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HEALTH-ENHANCING PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS

Prevalence, intervention and assessment

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ABSTRACT

Background and Aim: Rheumatoid arthritis (RA) is associated with poor health and functioning, and increased risk of cardiovascular disease. Health-enhancing physical activity (HEPA), defined in the present work as "a minimum of 30 minutes of at least moderately intense daily physical activity, whereof at least twice weekly circuit training sessions including both aerobic and muscular strength training", is a key component in the life-long management of RA as it reduces the risk of disability and comorbidity. The overall aim of the present work was to study the prevalence of HEPA and its correlates in people with RA, to describe the selection procedure for a one-year HEPA intervention, to explore the one-year adherence and response to the intervention program, and to examine the criterion validity of two assessment methods for estimation of aerobic capacity in people with RA.

Methods: Studies I and II, with cross-sectional designs, included 3,152 participants, mean age 56 years (SD 11.2). They were assessed with data retrieved from the Swedish Rheumatology Quality Registers (SRQ) and postal questionnaires. Study III is a study protocol describing a one-year HEPA intervention. Study IV, with a prospective longitudinal cohort design, included 220 participants mean age 59 years (SD 8.9), assessed with data from SRQ, questionnaires and physical performance tests before and after the one-year intervention. The HEPA program was performed in the participants' daily environment and at public gyms. Physiotherapists introduced daily physical activity and circuit training, and coached support groups applying behavioral change techniques. Twenty seven participants, mean age 62 years (SD 8.1) were recruited for Study V with a methodological design. The submaximal Fox-walk test and the Åstrand cycle ergometry test for estimation of maximal oxygen uptake (VO_{2max}) were validated against a maximal cycle ergometry test.

Results: A minority (11%) of the large, well-defined sample of people with RA reached recommended levels of maintained (>6 months) HEPA, while 69% reported HEPA the past week. Twenty-two percent of the variation in maintained HEPA was explained, and the most salient and consistent explanatory factors were exercise self-efficacy, social support and outcome expectations related to physical activity (Study I). Only 8% of the targeted sample for the one-year HEPA program was reached. Factors other than those related to the disease, i.e. sociodemographic and psychosocial factors mainly determined participation (Study II). High retention (88%) and reasonable attendance (50%) to the one-year HEPA program were observed. While no participant reported maintained HEPA at baseline, 37% did so after one year. A number of self-reported health outcomes improved as did physical capacity tests. Relations between adherence to the three main HEPA program components and response were not clear-cut (Study IV). The self-administered Fox-walk test overestimated aerobic capacity substantially while the Åstrand test displayed excellent criterion validity in a sample with fairly fit individuals (Study V). **In conclusion**, the results indicate a need for improved HEPA promotion, suggests that outsourced HEPA programs might be suitable for subgroups of persons with RA, and provides validity information on two submaximal tests of aerobic capacity.

SVENSK SAMMANFATTNING

Bakgrund och Syfte: Reumatoid artrit (RA) medför hälsoproblem och funktionshinder samt en ökad risk för kardiovaskulär sjukdom. Hälsofrämjande fysisk aktivitet (HFA), definierat i föreliggande arbete som "minst 30 minuters, minst måttligt intensiv, daglig fysisk aktivitet, varav minst två cirkelträningspass med konditions- och styrketräning i veckan", är en viktig del av den livslånga egenvården vid RA, eftersom detta minskar risken för funktionshinder och samsjuklighet. Det övergripande syftet med föreliggande arbete var att studera förekomsten av HFA och relaterade faktorer vid RA, att beskriva urvalsproceduren för en ettårig HFA-intervention, att utforska deltagande i och utfall av interventionsprogrammet samt att utvärdera kriterierelaterad validitet hos två utvärderingsmetoder för skattning av aerob kapacitet hos personer med RA.

Metoder: Delstudie I och II, med tvärsnittsdesign, inkluderade 3152 deltagare med medelåldern 56 år (SD 11.2). De utvärderades med data från Svensk reumatologis kvalitetsregister (SRQ) och postenkäter. Delstudie III är ett studieprotokoll som beskriver en ettårig HFA-intervention. Delstudie IV, med en prospektiv longitudinell kohortdesign, inkluderade 220 deltagare med medelåldern 59 år (SD 8.9). De utvärderades, före och efter den ettåriga interventionen, med data från SRQ, enkäter och tester av fysisk kapacitet. HFA-programmet utfördes i deltagarnas vardag och på allmänna gym. Fysioterapeuter introducerade deltagarna till daglig fysisk aktivitet och cirkelträning samt coachade stödgrupper med tillämpande av beteendeförändrings-tekniker. Tjugosju deltagare med medelåldern 62 år (SD 8.1) rekryterades till delstudie V som var en metodstudie. Det submaximala Fox-gångtestet (Hälsospåret) och Åstrands cykelergometertest för skattning av maximalt syreupptag (VO_{2max}) validerades mot ett maximalt cykelergometertest.

Resultat: En minoritet (11%) av det stora, väldefinierade stickprovet av personer med RA uppnådde rekommenderade nivåer av bibehållen (>6 månader) HFA, medan 69% rapporterade att de uppnått HFA senaste veckan. Tjugotvå procent av variationen i bibehållen HFA förklarades och de viktigaste förklaringsfaktorerna var self-efficacy, socialt stöd och förväntningar på effekter av fysisk aktivitet (Delstudie I). Bara 8% av dem som preliminärt uppfyllde kriterierna för det ettåriga HFA-programmet nåddes. Deltagande avgjordes huvudsakligen av faktorer som inte var relaterade till sjukdomen (Delstudie II). Bortfallet var litet (88%) och deltagandet var acceptabelt (50%) i det ettåriga HFA-programmet. Ingen deltagare uppfyllde kravet för bibehållen HFA vid studiestart, medan 37% gjorde det efter ett år. Ett antal självrapporterade hälsomått förbättrades, liksom fysisk kapacitetstester. Sambanden mellan deltagande i HFA-programmets tre huvudkomponenter och utfall var inte glasklara (Delstudie IV). Det självadministrerade Fox-gångtestet överskattade aerob kapacitet medan Åstrand-testet uppvisade utmärkt kriterierelaterad validitet i det aktuella samplet av personer i relativt god form (Delstudie V). Sammanfattningsvis visar resultaten på behovet av att förbättra främjandet av HFA, att utlokaliserade HFA-program kan passa subgrupper av personer med RA och ger information om validiteten hos två submaximala tester av aerob kapacitet.

LIST OF SCIENTIFIC PAPERS

This thesis is based on the following original papers. Each paper will be referred to their Roman numerals (Study I-V).

I. Demmelmaier I, Bergman P, Nordgren B, Jensen I, Opava CH. Current and maintained health-enhancing physical activity in rheumatoid arthritis - the PARA 2010 study. Arthritis Care Res (Hoboken) 2013 Jul;65(7):1166-76

II. Nordgren B, Fridén C, Demmelmaier I, Opava C. Who makes it to the base? Selection procedure for a physical activity trial targeting people with RA. Arthritis Care Res (Hoboken) 2014 May;66(5):662-70

III. Nordgren, B, Fridén C, Demmelmeier I, Bergström G, Opava CH. Long-term health-enhancing physical activity in rheumatoid arthritis. BMC Public Health 2012 Jun 1;12(1):397

IV. Nordgren B, Fridén C, Demmelmaier I, Bergström G, Lundberg IE, Dufour A, Opava CH, the PARA Study Group. An outsourced health-enhancing physical activity program for people with rheumatoid arthritis. Exploration of adherence and response. Rheumatology (Oxford). Accepted for publication

V. Nordgren B, Fridén C, Jansson E, Österlund T, Grooten W, Opava C, Rickelund A. Criterion validation of two submaximal aerobic fitness tests, the self-monitoring Fox-walk test and the Åstrand cycle test in people with rheumatoid arthritis. BMC Musculoskelet Disord. Accepted for publication

In addition to the above papers, the thesis includes additional results that have not previously been published

CONTENT

LIST OF ABBREVIATIONS

BCT	Behavioral change technique
DAS 28	Disease Activity Score 28 joints
ESAI	Exercise Stage Assessment Instrument
ESES	Exercise Self-Efficacy Scale
FABQ-m	Fear-avoidance Beliefs Questionnaire - modified
HAQ-DI	Stanford Health Assessment Questionnaire – Disability Index
HEPA	Health-enhancing physical activity
IPAQ	International Physical Activity Questionnaire
PARA	Physical Activity in Rheumatoid Arthritis
RA	Rheumatoid Arthritis
RM	Repetition maximum
SCT	Social Cognitive Theory
SDT	Self-Determination Theory
SSEB-Family	Social Support for Physical Activity - Family
SSEB-Friends	Social Support for Physical Activity - Friends
TTM	Transtheoretical Model
VO2max	Maximal Oxygen Uptake

HEPA DEFINITIONS USED IN THE PRESENT WORK

HEPA	A minimum of 30 minutes at least moderately intense daily physical activity, whereof at least twice weekly circuit training including both aerobic and muscular strength training.
Current HEPA	The above definition performed the past week, with no specification whether ‘vigorous exercise’ is targeting aerobic capacity or muscle strength.
Maintained HEPA	The above definition performed the past six months

1 INTRODUCTION

1.1 RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a chronic, autoimmune and progressive disease which, if untreated, is associated with destruction and deformity of the joints. RA is the most prevalent inflammatory rheumatologic condition, affecting 0.5-0.8% of the adult population (1, 2). The estimated prevalence in Sweden is 0.7-0.8%, with a higher prevalence in older age groups and in women (3). Common early clinical features include swollen and tender joints in finger and forefeet. Although any joint may be affected, there is a predisposition for peripheral joints (4, 5). Pain and fatigue are dominant symptoms of RA, but morning stiffness and depression are also prevalent (6, 7). Impairments such as decreased aerobic capacity and reduced muscular strength are common, causing activity limitation and participation restriction in daily life (8, 9). Moreover, mounting evidence exists that RA is associated with increased mortality and morbidity from atherosclerotic cardiovascular disease (CVD) (10, 11).

The prognosis of RA is predicted by non-modifiable and modifiable factors, where non-modifiable factors include age, gender, genetic factors and disease-specific factors such as autoantibody status (12). Modifiable factors include pharmacological treatment, and lifestyle factors such as smoking and physical activity (12). Pharmacological treatment has improved remarkable the past decades (13). Disease-modifying antirheumatic drugs and biologic agents reduce joint swelling and pain, limit progressive joint damage, and improve functioning in many patients (4). However, the drugs may cause both minor and serious adverse effects, the optimal onset of treatment and the selection of treatment still needs to be improved, and not all patients achieve clinical remission (12, 14). Despite low levels of inflammation, many patients still perceive high levels of pain, fatigue and sleep disturbances, and the lower survival rate in RA, mainly from CVD has not improved over time (6, 15, 16).

1.1.1 Non-pharmacological treatment in RA

To help patients cope with the consequences of the disease, a wide variety of non-pharmacological treatment for RA, are provided by health professionals (17, 18). While physical exercise, patient education and self-management interventions have proven effective, assistive devices, foot orthoses, and dietary interventions are less so (18).

Given that guidelines emphasize the importance of exercise therapy as well as providing information and advice about physical activity, health professionals need sufficient knowledge and skills within this field (17, 19). However, patients with RA perceive that health professionals lack certainty and clarity regarding exercise recommendation, and it is indicated that health professionals do not prescribe exercise according to the guidelines (20-23). With expert knowledge of the musculoskeletal system and exercise physiology, the physiotherapist plays a significant role when promoting physical activity (24). In addition to the traditional role as a clinical expert, the physiotherapist also needs adequate skills to

promote health-related behaviors, which may not always be part of the traditional education and training to become a physiotherapist.

1.2 PHYSICAL ACTIVITY

1.2.1 Definitions

Physical activity is defined, according to Caspersen et al (25), as "any bodily movement produced by skeletal muscles resulting in energy expenditure". It could be categorized as activities concerning e.g. household, occupational, leisure or any other kind of activity. Given that physical activity includes all kinds of movements or tasks a person performs, it is useful to recognize subcomponents of physical activity. Caspersen et al (25) defined *physical exercise* as physical activity that is "planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness". *Physical fitness* is defined as "a subset of attributes that people have or achieve that relates to the ability to perform physical activity" (25).

The distinction between these constructs is not always obvious and clear, and they are often used interchangeably in the literature, leading to difficulties in evaluating, comparing and interpreting studies.

1.2.2 Health-enhancing physical activity recommendations

It is widely acknowledged that physical activity and physical exercise confer multiple health benefits for the general population and for people with chronic conditions such as RA. The concept of health-enhancing physical activity (HEPA) refers to the physical activity and physical exercise recommendations developed by the American College of Sport Medicine (ACSM) and the American Heart Association (AHA) (26). The recommendations apply to healthy adults aged 18-65 years and state:

- Moderate intensity aerobic physical activity should be performed regularly for a minimum of 30 minutes, at least five days per week or substituted by 20 minutes of vigourus activity three days per week
- The 30 minutes of moderate intensity aerobic physical activity could be accumulated in several bouts performed 10 minutes or more
- Muscular strength exercising should be performed twice weekly, including ten exercises and 8-12 repetitions of each exercise

The ACSM and AHA have also outlined separate recommendations for older adults >65 years, or for adults 50 to 64 years with chronic conditions and/or functional limitation (27). These recommendations are similar to those previously described but also emphasize:

- The individual´s aerobic fitness should be taken into account when recommending intensity of aerobic activity
- Activitites that improve or maintain flexibility

- Balance exercises for patients with risk of falls
- An individual activity plan for achieving recommended activity

1.2.3 Physical activity in RA

Substantial evidence exists that physical activity is safe, beneficial and has no detrimental effect for individuals with RA. If exercise is performed with sufficient intensity and duration, aerobic capacity and muscular strength increase and activity performance improve (28, 29). Exercise can reduce pain, fatigue and morning stiffness, as well as improve psychological well-being and quality of life (29, 30). Further, regular physical activity before disease onset is associated with a milder disease at diagnosis (31). In reducing the risk for CVD in the general population, the role of regular physical activity is well documented. Whether this is the case in people with RA are until now sparsely studied. However, in a recent study, several CVD risk factors improved in patients with RA following six months of high intensity aerobic- and muscular strength training (32). Further, physically inactive individuals with RA, have a worse cardiovascular profile compared to those who are active, most likely contributing to the increased risk of CVD (33).

Despite the known benefits of physical activity, it is apparent that individuals with RA are less physically active than their healthy counterparts (8, 34, 35). However, it is not possible to date, to judge or conclude from existing literature, to what extent, individuals with RA reach the updated HEPA recommendations including both aerobic physical activity and muscular strength training (26). Recommendations for future research include larger sample sizes, use of objectively measurement of physical activity, use of outcome measures valid and reliable in the RA population, and definitions of terminology used (36).

1.2.4 Factors related to health-enhancing physical activity

For those involved in the care of patients with RA and for the development and improvement of physical activity interventions, it is important to understand factors associated with HEPA behavior (37). Although individuals and interpersonal variables are the most studied factors, environmental, policy and global variables are also thought to have widespread effects on physical activity behavior (38). Since a majority of studies reporting on correlates are of cross-sectional design, one should bear in mind that the findings do not provide evidence for a causal relationship between variables under investigation, and should therefore be interpreted with caution (39). For the general population some consistent correlates have been identified; male gender, reported health, intention to exercise, self-efficacy and previous physical activity (38). This mainly corresponds with correlates in people with RA, reported in a recent review; perceived health, self-efficacy, motivation, and previous physical activity (40). In this review comprising ten studies, age (examined in eight studies) and gender (examined in six studies) showed inconsistent or no correlation to physical activity, as was also the case with exercise beliefs and expectations (examined in three studies). However, due to the small number of studies included in the review, the wide range of variables investigated and the diversity of assessment methods and sometimes inappropriate statistical

analysis used, pooling of the results to make a definite conclusion of the strength of the associations could not be performed (40). To get a deeper insight in correlates associated with physical activity behavior in people with RA, more research is needed with larger and well-defined samples. It is also important to highlight that some correlates can be influenced by psychological interventions, which in turn can increase the level of physical activity, while other correlates such as age or gender are non-modifiable (41).

1.3 HEALTH-BEHAVIOR

1.3.1 Health-behavior theories

To better understand the psychological influences and processes which impact health behavior such as physical activity, different theories or models of behavior change have been developed. The Transtheoretical Model (TTM), the Social Cognitive Theory (SCT) and the Self-Determination Theory (SDT) are frequently applied in physical activity interventions (Figure 1). According to the TTM, behavior change occurs continuously through a cyclic process in five different stages; from the pre-contemplation stage at which there is no intention to change behavior, to the maintenance stage where a person has sustained the behavior for at least six months (42). Processes of change are activities that people use to progress through the stages. In intervention programs they are matched to each individual's stage of change to reach behavioral change. Other components of the TTM that have been applied to physical activity are decisional balance, i.e. reflecting the pros and cons of changing behavior, and exercise self-efficacy, i.e. the confidence in an individual's ability to complete a task under different circumstances. The SCT posits that learning occurs in a social context in a dynamic process in which personal factors, environmental factors, and behavior interact (43). According to learning theory, a person is more likely to be physically active when the right circumstances are in place, and beneficial consequences occur, as a result of physical activity. Important constructs in the SCT are reciprocal determinism, reinforcements, behavioral capability, observational learning, exercise self-efficacy and self-control. The SDT is a theory of motivation and personality where the focus is to understand why some people engage in positive and adoptive health behaviors and why others do not (44). According the SDT, individuals have inborn tendencies towards growth and development which can be facilitated by the social context, via the satisfaction of three key psychological needs; autonomy, competence and relatedness. SDT stress the extent to which behaviors are relatively autonomous (i.e., people engage in an activity because of internal factors, that is behaviors originate from the individual) versus relatively controlled (i.e. the extent to which behaviors are pressured or coerced by others). The above described model and theories are promising when applied in interventions promoting physical activity and exercise (45, 46).

1.3.2 Behavior change techniques

Behavior change techniques (BCTs) are frequently used in interventions to increase physical activity and are considered important in both the SCT and the SDT, and are also applied in the TTM (47). BCTs are defined as "observable, replicable, and irreducible component(s) of

an intervention designed to alter or redirect causal processes that regulate behavior", e.g. goal-setting, self-monitoring of behavior, feed-back, motivation, relapse prevention, problem solving (48). An extensive, consensually agreed hierarchically structured taxonomy of these BCTs used in behavior change interventions was recently published (49). The long-term goal of the this work on a taxonomy, is to reach consensus of a BCT taxonomy as a method for specifying, evaluating and implementing behavior change intervention that has internationally acceptance and use (49).

Many interventions include multiple or overlapping techniques from behavior theories, in order to maximize the effectiveness of an intervention (50, 51). This leads to difficulties in identifying which techniques or whether specific combination of techniques, are more effective than others.

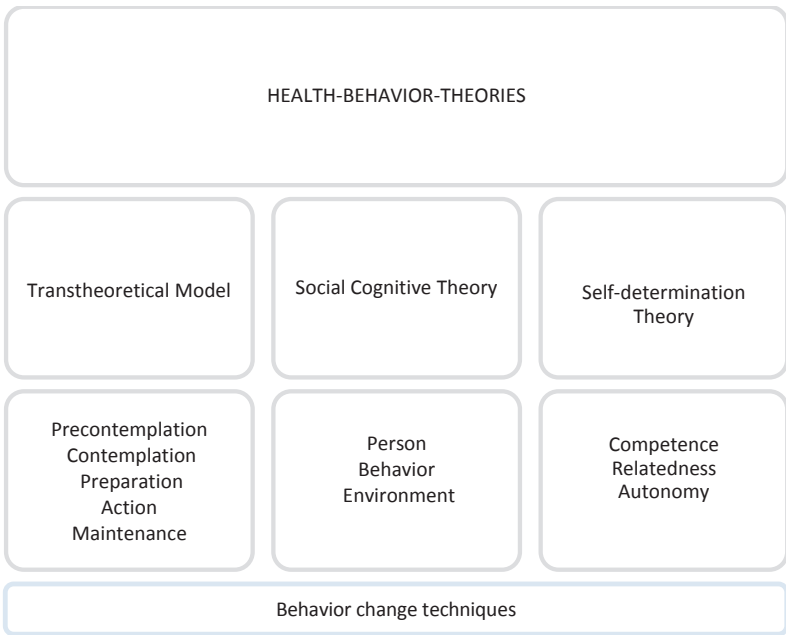


Figure 1. Health-behavior theories and behavior change techniques

1.3.3 Interventions to promote health-enhancing physical activity in RA

Only three randomized controlled health behavior change interventions in RA were identified in a recent systematic review aiming to determine whether those interventions can increase physical activity levels (52). However, none of the studies included utilized a specific behavior change theory, although several recognized elements from different theories were identified. It was not possible to conclude whether behavior change interventions can increase physical activity levels in RA due to poor quality of research (52). A review on the effectiveness of self-management interventions to promote exercise or physical activity, reported improvements in a number of outcomes, of which a majority assessed body function, activity performance, perceived health and disease activity (53). Only five (two of which

were included in the previous mentioned review) of the 15 studies included, used counseling, coaching or education with cognitive behavioral approaches. The intervention duration varied from four weeks to one year, a majority of the studies were performed in a clinical setting, and the exercise was supervised in most studies. For the majority of the studies, benefits from exercise generally did not persist at follow-up (53). A systematic review and meta-analysis of 27 randomized controlled trials of psychological interventions of increasing physical activity in RA indicated that several BCTs (goal-setting, planning, self-monitoring, feedback, relapse-prevention) had a positive impact on physical activity level among patients with RA (41).

The methodological quality of the trials included in the reviews by Iversen and Knittle have improved over time, as indicated by quality analysis performed (41, 53). However, methodological flaws, including insufficient description of recruitment methods and intervention components still exist and are in need of improvements to ensure internal and external validity.

Adjunct to supervised exercise, patient education for the promotion of physical activity is now recommended (17, 19). To optimize patients' self-management, some important factors enhancing the effectiveness of self-management have been identified, i.e. patient education should last at least six weeks, use of cognitive behavioral approaches, individualized weekly action plans, the use of protocols and handbooks, provision by the same trained leader, and the use of self-regulatory techniques (18).

In summary, up to this date very few interventions promoting health behavior changes in RA have taken a comprehensive theory-based approach to behavior-change, most likely contributing to initial ineffectiveness and long-term null effects of such interventions (54). Moreover, adherence and response related to physical activity are poorly described, and increased knowledge of what characterizes individuals that respond best to a certain intervention is needed.

As previously stated, the effectiveness of structured and supervised exercise in a clinical setting is evident, but physical activity also needs to be supported in other contexts, in order to encourage independence of health care. However, this is sparsely investigated in people with RA.

1.4 AEROBIC CAPACITY

1.4.1 Assessment of aerobic capacity

The internationally recommended core sets for outcome measures in clinical trials in RA include measures suitable for use when evaluating physical activity interventions (55). However, they do not include measures of aerobic capacity, which is crucial to evaluate physical activity interventions. Furthermore, aerobic capacity is not related to, or captured by, other measures of body function, frequently used in the management of patients with arthritis (56). The gold standard method to measure aerobic capacity or maximal oxygen uptake (VO_{2max}) is maximal testing by the collecting and analysis of respiratory gases performed in a

laboratory setting. However, the test requires maximal effort which is not always possible in people with RA, due to e.g. fatigue or pain. Instead, submaximal test for estimating VO_{2max} can be used.

1.4.2 The Åstrand cycle ergometry test

The Åstrand cycle ergometry test, which predicts VO_{2max} from the steady-state heart rate achieved after six minutes constant loading, at an individually chosen work rate, is one of the most commonly used cycle ergometry test (57). The test is feasible for people with RA, and is suitable for use by professionals in clinic and research (58). Although the Åstrand test is recommended as an assessment method in physiotherapy guidelines in the management of patients with RA, it has not been tested for validity in this population (19).

1.4.3 The Fox-walk test

In line with effective self-management strategies when promoting physical activity, self-administered test for estimating VO_{2max} should also be encouraged by health care providers (47). Different tests based on performance in walking for healthy individuals, as well as for persons with chronic conditions and older people, have been developed to estimate VO_{2max} (59-61). However, the distance in some of these tests could be considered too far for people with RA. The heart rate must be monitored or the speed needs to be paced, making it complicated to administer the test without equipment or help from another person. A novel and promising walking test, the Fox-walk test for estimation of VO_{2max}, is easy to perform and has previously been developed and also tested for reliability in individuals with RA (62). However, the test still needs to be validated in this population.

1.4.4 Validation

Simple and easy methods that are reliable and valid for evaluating aerobic capacity in RA are urgently needed, thus the Åstrand test and the Fox-walk test should be validated. The criterion-concurrent validity of the Åstrand and the Fox-walk tests need to be examined against a gold standard measure, e.g. a maximal cycle ergometry test, to establish the correlation between those measures.

1.5 THE SWEDISH RHEUMATOLOGY QUALITY REGISTER (SRQ)

The Swedish Rheumatology Quality Register was initiated the mid 1990s and is a web-based national surveillance system covering a majority of the entire RA population in Sweden (63). It is used in clinical practice and the number of variables to be collected is therefore minimized. The register contains information on date of diagnosis, onset of symptoms, age, gender, rheumatoid factor, disease-activity, perceived health, pain, fatigue and activity limitation. The information is collected at first entry and thereafter information on disease activity and pharmacological treatment is entered at subsequent visits in the out-patient clinics. Using the unique national identification number issued to all Swedish residents, data from other national and clinical registers on e.g. demographics, morbidity and mortality can be linked with data from the SRQ (64). The register provides excellent opportunities to

identify study samples and to perform long-term follow ups. However, complete data on individual patients may be missing and reporting from the rheumatologists to the register still needs to be improved (65).

1.6 THE PARA 2010 STUDY

The PARA 2010 Study is performed within the context of the SRQ, and is a further development of the original PARA Study, initiated in 1999. Since then, the previously mentioned physical activity recommendations have changed to also include strength training, defined as HEPA in this thesis (26, 66). Within the PARA Study, a number of studies have increased the understanding of physical activity, its promotion and outcome in people with RA (8, 67-69). Although beneficial one-year effects were found following the previous PARA interventions, follow-up indicated that improvements and physical activity behavior was not maintained long-term and the inclusion of further steps to include techniques for the long-term, maintenance of physical activity was recommended (67).

1.7 RATIONALE FOR THIS THESIS

RA is a major cause of disability, and individuals with RA have an increased risk of comorbidity related to cardiovascular diseases. As for the general population, physical activity confers health benefits, maintains functioning, and most likely prevents cardiovascular disease in individuals with RA. However, individuals with RA are less physically active compared to their healthy counterparts and it is still not known to what extent individuals with RA adhere to existing physical activity recommendations over time. Recent research shows that the adoption and maintenance of physical activity and exercise interventions is suboptimal in RA, and information is scarce regarding what characterizes the individuals that consent to participate in physical activity interventions compared to those that don't. Furthermore, adherence, response and maintenance of physical activity behavior still need to be explored to deepen the understanding of this behavior. Measuring physical activity is central in health promotion and is used to understand the relation between physical activity and health outcomes, to survey physical activity in populations and to measure the effectiveness of interventions designed to increase physical activity. To be used with confidence, existing methods for evaluating physical capacity need to be further developed and validated in individuals with RA.

2 AIMS

The overall aim of this thesis was to study the prevalence of physical activity levels, to explore adherence and response of a one-year HEPA intervention, and to validate assessment methods of aerobic capacity tests in people with established RA.

Specific aims of the studies included in this thesis were:

I. To describe and identify the explanatory factors of variation in current and maintained HEPA in a large and well defined sample of individuals with RA.

II. To compare individuals with RA at target for a HEPA trial, those who were finally included with those who were not.

III. To describe the recruitment procedure, design, assessments methods, and the intervention program of a HEPA study targeting individuals with RA.

IV. To document adherence and changes of HEPA levels, self-reported and assessed functioning, and to explore aspects of adherence and response during the first year of an outsourced two-year HEPA program in individuals with RA.

V. To examine the criterion-validity of the self-monitoring Fox-walk test and the submaximal Åstrand cycle test against a maximal cycle test in individuals with RA, and to study the influence of different formulas for age-predicted maximal heart rate when estimating VO_{2max} by the Åstrand test.

3 METHODS

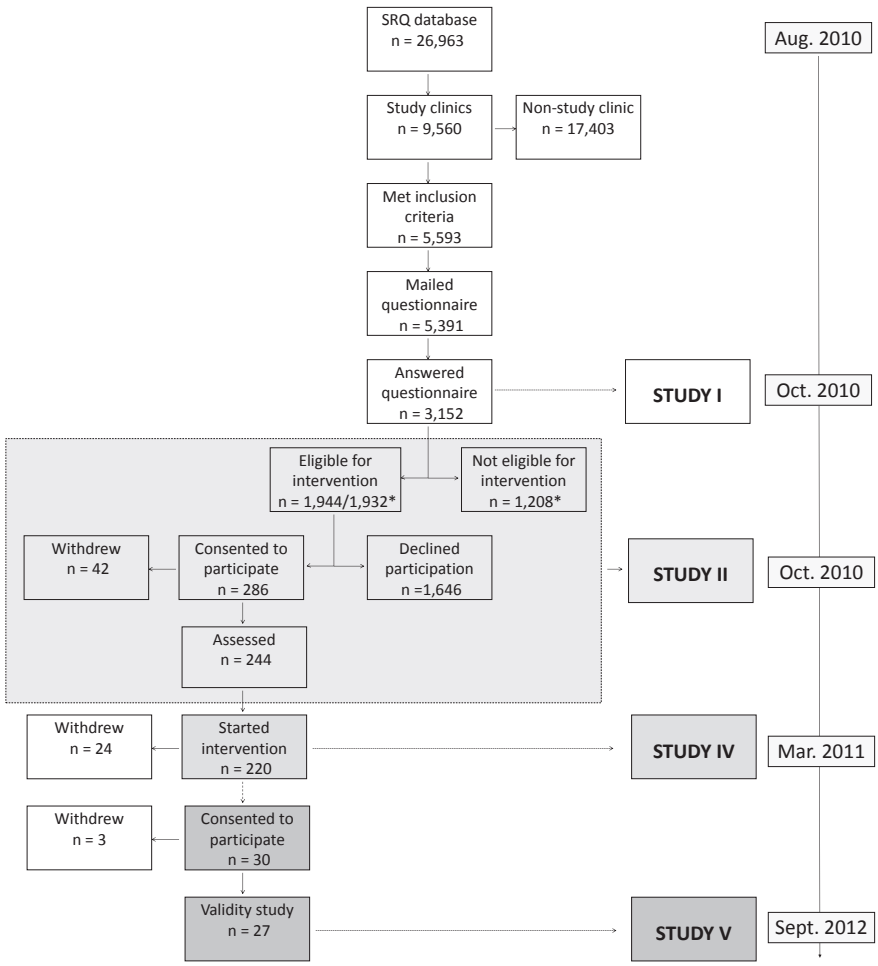
3.1 STUDY DESIGNS

Five studies are included in the thesis. **Study I** is of cross-sectional design, **Study II** of prospective descriptive design, **Study III** is a study protocol with a comprehensive description of the sample, assessment methods, and intervention evaluated in **Study IV**, which is of prospective observational design, and **Study V** is of methodological cross-sectional design.

3.2 PARTICIPANTS

The participants in all studies originate from the same study sample recruited from the SRQ. At the time for initial recruitment in 2010, the registers comprised almost 27, 000 cases with RA. An overview of sample sizes and time points for data collection for each study is depicted in Figure 2.

For the purpose of defining a target population for a HEPA program, the SRQ registers were searched in August 2010 to identify patients diagnosed with RA, aged 18-75 years and independent in daily living (Stanford Health Assessment Questionnaire Disability Index, HAQ ≤ 2) from six rheumatology clinics. The clinics were chosen to represent university and county hospitals in rural and urban areas and different parts of Sweden. Of 9,560 patients from the six clinics, 5,593 were identified as potentially eligible for the HEPA program. A questionnaire, including a question of interest in participating in a HEPA program, was mailed to the 5,391 patients that could be reached, of whom 3,152 responded, and thus constitute the sample in Study I and Study II. Of the 3,152 participants, 1,932 expressed an interest to participate in a HEPA program. They did not obtain maintained HEPA (> 6 months) and had no language difficulties and were therefore mailed a letter of invitation to the HEPA program. Two hundred and eighty six consented to participate in the HEPA program, 244 showed up for baseline assessments, and finally 220 started the intervention and constitute the sample in Study IV. A convenience sample of 44 participants in the intervention group from the Karolinska University Hospital study clinic were approached by e-mail or phone and asked to participate in Study V, 30 consented and 27 were included and constitute the sample in Study V. Demographics and disease-related characteristics of the participants are presented in Table 1.



* 12 patients were excluded due to participation in another study

Figure 2. Flowchart of sample sizes and time point for data collection for each study.

Table 1. Characteristics of the participants I Study I, II, IV, and V.

Characteristics	Study I+II	Study IV	Study V
Gender			
Men, n (%)	843(27)	41 (19)	5 (9)
Women, n (%)	2309 (73)	179 (81)	22 (81)
Age (years), mean (SD)	56 (11.2)	59 (8.9)	62 (8.1)
Education, university, n (%)	1025 (33)	112 (51)	5 (18)
Income, above average	1431 (45)	152 (69)	22 (81)
Children < 18 years, n (%)	505 (16)	35 (16)	3 (11)
Disease duration, years, median (IQR))	9 (4-16)	10 (4-17)	15 (7-30)
Disease activity DAS28, 0-10 median (IQR)	2.82 (2-3)	2.64 (1.99-3.51)	2.37 (2.15-2.8)
Pain VAS, 0-100, median (IQR)	25 (10-48)	21 (11-45)	19 (7-28)
Perceived health VAS, 0-100, median (IQR)	25 (10-49)	25 (14-47)	14 (7-25)
Activity limitation HAQ-DI, 0-3, median (IQR)	0.5 (0.125-1)	0.375 (0.13-0.875)	0.379 (0-0.75)

3.3 ASSESSMENTS

An overview of assessments used in Study I, II, IV and V is presented in Table 2, page 14. Data on age, gender, disease activity, disease duration, and activity limitation were retrieved from the SRQ when searching the target population for the HEPA trial in August 2010. These data were supplemented with data from a mailed questionnaire including a number of separate questionnaires on sociodemographic, disease-related, psychosocial characteristics and on HEPA-levels. Participants in Study IV and V were in addition assessed with performance tests and anthropometrics. In Study IV, adherence to HEPA was assessed with weekly text messages. A detailed description of each assessment method used in Study I, II and IV is given in paper III. A detailed description of the tests in Study V is given in paper V.

Table 2. Assessments used in Study I, II, IV and V.

	Method	Measurement unit	Study
SRQ and patient records			
Activity limitation	HAQ-DI	0-3	I, II
Age	-	Years	I, II
Disease activity	DAS28	0-10	I, II, IV, V
Disease duration	-	Years	I, II, IV, V
Gender	-	Female/male	I, II
Medication	-		V
Questionnaire			
Activity limitation	HAQ-DI	0-3	I, II, IV, V
Exercise self-efficacy[1]	ESES	6-60	I,II,IV
Fatigue	VAS	0-100	I, II, IV, V
Fear-avoidance beliefs[1]	FABQ-m	0-24	I, II, V
Health perception[2]	VAS	0-100	I, II, IV, V
Health status	EQ-5D	0-100	I, II, IV
HEPA - current	IPAQ	Yes/No	I, II, IV
HEPA - maintained	ESAI	Yes/No	I,II,IV,V
Pain	VAS	0-100	I, II, IV, V
Outcome expectations - health		0-10	I, II, IV
Outcome expectations - RA		0-10	I, II, IV
Social support for physical activity - family	SSEB-Family	0-65	I, II, IV
Social support for physical activity - friends	SSEB-Friends	0-65	I, II, IV
Performance tests			
Grip strength-average[1]	Grippit	Newton	IV
Grip strength-max, right[1]	Grippit	Newton	IV
Oxygen uptake, estimated[1]	Åstrand cycle test	l/min, ml·kg^{-1}·min^{-1}	IV, V
Oxygen uptake, estimated[1]	Fox-walk test	l/min, ml·kg^{-1}·min^{-1}	V
Oxygen uptake, maximal[1]	Maximal cycle test	l/min, ml·kg^{-1}·min^{-1}	V
Time standing (lower extremity function)	TST	s	IV
Anthropometrics			
Blood pressure, diastolic	Sphygmomanometer	mmHg	IV, V
Blood pressure, systolic	Sphygmomanometer	mmHg	IV, V
Body mass Index	Weight/length scale	kg/m^2	IV, V
Waist circumference	Tape measure	cm	IV
Adherence			
Weekly number of short text messages	SMS	0-7	IV, V

[1]secondary response variable, [2]primary response variable in Study IV

3.4 INTERVENTION

The one-year HEPA intervention program included three main components; moderate-intensity physical activity, circuit training sessions, and support group meetings. An overview of the different components is presented in Figure 3.

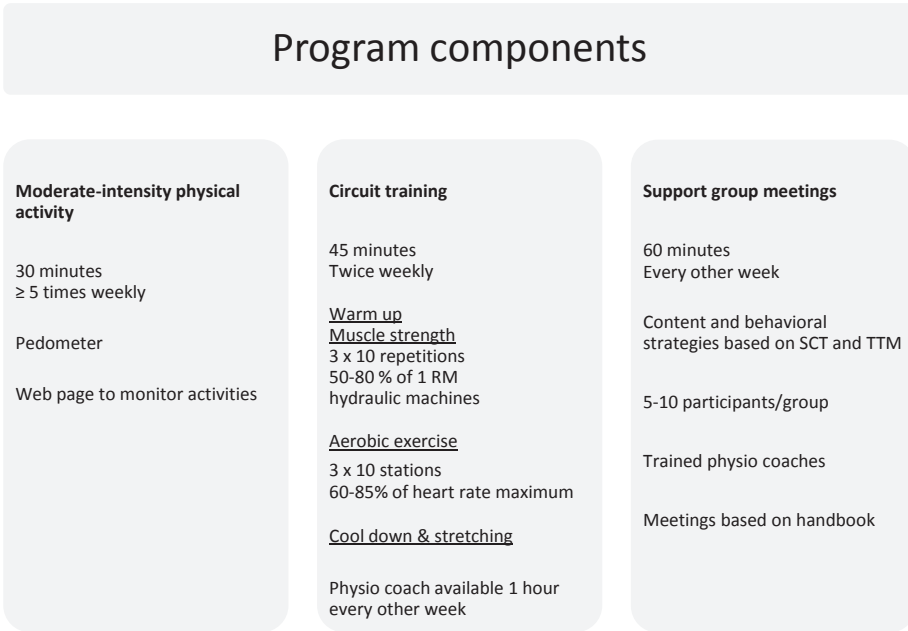


Figure 3. Program components

3.4.1 Moderate-intensity physical activity

The participants were encouraged to perform at least 30 minutes of physical activity on a moderate-intensity level on most days of the week. They were provided with a pedometer and free access to a web page for optional registration and monitoring of their physical activity.

3.4.2 Circuit training

Participants were encouraged to take part in at least two weekly 45-minutes circuit training sessions at a public gym, and they committed to pay the costs related to the training. The circuit consisted of 20 stations; providing both muscle strength training and aerobic exercises. The equipment was hydraulic and produced concentric resistance relative to exercise speed. Each station took 30 seconds, and three circuit laps were expected to be performed. A physiotherapist was initially present to instruct and assist in adjusting the program to each participant's needs and preferences and the same physiotherapist was also available at the gym one hour every week at fixed times. The physiotherapists' role was also to encourage the participants to exercise at a sufficient intensity and load.

3.4.3 Support group meetings

During the intervention, 13 physiotherapists at 8 different gyms, guided one hour bi-weekly support group meetings with 5-10 participants. The group meetings aimed to facilitate learning of specific behavioral skills to enable incorporation of circuit training and moderate-intensity HEPA into daily routines. The idea of the group format was to enable social support, positive reinforcement of HEPA, and observational learning by sharing experiences with

other participants. The meetings were based on a study-specific handbook, designed for the intervention. It comprised topics (e.g. pain, sleep and stress, fatigue, beliefs, risk situations) to discuss at each meeting, and it also included general information on behavior change, HEPA, aerobic exercise, muscle strength training, and the performance tests used in the study. At each group meeting, specific and individual goal-setting were systematically evaluated and adjusted, participants gave each other feedback on performance and they practiced problem-solving to help overcome present and future barriers. Knowledge, attitudes, and self-efficacy for HEPA based on the participants' previous experiences were discussed, and relapse-prevention was practiced.

3.4.4 Tools for maintenance

Alternative types of activities, e.g. Nordic walking, yoga, and out-door gym were encouraged and practiced, individually or together with group peers. Challenge competitions were organized to prevent relapse during holidays. The participants were taught and encouraged to regularly monitor aerobic capacity with the Fox-walk test and muscle function with the timed stands test. They were also provided with short message service (SMS), weekly text messages to monitor and encourage their HEPA.

3.4.5 Extras

Expert lectures on participants' preferred topics, e.g. medication, diet and complementary medicine, were offered, once or twice during the year depending on study site.

3.4.6 Preparing delivery

Physiotherapists experienced in rheumatology ('physio coaches') were trained to deliver the intervention. They were provided with a tailored six-days course spread over two two-day sessions before the intervention and two one-day booster sessions during the intervention. The focus was on learning coaching skills to support the strategies used in the group meetings. The physio' coaches were provided with a manual, based on the content of the participants hand books. A study specific treatment protocol was presented stating which core components should be included in the early, intermediate and late phases of the intervention. The course days also included lectures on exercise physiology, evidence based physical activity in RA, pedometer use, and self-administered tests for evaluating body functions.

On-site visits were made by one of the researchers to the physio coaches local gyms to instruct and discuss correct performance of the circuit training in order for the participants to obtain enough exercise intensity and load. Each physio coache was also introduced to, and provided with a heart rate monitor enabling them to give feed-back on their participants' performance.

The physio coaches were video recorded and given feed-back on behavioral performance by one of the researchers at two selected group meetings during the first year. Sequences from the video recordings, selected to serve as good examples of coaching and enabling observational learning among the coaches, were published on an internet community. On the

internet community the coaches could exchange experiences during the year and get feedback from the fellow researchers on selected issues.

3.4.7 Procedures for the intervention

Before the HEPA program started, 14 trained physiotherapists conducted baseline assessments including performance tests and collection of self-reported data at the six rheumatology clinics. The participants then took part in the one-year HEPA program, and follow-up assessments were performed by the same physiotherapists after one year. To assure the quality of the assessments, the physiotherapists were trained to administer the questionnaires, perform all the physical performance tests as well as calibrate the test equipment in a standardized setting during four days prior baseline assessments and two days prior follow up.

3.5 CRITERION VALIDATION

The submaximal Fox-walk for estimation of VO_{2max} was carried out by trained test-leaders at an outdoor track

The submaximal Åstrand cycle test (57) for estimation of VO_{2max} and a maximal cycle test (measured VO_{2max}) for direct measurement of VO_{2max} were carried out in a laboratory setting by an experienced biomedical scientist under close observation of a physician. The Åstrand test and the maximal cycle test were performed at the same test occasion separated by five minutes' rest in between.

All tests were conducted within a week.

3.6 DATA MANAGEMENT AND ANALYSES

3.6.1 Study I

The participants were classified as obtaining current and maintained HEPA in order to describe and identify explanatory factors of variation of HEPA levels. Current HEPA was defined as having performed at least moderate intensity aerobic physical activity for a minimum of 150 minutes during the past week prior to baseline assessment. Maintained HEPA was defined as having performed at least moderate intensity aerobic physical activity for a minimum of 150 minutes per week and/or muscle strength training at least twice weekly during the past six months prior to baseline assessment.

3.6.2 Study II

In the selection procedure for the HEPA program, differences between individuals making it to the baseline assessments and those who did not were analyzed in three steps, described in Figure 4.

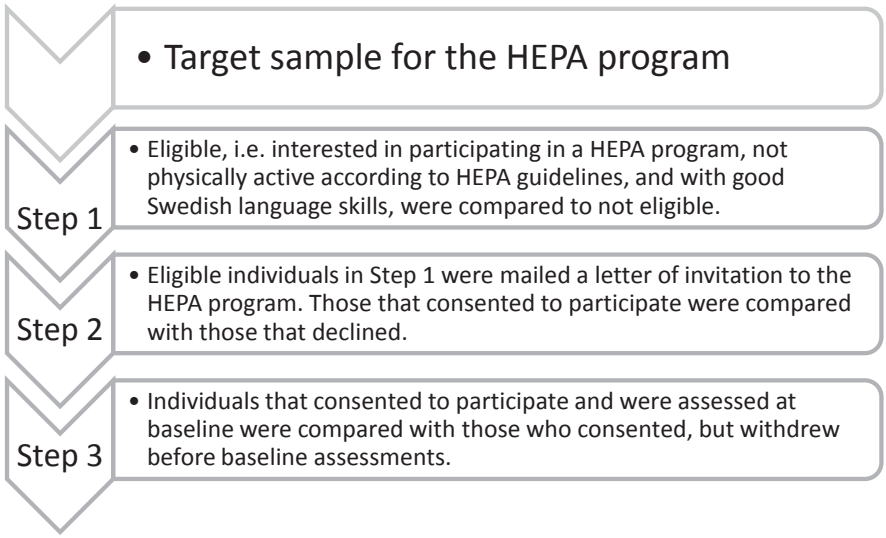


Figure 4. The selection procedure for the HEPA program described in a three steps process.

3.6.3 Study III

Study protocol describing the HEPA program.

3.6.4 Study IV

To explore and examine adherence and response to the intervention, the three intervention components: circuit training, total HEPA (including circuit training), and support group meetings along with the primary and secondary response variables were incorporated. The maximal expected number of circuit training sessions during the year was 104, the total maximal number of HEPA sessions were 365 (including circuit sessions), and support group meetings were 20-22 depending on study site.

Adherence
The participants were categorized into adherers or non-adherers based on 50%, 70% and 90% participation in circuit training sessions, total HEPA, and support group meetings. The mean changes in the primary and secondary response variables from baseline to follow-up were compared in adherers versus non-adherers.

Response
Participants were categorized into responders or non-responders based on 10%, 20% and 30% one-year improvement in the primary and each of the secondary response variables. Differences between mean adherence to each of the three program components in the responders and non-responders were examined.

A total response variable, in addition to the individual response variables, was also created. The total response variable was based on improvement in general health perception and at least two out of three performance tests. Using the total response variable at the 10% level of

improvement at the end of the intervention year, baseline characteristics of participants were compared in responders versus non-responders.

3.6.5 Study V

A previously developed equation was used to estimate VO_{2max} by the Fox-walk test using gender, age, height, BMI, walking speed, length and ascendance of the track.

The assessed maximal heart rate from the measured VO_{2max} test and the age corrected heart rate from the Åstrand-Rhyming nomogram (57) were used to estimate VO_{2max} for the Åstrand test. To study the influence of other formulas for age-predicted maximal heart rate to estimateVO_{2max} by the Åstrand test, the Fox-Haskell formula (220 - age) (70), the Tanaka formula (208 - 0.7·age) (71) and the Nes formula (211 - 0.64·age) (72) were used.

The estimated values from the submaximal tests were compared to the value obtained from the measured VO_{2max} test.

3.6.6 Data analyses

Table 3 lists the statistical methods used in the thesis. Alpha levels were set to 0.05 in all studies. To account for multiple testing in Study II and IV, alpha levels were set to 0.01. Statistical analysis were performed using Statistical Package for Social Sciences for windows (SPSS), version 20.0 (IBM) (Study I), StatSoftTM, STATISTICA, version 10.0 (Study II), version 12.0 (Study V) and Statistical Analyses Software (SAS), version 9.3 (SAS Institute) (Study IV).

Table 3. Statistical methods performed in Study I, II, IV and V.

	Study I	Study II	Study IV	Study V
Descriptive statistics				
Frequency (n), percent (%)	X	X	X	X
Median, inter quartile range	X	X		X
Mean, standard deviation			X	X
Statistical methods				
Chi-square test for homogenity	X	X	X	
Mann-Whitney U test	X	X		
Students paired T-test		X	X	X
Pearson´s correlation coefficient	X			X
Multiple imputation for missing data	X			
Multiple logistic regression	X			
Generalized linear models/repeated measures			X	
Bland-Altman method				X

3.7 ETHICS APPROVAL

All studies in this thesis were carried out in compliance with the Helsinki Declaration and were approved by the Stockholm Regional Ethical Review Board (Study I: 2011/1241-32, Study II: 2010/1232-31/1, 2011/1241-32, Study III: 2010/1232-31/1, Study IV: 2010/1232-31/1, Study V: 2011/1241-32).

4 RESULTS

4.1 STUDY I

Current HEPA (the past week) was reported by 69% of the participants and maintained HEPA (past six months) was reported by 11 %. Maintained HEPA separated into aerobic physical activity was reported by 21%, and maintained muscle strength training by 14%.

Eighteen percent of the variation in current HEPA was explained by the following factors; low age, higher education, good Swedish language comprehension, low activity limitation, moderate/high exercise self-efficacy, and high outcome expectations of physical activity on RA symptoms.

Twenty-two percent of the variation in maintained HEPA was explained by male gender, low age, low income, low/moderate fatigue, moderate/high self-efficacy, moderate social support, and outcome expectations of physical activity on health and RA symptoms.

The most consistent factors explaining variation in both current and maintained HEPA were self-efficacy, social support, and outcome expectations related to physical activity.

4.2 STUDY II

Of the total target sample, n = 3,152, for the HEPA program, 244 (8%) took part in the baseline assessments. In *Step 1*, 1,944 (62%), were identified as eligible for the PA trial and 1,208 (38%) were not. In *Step 2*, 12 individuals were excluded from the 1,944 eligible individuals due to participation in another study. Of the remaining 1,932 that were asked to participate, 1,646 (85%), declined participation, either actively (n = 965) or by not answering the invitation (n = 681). In *Step 3*, 244 of 286 (85%) individuals accepting participation were assessed at baseline and 42 (15%) withdrew. Differences between individuals making it to the baseline assessments and those who did not are described in Figure 5.

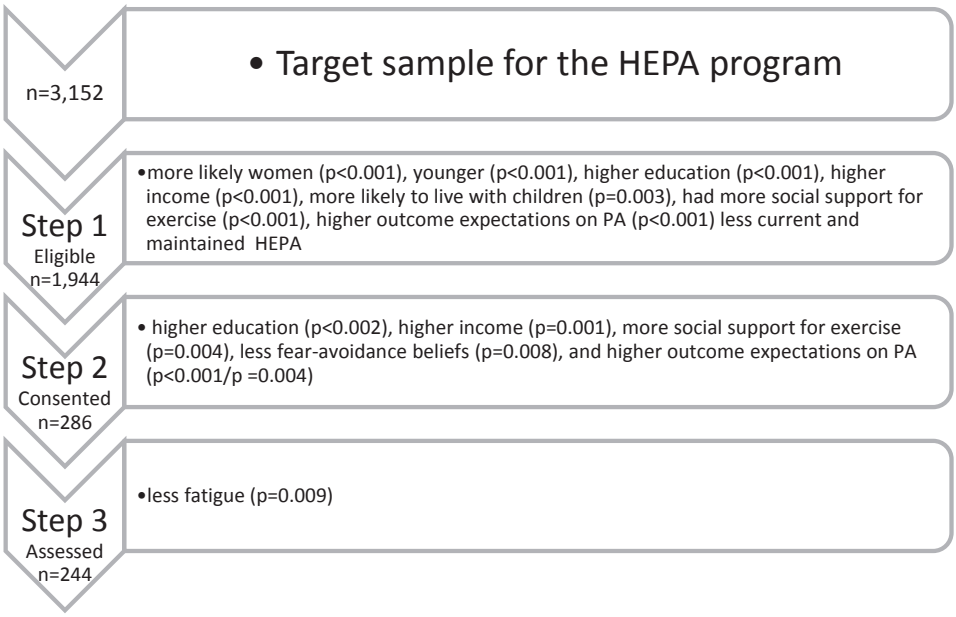


Figure 5. Differences between individuals making it to the baseline assessments and those who did not.

Reasons for withdrawals in *Step 2* included economics, logistic problems related to time and place of training center, and injury/co-morbidity. Reasons for withdrawals in *Step 3* were logistic problems related to time and place of training center, other diagnosis, dislike of training center, and change of mind about participation.

4.3 STUDY III

Study protocol describing the HEPA program

4.4 STUDY IV

One hundred and ninety four (88%) participants completed the one-year follow up assessments with questionnaires (87%) and/or performance tests (85%) and short text messages (83%). The dropouts (12%) did not differ from the remaining sample at any of the variables assessed at baseline.

Reported mean circuit-training sessions were 48 (SD = 36.2) of 104 recommended sessions, the mean number of days with total HEPA were 189 (SD = 92.3) of 365 possible days, and mean registered support group meeting attendance was 9 (SD = 6.4) of 20-22 possible meetings.

The proportions meeting current HEPA criteria changed from 55% to 82% (p = 0.0004) for those that were assessed at both baseline and at one-year assessments (n = 186). The

proportions for maintained HEPA at baseline were none, and changed to 37% ($p = 0.0495$) at the one-year follow up ($n = 178$) assessments.

The participants improved their general health perception ($p = 0.0255$), quality of life ($p<0.0001$), social support from friends ($p = 0.0290$), pain ($p = 0.0388$), activity limitation ($p<0.0001$) and fear-avoidance beliefs ($p = 0.009$), while exercise self-efficacy ($p = 0.0006$) declined during the one-year program. The outcome of the performance tests indicated improved aerobic capacity ($p = 0.0025$), timed standing ($p<0.0001$), and grip strength ($p = 0.0001$). Waist circumference ($p<0.0001$) was reduced.

Adherence at 50%, 70%, and 90% levels to circuit training or group meetings, total HEPA, and support group meetings showed that exercise self-efficacy improved in those with higher adherence to circuit training and those with higher attendance at support group meetings, while it decreased in the non-adherers (Table 4). Higher attendance at support group meetings was related to greater improvement in timed standing compared to the non-adherers (Table 4). Total HEPA adherence did not influence any of the response variables (Table 4).

Table 4. Adherence at different levels to the three intervention components in relation to one-year changes in primary and secondary response variables. 0 = non-adherer, 1= adherer.

Intervention component		Health, 0-100			Exercise self-efficacy, 6-60			Fear-avoidance beliefs, 0-24		
		n	ΔMean(SD)	p	n	ΔMean (SD)	p	n	ΔMean (SD)	p
Circuit training, 50%	0	91	-2(24.8)	0.4648	85	-7(13.0)	**<.0001**	95	-1(4.6)	0.7515
	1	91	-4(19.1)		88	1(12.1)		91	-1(4.6)	
Circuit training, 70%	0	134	-2(23.7)	0.2131	126	-5(13.2)	**<.0001**	137	-1(4.5)	0.8878
	1	48	-6(16.9)		47	3(10.5)		49	-1(49)	
Circuit training, 90%	0	160	-2(23.3)	0.0308	151	-4(13.0)	**0.0042**	163	-1(4.5)	0.5932
	1	22	-8(8.2)		22	4(11.5)		23	-(5.4)	
Total HEPA, 50%	0	76	-4(24.2)	0.7018	69	-6(14.1)	0.0168	77	-0(4.9)	0.7048
	1	106	-2(20.7)		104	-1(121)		109	-1(4.38)	
Total HEPA, 70%	0	128	-2(23.7)	0.4266	119	-4(14.2)	0.2019	129	-1(4.45)	0.3592
	1	54	-5(18.1)		54	-2(10.2)		57	-1(4.85)	
Total HEPA, 90%	0	167	-2(22.3)	0.0775	159	-3(13.5)	0.2832	171	-1(4.65)	0.1075
	1	15	-13(18.1)		14	-1(8.1)		15	9(3.16)	
Group meetings, 50%	0	83	-5(20.2)	0.0663	81	-6(13.5)	**0.0091**	87	-1(4.68)	0.6144
	1	99	-2(23.6)		92	-1(12.3)		99	-18(4.5)	
Group meetings, 70%	0	124	-5(21.1)	0.3058	118	-5(13.4)	**0.0025**	128	-1(4.77)	0.8495
	1	58	1(23.7)		55	1(11.5)		58	-1(4.16)	
Group meetings, 90%	0	170	-3(22.5)	0.3058	162	-4(12.9)	0.0125	174	-1(4.54)	0.4539
	1	12	3(15.9)		11	6(13.7)		12	-2(5.21)	

Table 4 ctd.

Intervention component		Oxygen uptake, ml·kg^{-1}·min^{-1}			Time standing, s			Grip strength, N		
		n	ΔMean (SD)	p	n	ΔMean (SD)	p	n	ΔMean (SD)	p
Circuit training, 50%	0	66	0.76(4.55)	0.1396	89	-3(6.4)	0.0626	91	17(51.49)	0.3099
	1	70	2.04(5.46)		92	-5(4.4)		93	10.09(39.7)	
Circuit training, 70%	0	97	1.25(4.82)	0.5502	132	-4(6.0)	0.3742	134	14.01(48.08)	0.8061
	1	39	1.83(5.65)		49	-4(3.9)		50	12.14(39.95)	
Circuit training, 90%	0	116	1.35(4.81)	0.6969	158	-3(5.7)	0.7080	161	12.63(46.6)	0.4940
	1	20	1.83(6.44)		23	-3(4.0)		23	19.65(41.17)	
Total HEPA, 50%	0	51	1.32(4.82)	0.8602	76	-4(5.1)	0.6164	77	15.97(44.12)	0.5376
	1	85	1.48(5.23)		105	-4(5.8)		107	11.73(47.28)	
Total HEPA, 70%	0	93	1.57(5.23)	0.6181	127	-4(6.0)	0.8310	128	12.31(48.59)	0.5955
	1	43	1.1(4.73)		54	-4(4.1)		56	16.23(39.39)	
Total HEPA, 90%	0	124	1.47(5.04)	0.6894	167	-4(5.6)	0.6334	169	13.86(47.39)	0.5481
	1	12	0.86(5.42)		14	-4(4.4)		15	9.47(24.15)	
Group meetings, 50%	0	60	1.11(5.74)	0.5456	82	-2(6.6)	**0.0039**	83	13.22(51.7)	0.9400
	1	76	1.66(4.48)		99	-5(4.2)		101	13.74(40.81)	
Group meetings, 70%	0	88	1.52(5.32)	0.7632	122	-3(6.1)	0.0755	124	14.38(47.72)	0.7117
	1	48	1.24(4.59)		59	-5(3.9)		60	11.7(42.26)	
Group meetings, 90%	0	128	1.23(4.99)	0.0758	168	-4(5.6)	0.4886	171	14.36(46.46)	0.3631
	1	8	4.5(5.53)		13	-5(3.9)		13	2.31(37.65)	

Changes in response in relation to the intervention components showed that response at 10% and 20% levels in general health perception was more likely to occur among participants that adhered better to circuit training compared to those adhering less (Table 5). No statistically significant changes were found for the other response variables in relation to adherence to the intervention components (Table 5).

Table 5. One-year changes in primary and secondary response variables general health perception in relation to each of the three program components. 0 = non-responders, 1 = responders.

Response variable		Circuit training			Total HEPA			Support group meetings		
		n	mean (SD)	p	n	mean (SD)	p	n	mean (SD)	p
ΔHealth[1], 10%	0	83	46(32.9)	**0.0087**	83	195(82.5)	0.1198	83	10(5.6)	0.9770
	1	99	60(36.5)		99	214(78.7)		99	10(6.5)	
ΔHealth, 20%	0	91	46(32.4)	**0.0037**	91	196(83.0)	0.1216	91	10(6.0)	0.4201
	1	91	61(37.0)		91	215(77.9)		91	10(6.5)	
ΔHealth, 30%	0	101	48(33.2)	0.0239	10	198(83.6)	0.1773	101	10(6)	0.8210
	1	81	60(37.4)		81	214(76.7)		81	10(6.6)	
ΔSelf-efficacy, 10%	0	122	52(36.9)	0.0659	12	212(75.3)	0.5763	122	10(6.1)	0.6397
	1	51	62(30.8)		51	205(78.7)		51	11(6.2)	
ΔSelf-efficacy, 20%	0	132	52(36.1)	0.0762	13	212(76.9)	0.4737	132	10(6.1)	0.9223
	1	41	63(32.2)		41	203(74.)		41	11(6.9)	
ΔSelf-efficacy, 30%	0	140	52(35.9)	0.0310	14	210(77.9)	0.9207	140	10(6.1)	0.8709
	1	33	66(31.5)		33	211(69.7)		33	11(6.7)	
ΔFear avoidance beliefs, 10%	0	67	54(39.6)	0.6999	67	201(81.7)	0.5461	67	11(6.3)	0.4129
	1	120	52(33.3)		12	209(81.4)		120	10(6.2)	
ΔFear avoidance beliefs, 20%	0	73	54(38.4)	0.7122	73	201(82.0)	0.4649	73	11(6.3)	0.0376
	1	114	52(33.8)		11	209(81.1)		114	10(6.1)	
ΔFear avoidance beliefs, 30%	0	79	55(37.4)	0.4245	79	204(83.0)	0.7485	79	11(6.2)	0.0510
	1	108	51(34.3)		10	208(80.5)		108	9(6.1)	
ΔOxygen uptake[2], 10%	0	89	53.0(39.3)	0.2028	89	203(83.6)	0.1775	89	10(6.4)	0.2443
	1	47	61.5(31.2)		47	222(74.8)		47	12(5.7)	
ΔOxygen uptake, 20%	0	109	55.2(36.9)	0.6096	10	211(85.3)	0.7287	109	11(6.2)	0.8095
	1	27	59.2(36.4)		27	205(61.3)		27	10(6.1)	
ΔOxygen uptake, 30%	0	121	54.6(37.2)	0.2337	12	211(83.9)	0.4700	121	10(6.2)	0.2049
	1	15	66.7(32.7)		15	199(52.3)		15	12(6.0)	
ΔTime standing, 10%	0	60	50(40.7)	0.3038	60	206(81.7)	0.7076	60	8(5.8)	0.0380
	1	121	56(32.9)		12	201(84.3)		121	11(6.2)	
ΔTime standing, 20%	0	107	49(36.4)	0.0445	10	198(77.9)	0.3776	107	9(6.0)	0.3930
	1	74	60(33.9)		74	209(90.6)		74	12(6.1)	
Δ Time standing, 30%	0	144	53(36.9)	0.6331	14	205(81.1)	0.5600	144	10(6.3)	0.2733
	1	37	56(31.0)		37	196(92.1)		37	11(5.9)	
ΔGrip strength,10%,	0	108	56(35.1)	0.3335	10	207(83.2)	0.5141	108	11(6.1)	0.6904
	1	76	51(36.2)		76	199(84.8)		76	10(6.3)	
ΔGrip strength, 20%	0	126	54(33.8)	0.8138	12	205(82.4)	0.7903	126	11(6.1)	0.9146
	1	58	53(39.4)		58	201(87.2)		58	10(6.5)	
ΔGrip strength, 30%	0	147	55(35.9)	0.3184	14	207(82.5)	0.3735	147	11(6.1)	0.7940
	1	37	48(33.9)		37	193(88.8)		37	9(6.7)	

[1]General health perception, [2]Oxygen uptake, estimated

Characteristic differences at baseline between responders at a 10% level and non-responders, showed a higher proportions of responders having university education ($p = 0.0489$), income above average ($p = 0.0485$), and less co-morbidities ($p = 0.0335$) compared to non-responders. The proportion of responders meeting current HEPA ($p = 0.0165$) at baseline was lower as was mean standing time ($p = 0.0267$), mean grip strength ($p = 0.0390$) and mean systolic blood pressure ($p = 0.0259$) compared to non-responders.

4.5 STUDY V

The Fox-walk test, the Åstrand test and the measured VO_{2max} test were completed by all participants (n=27). When performing the measured VO_{2max} test, a majority of the participants (n=24) achieved a respiratory exchange ratio greater than 1.10, and all reached a maximal heart rate close to, or exceeding, the age-predicted maximal heart rate according to the Fox-Haskell formula (220-age) (70).

As displayed in Table 3 in paper V, the correlation between estimated and measured $VO_{2\ max}$ ranged between $r = 0.52$ and $r = 0.82$ ($p < 0.001$-0.006), for the Fox-walk test and the Åstrand test, respectively, including the use of the three different formulas for age-predicted maximal heart rate (70-72).

The Fox-walk test overestimated VO_{2max} by almost 30%, and the Åstrand test underestimated VO_{2max} by almost 10%. The distribution of differences between the submaximal tests and the measured VO_{2max} test was independent of VO_{2max} levels regardless if expressed in l/min or expressed in $ml \cdot kg^{-1} \cdot min^{-1}$.

Good agreement was found between the Åstrand test and the measured VO_{2max} test when the Åstrand test was corrected for assessed maximal heart rate (Table 3, paper V).

When heart rate was corrected according to the three age-predicted maximal heart rate formulas for the Åstrand test, only the Fox-Haskell formula (220-age) was statistically significant from the measured VO_{2max} test ($p < 0.0001$), and VO_{2max} expressed in l/min was underestimated using this formula (Table 3, paper V).

5 DISCUSSION

The present work describes the prevalence of physical activity levels and their correlates in a large and well-defined sample of individuals with RA, the selection procedure for a long-term HEPA intervention, adherence and response after one year, as well as the criterion validity of two assessment methods for estimation of aerobic capacity in people with RA.

5.1 MAIN FINDINGS

A minority of individuals with RA reach the recommended levels of HEPA. Only 11% reported to reach maintained HEPA according to the definition in the present work, while 21% reported performing a minimum of 30 minutes' of at least moderately intense daily physical activity the past six months, 69% reported the same amount of physical activity (current HEPA) performed the past week. The most salient and consistent factors explaining variation in HEPA were exercise self-efficacy, social support and outcome expectations related to physical activity.

Only eight percent of the targeted sample for the long-term HEPA program was reached. Factors other than those related to the disease seem to mainly determine participation, and largely resemble determinants in the general population.

Evaluation of the one-year HEPA program in a real-life setting, including daily moderate intensity physical activity and twice weekly circuit training with bi-weekly support group sessions, indicated high retention and reasonable adherence to the program components. Self-reported physical activity and a number of reported health outcomes as well as physical capacity increased to a large extent during the year. However, relations between adherence to the program components and response were not clear-cut. A number of characteristics to help target potential responders for HEPA programs such as the present were also identified.

The results of the validation of two aerobic capacity tests for estimation of VO_{2max} in individuals with RA showed that the self-administered Fox-walk test overestimated VO_{2max} substantially, while the Åstrand cycle ergometry test was considered valid in the present sample for individuals in fairly good condition.

5.2 STUDY I

5.2.1 Prevalence of physical activity in RA

While previous studies have mainly reported current physical activity in relatively small samples, this is the first study to explore self-reported maintained HEPA in a large and well-defined sample with RA (34-36, 73). The reason for using different time frames when assessing HEPA; the past week for current HEPA (the IPAQ) and the past six months for maintained HEPA (the ESAI), was to contrast the two methods, and particularly, to gain insight in regularly performed HEPA in the RA population over time. As it is evident that HEPA confer health benefits, improve physical capacity, and is likely to reduce cardiovascular risk factors in RA the very low adherence (11%) to current recommendations

found in the present study, including both maintained aerobic physical activity and maintained strength training, is of concern (32, 74, 75). Whether the low prevalence of HEPA in this sample, although large and well-defined, is true for the RA population in general is questionable, since those responding to the questionnaire might have had an interest in physical activity and health, thus representing a more selected group. However, one fourth of the sample reported no intention to become physically active on a daily basis the following six months, and half of the sample reported no intention to initiate muscular strength training the following six months, indicating that those included in the sample were not just individuals with a preference for physical activity. It is conceivable that the prevalence of physical activity in the non-responder group is even lower compared to those who responded, since their health and disease-related factors were worse, previously shown to be associated with physical inactivity (35).

In a smaller sample of 87 individuals, maintained HEPA was assessed using the same method, as in the present study, the ESAI (76). Of their sample, close to 40% reported maintained HEPA the past six months. The reported high proportion in the maintenance stage in that study is in line with the 21% in the present study, since their definition of maintained physical activity did not include strength training.

5.2.2 Correlates to physical activity

Unlike other studies reporting on correlates to physical activity in RA, the present study used a comprehensive set of sociodemographic, disease-related and psychosocial factors, several of which have previously never been studied in relation to physical activity. Although several factors were found to significantly contribute to the explanation of variation in current and maintained HEPA, the proportion of variation explained was low, 18% for current HEPA and 22% for maintained HEPA. Inclusion of e.g. environmental, policy or global factors in addition to the comprehensive set of factors used in the present study might increase the proportion of variation explained. In healthy adults, some consistent environmental correlates to total physical activity have been identified, i.e. recreation facilities and locations, and transportation environments and aesthetics (38). Addressing such factors in future studies may further increase understanding of HEPA correlates among persons with RA.

Nevertheless, despite some similarities and differences between the IPAQ and the ESAI models, the majority of contributing variables were demographic and psychosocial, with exercise self-efficacy as the most salient one. Exercise self-efficacy has been identified as a key determinant for behavior change towards more physically active behavior in the adult population and in addition recognized as a correlate to physical activity in RA (38, 40). Consequently, it is imperative to target exercise self-efficacy in order to change physical activity behavior, as well as to identify BCTs effective in increasing self-efficacy, when designing physical activity interventions, or by health professionals when promoting health behavior change. In a systematic review and meta-analysis in healthy adults, a number of BCTs were associated with increases in exercise self-efficacy, i.e. feedback on performance,

feedback in comparison to others' performance, and vicarious experience (77). Whether those BCTs are associated with physical activity behavior was however not studied in the review.

5.3 STUDY II

5.3.1 The selection procedure for the HEPA program

This is the first study to describe in detail the entire selection procedure for a physical activity trial in RA including a comprehensive set of factors potentially influencing participation. The selection procedure for the long-term outsourced HEPA program outside a clinical setting clearly illustrates the difficulties in recruiting participants for such trials and the consequences for the generalization of the results. The eight percent of the targeted population of 1,944 individuals that consented to participate, and were assessed at baseline, could thus be considered very low.

5.3.2 Factors related to interest and acceptance in participating

The findings of the present study reveal new insight in factors influencing participation in HEPA trails. The sociodemographic factors related to eligibility and acceptance for the program, mainly resemble those previously described as correlates or determinants for physical activity in the general population (78). Surprisingly, disease-related factors did not seem to have much importance for eligibility or acceptance. This is in contrast to a Dutch study, carried out in the end of the 1990's, and might indicate that RA is generally better controlled today (79, 80). Another explanation could be that modes and settings of the Dutch program and the present HEPA program differed, and thus attracted different target groups. Important to underline is that one disease-related factor, perceived fatigue, was higher among participants who withdrew from baseline assessments, which might indicate that people with more fatigue, although eligible and willing to participate in physical activity trials, withdraw in late stages. As fatigue in RA is associated with physical inactivity and potentially reversible by it, this finding is of great concern (35, 81, 82). Another concern is that fear-avoidance beliefs were higher among those declining participation, indicating that fear of exercise-related injury, or risk of increased symptoms are still present among people with RA, despite the increasing body of knowledge contradicting such disadvantages (28). Several factors, i.e. lack of time, being too busy, training center being too far away and co-morbid conditions have previously been reported as barriers to physical activity and resemble the result in the present study (83).

Other factors than those explored in the present study could most likely offer additional explanations for participation in physical activity trials, but the participants had the opportunity to provide additional reasons for non-participation in each step of the procedure.

5.4 STUDY IV

5.4.1 HEPA levels

This is the first study to investigate promotion of long-term HEPA with a novel combination of intervention components, integrating physiological and behavioral aspects of HEPA, and carried out in a real-life setting.

Self-reported HEPA levels increased significantly from baseline to the end of the year, while adherence to the circuit training sessions and daily physical activity was moderate, reported with weekly text messages. The intended expectations when designing the study, to reach the recommended levels of HEPA within a year, were probably set too high, and seemed to be perceived too overwhelming for some participants. However, in comparison with the previous PARA study, the participants in the present study reported substantially increased HEPA levels, indicating that the delivery of the present HEPA program was more efficient (67).

Nevertheless, only 15 minutes per day of physical activity on a moderate intensity level may be sufficient to produce health benefits as reported in a recent large prospective study in Asian adults, and would most likely have been more realistic and achievable for some of the participants in the present study (84). To improve long-term maintenance of physical activity it is important to find the proper context and support for each participant's needs, which was the intention in the group meetings with support from the coaches (85). However, it was probably challenging from time to time to guide the group meetings in order to tailor the content and support, to each participant's needs and preferences.

5.4.2 Physical capacity

Although a majority of the participants' did not reach the HEPA recommendation, physical capacity was significantly changed from baseline. The change in VO_{2max} after one year could be considered rather modest in comparison with the outcome after a 21 week exercise intervention, with perfect compliance to all training sessions, performed three times/week, in patients with longstanding and early RA (86). In that study, $VO_{2\,max}$ increased by 20% for those with longstanding RA and by 10% in those with early RA, compared to 4% in the present sample, when expressed in $ml \cdot kg^{-1} \cdot min^{-1}$. If expressed in l/min, the increase in the present sample was 10%. Compared to the participants in the Hakkinen et al study (86), the present sample was older, with longer disease duration and higher VO_{2max} values at baseline, leaving less room for improvements. As the participants in the Hakkinen et al study (86) were supervised at every single training session and guided on how to perform the exercises properly with the right predetermined intensity, the improvements of the participants in the present study could be considered satisfying in relation to the minimal support received at the training centres. The improvements in $VO_{2\,max}$, lower limb function (17%) and grip strength (7%) are most likely related to the 37% reduction of activity limitation, and should thus be considered clinically relevant. The reduction of activity limitation differed to a very large extent in comparison with the participants in the previous PARA study (67).

Participants with higher adherence to group meetings showed more improvements in lower limb function. This may be explained by the information provided and discussed at the meetings on how to perform exercises with good quality, and with sufficient intensity and frequency. The participants in the present study were aware of the benefits of being physically active when they started the program, but acknowledged that the meetings gave a deeper understanding and insight about physical activity and exercise (87). Previous research has found that patients with RA, have knowledge about the benefits of physical activity but have concerns about how to exercise and the effect of exercise on joints, which is in accordance with the present study (23, 76). Health professionals' knowledge in exercise physiology and in particular in relation to RA is thus instrumental when giving advice on physical activity and exercise.

5.4.3 Exercise self-efficacy and health perception

Exercise self-efficacy was one of the psychosocial variables that changed significantly during the one-year HEPA program. Surprisingly, in contrast to what was expected, exercise self-efficacy declined for the entire group. The decline may be an effect of response shift, i.e. self-efficacy may decline once a person realizes how difficult it is to obtain the intended physical activity intensity and frequency. However, in a recent systematic review of physical activity interventions targeting adults over 60, a number of BCTs, i.e. goal-setting, self-monitoring of behavior, planning for relapse, receiving feedback on performance and planning how to elicit social support were associated with lower levels of exercise self-efficacy as well as lower levels of physical activity (88). This is of concern since these BCTs were frequently practiced in the HEPA-program. It is indicated that BCTs that are effective fort increasing exercise self-efficacy and physical activity for younger adults may not be effective for older adults, and may also differ for the RA population (89). It should also be highlighted that specific combinations of BCTs can be more effective in increasing physical activity and changing dietary behaviors (90). Interestingly, the participants in the HEPA program that adhered more to the support group meetings as well as to circuit-training sessions improved their exercise self-efficacy compared to those that adhered less. An explanation for this might be that they had the chance to practice BCTs such as goal-setting, and that they received more guidance from the coaches. Improvements in health perception was related to better adherence to circuit training sessions, in line with recent findings of positive associations between physical activity and perceived health, and may be attributed to potentially improved physical capacity following circuit training, rather than moderate-intensity physical activity (91).

5.4.4 Characteristics of responders versus non responders

A number of variables that differed between those responding to the HEPA program compared to those who did not, were identified. Responders tended to have more comorbidities, less current HEPA, and lower physical capacity at baseline. This might indicate that those with low functioning benefit more from a HEPA program, which is in agreement with previous studies involving persons with arthritis and healthy individuals (69). Compared to individuals in good physical condition, less physically fit individuals respond

quicker and increase their capacity more when exercising with the same intensity, frequency, and duration (92). Moreover, the intensity of physical activity may be a stronger determinant of fitness response than the total volume (93). With this in mind, to achieve better improvements in physical capacity, more attention should be paid to the quality of the HEPA performance.

Also notable is that a higher proportion of the responders was educated at university level and had higher income compared to non-responders, which is in accordance with previous findings (79). Those with higher education might have adapted and absorbed the information provided at group meetings better, which in turn could have led to initiation and maintenance of physical activity to a higher extent.

5.4.5 Delivery of the intervention

As HEPA is a lifelong commitment, outsourcing of HEPA programs are necessary in order to support people with RA who cannot constantly be supervised in healthcare environments. Experienced physiotherapists in rheumatology, were trained to coach HEPA behavior change, and although initially uncomfortable with changing their role from experts to coach, they gradually adjusted and even started to use the new skills in regular clinical work (94). With expert knowledge in exercise physiology and musculoskeletal conditions, physiotherapists, need to be involved in hands-on HEPA instructions. Although, it is possible that trained lay people could lead the support groups as has successfully been done in the Arthritis Self-management Programs (95). Nevertheless, it has been claimed that the most positive effects of health coaching, were found in studies in which the coaches were educated coaches or trained psychologists (96, 97). However, for individuals with RA, tailored advice regarding physical activities and exercise needs to be delivered by experienced physiotherapists during periods of flares or pain.

High retention and reasonable adherence indicated good feasibility of the outsourced HEPA program, delivered outside a clinical setting. Circuit training at public gyms and physical activity in daily life were the most valued program components (87). Furthermore, adoption and maintenance of HEPA and improvements of a number of outcomes found among the participants in the present study indicate that the present HEPA program had advantages over the previous one (67).

5.5 STUDY V

5.5.1 The Fox-walk test

This is the first criterion validation of a self-administered test for estimating VO_{2max} for individuals with RA. The Fox-walk test overestimated VO_{2max} by almost 30%, independent of the participants' levels of fitness, and cannot be used confidently for estimating VO_{2max}. Nevertheless, the test may still be used but with consideration of its limitations when interpreting the results. Lower limb pain was expected to be a limitation when performing the

test. However, the participants rated pain as very low after walking the track, although they were encouraged to walk at a fast pace.

As walking is a preferred activity among individuals with RA and also suitable for monitoring progress after a period of exercising, it is warranted that easy and simple tests such as the Fox-walk test are developed (76, 98). The Fox-walk tracks differ in lengths and ascendance, and are therefore situated in different environments. Tracks can be found both in cities and along jogging tracks making them suitable for testing or exercising.

5.5.2 The Åstrand test

The Åstrand test, although extensively used in clinic and research, has never been validated for the RA population. The test underestimated VO_{2max} by 10% (57). This is in accordance with previous studies on healthy individuals, although an overestimation has also been indicated (99-101). When age-correction was made with the use of three alternative age-predicted maximal heart rate formulas, the widespread Fox-Haskell formula underestimated VO_{2max} by the same degree as Åstrand corrected for age (70-72). The formulas by Tanaka and Nes are preferable since the associations to the measured VO_{2max} values were slightly better.

Provided that the Åstrand test is standardized according to the test manual, it should be considered as highly valid in people with RA. It should however be pointed out that the sample was recruited from the HEPA program, and consequently rather fit compared to individuals with RA in general.

5.6 METHODOLOGICAL CONSIDERATIONS

5.6.1 External validity

The analyses (Study I, II) were based on a large, and well-defined sample of people with RA recruited via a national patient register. The response rate of the questionnaire in Study I and II was nearly 60%, which is in line with a previously reported mean response rate of 62 % in postal surveys (102). Nevertheless, the risk of response bias needs to be considered. Thus the non-responders were younger, had shorter disease-duration, poorer health, and worse disease-conditions compared to the responders. This indicates that the results of the present work are valid for a slightly less affected RA population. However, the intention with Study IV was not merely to generalize the findings to the RA population as a whole, but to study and identify which individuals that would best be suited to manage their physical activity with limited support from a health professional and in a context outside a health care setting. Furthermore, the sample in Study V was recruited from the intervention sample, of which a majority had been regularly physically active during the past year and was consequently physically fit and active, compared to people with RA in general. This certainly limits the external validity.

5.6.2 Internal validity

5.6.2.1 Data collection

One strength in the present work is the use of a comprehensive set of questionnaires, of which several are part of internationally recommended core sets for outcome measures in RA, while others are validated for people with musculoskeletal diseases (103). However, it should be recognized that some are not yet validated for people with RA. Self-reports of physical activity are useful and feasible to gain insight in physical activity levels for a large population, but may be influenced by recall and response bias (104). Another issue to consider in self-reports is individual differences in understanding the various intensity levels of physical activity (104, 105). Although the IPAQ have sufficient validity and reliability in adults, the responsiveness is poor (106). To our knowledge, no existing questionnaire on physical activity is valid for detecting changes over time. In fact, in a systematic review, reporting on measurement properties of 85 physical activity questionnaires, only two (including the IPAQ) were found to have been tested for responsiveness (106). However, the IPAQ has not yet been validated for the RA population. The ESAI questions, modified for the present study, still need further evaluation regarding measurement properties in RA. Despite this, the ESAI is a concise, straight forward assessment that leaves little room for misunderstanding.

The physiotherapists conducting the performance tests were trained during a four-day course prior to baseline assessments, and an additional two days prior to follow up. Differences in equipment and other local facilities as well as variations in rigor and correctness may nevertheless have caused bias. However, since the same participants were tested at the same units on both occasions, this might be of minor importance.

In the criterion validation of the Åstrand test, the fact that it was performed in a laboratory setting and conducted by the same experienced biomedical scientist is considered a strength. Furthermore, all participants had previously performed the test at least twice and were familiar with exercise testing. The criterion validation of the Fox-walk test was conducted by two trained test leaders under supervision of one of the researchers (BN). The fact that only one of all available Fox-walk tracks was used for all tests is though a limitation. Moreover, some participants should have performed the test running, as suggested in the instructions, since they were too fit to walk the test. On the other hand, jogging might not have been possible due to deformities of feet or lower limb pain.

5.6.2.2 Design

The present findings contribute to existing knowledge of correlates to physical activity in RA since no previous study has included such a large and well-defined sample as well as a comprehensive set of sociodemographic, disease-related and psychosocial factors to explain variation in physical activity. However, longitudinal studies are still needed to identify causal associations between potential determinants and physical activity behavior (39).

Initially, the intention was to use those who declined participation in Study IV as a comparison sample, to demonstrate the natural course of functioning and health. However, this had to be discarded since the intervention and the comparison samples differed considerably already at baseline on a number of sociodemographic, disease-related and psychosocial variables. Furthermore, the choice of an observational longitudinal prospective design is more appropriate than a randomized controlled design, since long-term compliance to physical activity will be better in a supportive environment at a participating center, where contamination effects between groups as well as effects of repeated measurements of controls are avoided. The present study was never designed to evaluate effects of the HEPA program per se, but rather to explore feasibility and aspects related to adherence and response.

5.6.3 Statistical considerations

Logistic regression models as carried out in Study I as well as exploration of adherence versus response as performed in Study IV require cut-offs, for which a clear rationale is not always present. Thus, in Study I the dichotomizations of variables were based in literature, on clinical reasoning or on statistical considerations. This is clearly not ideal, but a pragmatic approach to enable this type of analyses. Similarly, the 50%, 70%, and 90% adherence levels to the intervention components in Study IV, and, the 10%, 20% and 30% response levels were, in the absence of previous research with similar approaches, based on reasoning within the research group. Thus, the approach in this part of Study IV must be considered explorative rather than confirmative.

As recommended, multiple imputations were run before the analyses in variables with missing data, predominantly the variable social support for physical activity in Study I (107). In Study IV, a majority of participants reported outcome expectations as 10 on a 1-10 scale. Those variables were therefore dichotomized into 10 versus <10 for analysis.

It should be acknowledged that intention-to-treat analyses were not performed in Study IV. One reason for this was the high retention rate of 88%, another that the 26 drop-outs did not differ ($p > 0.05$) from the remaining sample at any of the variables assessed at baseline. It also seems that reasons for dropping out were mainly related to logistics, costs, work or family responsibilities, injuries and comorbidities. Nevertheless, it cannot be excluded that the present analyses, including only complete cases, resulted in better response than that of an intention-to-treat approach.

5.7 CLINICAL IMPLICATIONS

Previous research indicates that health professionals very seldom discuss physical activity with their patients, which is of concern since tailored advice increases physical activity participation in people with arthritis (83, 98, 108) The present findings of low HEPA levels in individuals with RA reinforce the need for health professionals to initiate discussions about physical activity and to use behavior change techniques in order to promote a more physically active lifestyle among their patients.

Higher levels of exercise self-efficacy increase the likelihood that individuals with RA will achieve their physical activity goals (109). It is therefore important that those involved in the care or rehabilitation of patients with RA foster goal achievement in a number of ways to increase exercise self-efficacy, so that lifelong maintenance of physical activity will be reached in a long-term perspective.Having in mind that HEPA is a lifelong commitment, the physiotherapists' role of supporting adoption and maintenance of HEPA in individuals with RA could possibly be performed in contexts outside the healthcare system, as in the present HEPA program. It might be that new arenas situated in a real life environment would attract individuals difficult to reach in the traditional health care. Since walking is a preferred activity among individuals with RA, health care professionals are recommended to prescribe this activity and to encourage patients to perform self-administered tests regularly to monitor their progress. According to evidence based practice, physiotherapists should assess and evaluate a period of exercise with valid and reliable methods when prescribing physical activity. If performed according to standardized manuals, the Åstrand test is excellent for this purpose.

5.8 FUTURE RESEARCH

Development and evaluation of HEPA programs tailored to each individual's needs and preferences in order for them to adopt and maintain HEPA, is a major challenge for future research. It is of particular importance to explore the needs and barriers among people with poor socio-economic conditions, low social support for exercise, low physical activity expectations, and high fear-avoidance beliefs in order to develop and evaluate physical activity programs that are feasible and attractive to them. To improve the evaluation of interventions including a multitude of components, it is fundamental that researchers use guidelines on the development, evaluation, and implementation of complex interventions (51, 110). Accurate definitions and measurements are central to our understanding of physical activity levels. Development and use of physical activity measurement standards in RA that enhance international comparison is therefore crucial (111). In contrast to self-reports, accelerometry is an objective way to measure physical activity that has been used in the RA population in a number of physical activity studies with different aims (112-114). However, only few accelerometers have been validated for the RA population and it is thus urgent to validate them for this specific population to be used in studies with smaller samples (115). Further development of tests to monitor progress after a period of physical activity that are easy and simple to administer for individuals use is strongly recommended.

5.9 CONCLUSIONS

Despite the above discussed limitations in the present work it can be concluded that:

- Only a minority of people with RA reaches HEPA in accordance with current recommendations, and psycho-social factors, such as self-efficacy, social support and outcome expectations related to physical activity, are the most salient factors explaining variation in HEPA.

- Only a small minority of individuals with RA is reached for physical activity trials and factors other than those related to the disease, i.e. sociodemographic and psycho-social factors, seem to mainly determine participation.

- Outsourced HEPA programs are feasible for a subgroup of people with RA. HEPA levels increase substantially, and a number of self-reported health outcomes and assessed physical capacities improve after a one-year intervention.

- The relation between adherence to the HEPA program components and response is not clear-cut, but improvements in health perception, exercise self-efficacy and lower limb function respectively are related to higher adherence to one or more of the program components.

- Potential responders to outsourced HEPA programs are those characterized by high education, high income, less co-morbidities, poor physical capacity and low levels of HEPA.

- The self-adminstered Fox-walk test to estimate VO_{2max} needs further development, but it is a promising tool for self-monitoring of aerobic capacity.

- The Åstrand test is a valid method to estimate VO_{2max} but it is preferable to combine it with two newly developed formulas for age-predicted maximal heart rate.

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