest maintenance of MSH at long-term follow-up had a lower mean MSH (cm) (SD) at baseline, 26.7 (4.1) compared to 29.6 (6.0) in the group with the lowest maintenance of MSH. At baseline, the group with the highest maintenance compared to that with the lowest included some patients on sickness benefits or with disability pensions, which may be a possible cause of lower MSH. No significant difference was seen in mean levels of sick leave between groups at baseline. The opposite was the case for the group with the lowest maintenance at long-term follow-up when one fourth of the patients received either sickness benefits or disability pension, and nearly half (44%, n=22), compared to one third (27%, n=27) of patients in the group with the highest maintenance, were being assigned sick leave. When a person with overweight changes lifestyle in a short time – for example, going on sick leave and becoming less physically active without simultaneous weight loss – the decline in leg muscle strength gives reduced ability to move the body vertically as assessed by the MST. Accordingly, the MSH decline we found in our study at long-term follow-up can be an early finding indicating effects of sick leave and lower leg muscle strength on the potential for increased cardio-metabolic and functional risks. Also, with rapid reduction in muscle strength and function and no change in energy intake, an increased weight may start a negative spiral towards an even higher BMI, leading to further decline in MSH. A majority of our patients were overweight.

Another notable lifestyle change was that eleven out of twenty smokers had stopped smoking at long-term follow-up. The only tobacco cessation intervention strategy that was used in the project was instructions that no smoking must take place within two hours of tests or of group exercise. The medical and physiological reasons for this were explained and some general information about the adverse effects of smoking on fitness and general health were given.

5.3.7 MSH, obesity and unhealthy obesity

Our data presented in additional file 2 show that patients with obesity (BMI≥30) had a higher MSH at baseline than the group with overweight and normal BMI, in our subgroup of female patients, and that the body height did not differ. Furthermore, the obese patients showed less improvement of MSH during intervention and a steeper decline at long-term follow-up. More information about baseline MSH and the MSH changes in different subgroups are presented in additional file 2. A steep decline in MSH was seen for patients with T2D indicating loss of muscle strength and function and comparative reduction in metabolic capacity. In attempting to find an assessment method for detecting unhealthy obesity – that is, obesity with low leg muscle strength and metabolic function – the MST assessment of MSH could be considered useful when planning for future research.

5.3.8 Changes in SF-36 scores and SF-36 physical function items

In addition to patients' increased metabolic and cardiovascular risks, mentioned above, lower self-reported quality of life in itself gives an increased risk of ill health. Comparing our patients' mean SF-36 scores (broad standard deviations) in table 1b with normative Swedish female population scores (narrow confidence interval) for women in the age groups in question (45-54 years) [53] the differences in scores are PF 19, RP 49, BP 31, GH 30, VT 32, SF 22, RE 33 and MH 16. Significantly improved values compared to baseline were in our study measured at both follow-ups, see table 1b, and we suggest that an intervention of this kind should be further investigated in a larger context.

A recent study investigated whether physical activity and sedentary behaviours interact to influence feelings of energy and fatigue in women in their 40s. When insufficiently active, being less sedentary was associated with lower levels of fatigue comparable with women meeting the recommendations [107]. To join the regular group exercise in MABRA hugely influenced our patients' feelings of energy and reduced fatigue. Patients showed strong positive improvements in self-reported health. The extremely positive feedback reported during and after the intervention, showing the great enjoyment gained by being physically active and by being so in a group [104], appear plausible reasons for the wide-spread tendency in patients to continue with daily walks to long-term follow-up.

We analysed in more detail some questions in SF-36, PF, which measure the ability of completing activities at moderate strain level where leg strength might have importance for the estimated function, see table 1b. The ability to walk more than 2 km at a time without strain was the easiest task to achieve and keep until the long-term follow-up, but also those who improved their ability to escalate several flights of stairs without large or small difficulty could maintain this ability long-term. One third of the patients with reported large problems, mostly with knee bending, reported decreased limitations at the follow-up shortly after the 3-month period of group training. At long-term follow-up the positive effect on knee function had returned to baseline, indicating the need for regular mixed aerobic fitness and strength training to sustain MSH. We conclude that the SF-36 items 3b, 3d, 3f and 3g are useful in clinical practice, primarily for screening leg muscle strength and leg function, to enhance individually prescribed exercise and to support patients in setting realistic goals.

5.3.9 Strengths and limitations of Study III

The study population was representative of female patients in Swedish primary health care.

The intervention programme was received well by patients, despite substantial burdens of disease. There were no accidents requiring medical attention during or after the training sessions. All training sessions, except Nordic Walking, included music and in a recent study this was recommended to promote physical activity among sedentary individuals [108].

The baseline and 3-month follow-up tests were distributed across three out of four seasons because of the way in which patients were added to the programme, and no seasonal influence was discovered.

One limitation is that we have not measured the sedentary behaviour or the physical activity more objectively, including intensity with an accelerometer or posture with an inclinometer. If so, we could have addressed some of the remaining questions about what is important for maintaining MSH. Another limitation is that when long-term results from subgroups are presented, each subgroup is comparatively small. Because this study is the first to describe the long-term results of MSH change after the intervention is completed, we believe it is useful to present the results to help plan future intervention studies, see additional file 2. Another limitation is that the study did not investigate the findings in a population of men.

5.4 MAXIMAL STEP-UP TEST – ADVANTAGES AND POSSIBILITIES

A recently published study showed that handgrip strength may not be an appropriate surrogate for lower body strength, power or balance, and is proposed only to be used describing upper-body strength or functionality [109]. MST is a weight-bearing test that in an integrated and functional way assesses leg muscle strength, power, mobility, balance and coordination and is also indirectly a test of metabolic and cardiovascular risks as it is measuring the function of the body's largest tissue with secretory capacity – the skeletal muscle.

We suggest that MST can be used for future research to study the natural course of sarcopenia and osteoarthritis, the influence of exercise interventions on the risk of falls, as well as the morbidity and mortality in cardio-metabolic diseases, COPD and several other chronic diseases [110, 111]. Exercise has been recommended as a first-line treatment of degenerative joint disease of the knee and new research recommends that exercise should more closely target the sensorimotor deficiencies and functional instability associated with the degenerative joint disease of the knee than is the case in traditionally used training methods [50]. The 30-s chair-stand test, the 40-m fast-paced walk test and a stair-climb test were recently recommended as the minimal core set of performance-based tests for hip or knee osteoarthritis to be used in clinical practice [41, 112]. Also, the MST has been proposed as a recommended performance-based test to assess leg strength and function as well as differences between legs in people diagnosed with knee osteoarthritis [113].

The measurement of MSH has many advantages, already presented [1]: it is easy and safe to perform and immediately delivers a measurement value. Furthermore, it is inexpensive, and after brief instruction MST can be performed by health care staff with the help of step-up boards with different heights. Potentially, MST could, in everyday clinical practice on consecutive patients, allow the clinician and nurse to detect low muscle strength and abnormalities in the locomotor system not observed with the patient in a resting position. A review has recently provided evidence that suggests aerobic exercise assessment to be a vital sign status in future clinical practice [114]. After the same considerations about the health effects and usefulness of assessment of leg strength, we suggest that assessment of MSH may serve as a vital sign status for assessment of muscle strength and function which could be used as a 'health check', both in clinical practice and when used as a self-test. Muscle strength, power and joint mobility are perishable, which is why repeated testing is needed, especially in patients with symptomatic degenerative joint disease of the knee and hip.

6 FUTURE PERSPECTIVES

6.1 eMSH – ESTIMATED MAXIMAL STEP-UP HEIGHT

When assessing leg muscle strength and function with MST, it is useful to compare the person's actual MSH level with her or his theoretical highest possible MSH when physically fit, according to standardisation. This enables us to give the person a 'visualised individual goal' for each leg as a target, the so-called estimated MSH (eMSH), to reach and maintain throughout life, from puberty onwards. During growth in adolescence, the eMSH will increase in parallel with body height.

MST is likely to be a robust and easy-to-use test for assessing strength development, flexibility, joint mobility, side differences, balance and coordination in puberty, to be used in parallel with traditional measurements of increases in height and body weight. During growth in adolescence it is not unusual that sport injuries appear and an imbalance in flexibility and strength development can be found at examination. Future research will appraise what benefits MST may have for growing adolescents. Can repeated assessments of MSH during adolescence be beneficial for discovering imbalances in muscle strength and flexibility, to then be improved and trained during exercise in school (PE), not least to prevent excessive weight gain without enough parallel increase in muscle strength with increased health risks as a consequence?

A few subjects of either sex in Study I managed to step up to a high level (39-45 cm). Their quadriceps strength assessed by IKEPT was high, they had good joint mobility, coordination and balance, and they reported no or tolerable pain. At this high level the femur was parallel to the floor, and the hip and knee angles were about 90 degrees at the starting position for the step-up leg, with the floor foot flat on the floor. This has been the routine for assessment of eMSH so far.

To further increase the level of difficulty, beyond the scope of good and very good fitness (possibly primarily applicable to certain age groups), an advanced estimated MSH may be standardised. For this, the advanced estimated MSH (aeMSH) would be measured with the person being assessed standing with an angle of 90 degrees at hip and knee when the floor foot is in the tip-toe position, compared with keeping the floor foot flat on the floor at the point of assessment as for eMSH. To reach one's advanced estimated MSH according to our step-up standardisation, the person would need to be extremely fit with regards to leg muscle strength, maximum mobility, balance and coordination in relation to age, sex, body weight and, to a lesser extent, height.

In summary, the highest MSH level in theory has been named the estimated maximal step-up height and will be abbreviated as eMSH. The most advanced estimated MSH, only applicable to extremely fit persons, will be abbreviated as aeMSH.

aeMSH standardisation has been made in clinical practice in a pilot study (not published) on male middle-aged patients with type 2 diabetes (T2D) and on men from a recreational joggin group (11/13), already familiar with MST from taking part in Study I. Preliminary data showed additional clinically important information when calculating the change in difference between aeMSH and assessed MSH before and after a short daily training programme. The training programme consisted of repeated MST on each leg and slow controlled knee-bending exercises, using both legs, performed regularly during six weeks. Further investigation on the clinical usefulness of assessing MSH in relation to aeMSH, and to follow the change in the difference between aeMSH and MSH after intervention, is recommended for further research.

6.2 MAXIMAL STEP-UP TEST (MST) AS A SELF-TEST

People across the globe have vastly different opportunities for leading healthy lives. Wide-spread changes in lifestyle over the last few decades that have meant reduced everyday physical activity – with increased sedentary behaviour, low aerobic fitness and low muscle strength as important consequences – have brought about many health risks for a very large number of people. Based on the findings presented in this thesis, and while awaiting further research to provide different easy-to-use functionality tests for routine testing of patients' leg muscle strength – a perishable article! – we want to encourage clinical staff within both primary and specialised health care to try out the clinical benefits of MST on individual patients. We would also like to recommend that health care professionals teach their patients to use MST (on two steps of a flight of stairs, on a number of step-up boards on top of each other or on another everyday device) as a self-test for leg strength and leg functionality. This would enable patients themselves to react to differences in functionality between legs and to reduced strength and functionality in relation to age and weight, or after symptom-inducing osteoarthritis in the hip or knee, when detecting a decrease in MSH.

7 CONCLUSIONS

In clinical practice, objective measurements of physical function are seldom used and routines are generally not in place. The maximal step-up test – assessing maximal step-up height on each leg – represents one aspect of current individual leg function, and is most likely dependent on leg muscle strength, but also on mobility, coordination, joint stability, balance and degree of pain.

From this thesis is concluded that a maximal step-up test is simple to conduct, requires little equipment and space and can be performed by subjects in everyday clothing. We suggest that the maximal step-up test could be a useful and valid test of leg muscle strength and physical function and could be integrated into ordinary clinical routines.

This new standardised maximal step-up test is robust and safe and maximal step-up height could be valuable as a relevant health indicator in clinical practice, not least when assessing patients of all ages in order to prescribe physical activity as treatment.

A 3-month group exercise intervention significantly improved maximal step-up height, aerobic fitness and self-reported health, and decreased risk in female patients with reduced capacity to work, elevated cardio-metabolic risk and low self-reported health. At an average of 22-month follow-up investigation, when brisk walking was reported as the main exercise, the maximal step-up height was reduced to lower than baseline. However, significant positive effects remained for waist circumference, VO_2 max, self-reported health, physical function as well as exercise and physical activity. Regular group exercise 2-3 times per week with mixed aerobic fitness and strength training, and with support from health care professionals, is probably needed to maintain improved leg muscle strength and function among these primary health care patients.

However, regular group exercise 2-3 times per week with mixed aerobic fitness and strength training was associated with maintenance of maximal step-up height, whereas brisk walking for at least 150 minutes per week was not sufficient to maintain maximal step-up height in a subgroup of women.

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Figur 4. Standardiserat maximalt klivhöjdstest (MST) – instruktioner på svenska

Bild 1. Ena foten stadigt i golvet, den andra på brädan i klivlådan. Gå upp så högt som möjligt på tå med golvfoten, stå stilla och hitta balansen.

Bild 2. Titta framåt, sträck på ryggen, för över kroppsvikten till klivfoten på brädan. Stå stilla och hitta balansen.

Bild 3. Kliv långsamt upp utan att skjuta ifrån med golvfoten genom att pressa klivfoten mot lådan (brädan) samtidigt som överkroppen lutas lite framåt, därefter räta ut i knä och höft.

Bild 4. Klivet avslutas med att golvfoten placeras på brädan tillsammans med klivfoten.

Efter godkänt test höjs klivnivån tills den högsta godkända nivån nåtts. Tre försök på varje höjd är tillåtet. Testaren får gärna uppmuntra personen som testas under klivtestet. Högsta uppmätta klivhöjden (MSH) noteras för respektive ben och ett medelvärde för båda klivhöjderna kan användas för jämförelser och vid statistiska beräkningar. En låg maximal klivhöjd respektive sidoskillnad kan upptäckas.