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Rehabilitation in warm climate for young adults with inflammatory arthritis

A 12 months randomized controlled trial

Master's thesis in Clinical Health Science
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Abstract

Background: Rehabilitation in warm climate has long been an established non-pharmacological treatment for patients with inflammatory arthritis (IA) in Norway. It has however not been tailored to the needs of young adults, who often have different challenges than older adults with IA.

Aims: The aim was to investigate if a rehabilitation program in warm climate especially developed for young adults with IA showed indications of a long term effect on general health status compared to usual care.

Method: We did an open randomized controlled trial. Patients aged 20-35 years, with inflammatory arthritis (IA) were randomized to the intervention (n=20) or usual care (n=20). The intervention was a 17 day long rehabilitation program in warm climate, and the main component was intensive exercise, individual physiotherapy and patient education. The primary outcome measures was physical function assessed by the "30 second Sit to Stand test" and self-management/coping measured by the "Effective Musculoskeletal Consumer Scale" (EC17).

Results: Forty patients (mean age 27.5, 65 % female) with IA were randomized. 19 out of 20 patients completed the intervention. At twelve months follow up there were 3 patients lost to follow up from the intervention group, and 2 in the control group. The intervention group had a significant improvement in the physical function test at 3 months; mean difference (95% CI): 7.6 (4.3 to 10.9), 6 months 4.7 (0.7 to 8.8) and 12 months 6.8 (2.3 to 11.3), compared to the control group. There were no difference in self-management/coping measured with EC17 between the two groups at 3, 6 or 12 months.

Conclusion: This study indicates that a rehabilitation program in warm climate especially developed for young adults with IA improves patient's physical function, but not self-management/coping up to one year after the intervention. Further studies are needed to confirm these findings.

Relevance: This is the first study to investigate a rehabilitation program in warm climate especially for young adults with IA. Bringing new knowledge in this field is important as this patient group often encounter complex challenges, and have a need for multidisciplinary rehabilitation. Yet, there is a lack of rehabilitation programs targeted toward young adults with IA, and for young adults with chronic disease overall.

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Working with this master thesis has been challenging, but most of all it has been a very meaningful and informative process, which have given me valuable knowledge and experience.

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Abbreviations

30sSTS	30 second sit to stand test
AS	Ankylosing Spondylitis
ASAS	Assessment of Spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
CI	Confidence Interval
COOP/WONKA	The Dartmouth Coop Functional Health Assessment/ World Organization of National Colleges, Academies and Academic Association of General Practitioners
COXIBS	Cox-2 inhibitors
DMARD	Disease Modifying Anti Rheumatic Drug
EC17	Effective Consumer Scale 17
EULAR	European League Against Rheumatology
ILAR	International League Against Rheumatology
IA	Inflammatory Arthritis
ITT	Intention to Treat
JIA	Juvenile Idiopathic Arthritis
HAQ	Health Assessment Questionnaire
NSAID	Non-steroidal anti-inflammatory drug
NTNU	Norwegian University of Science and Technology
PP	Per Protocol
PsA	Psoriatic arthritis
PSFS	Patient Specific Functional Scale
RA	Rheumatoid Arthritis
RCT	Randomized Controlled Trial
RMD	Rheumatic and Musculoskeletal Diseases
SD	Standard deviation
SpA	Spondyloarthritis

1 Background

1.1 Chronic disease and rehabilitation for young adults

Having a chronic disease as a young adult can be challenging in a number of ways (Verhoof, Maurice-Stam, Heymans, Evers, & Grootenhuis, 2014). Many at this age are choosing their educational path, establishing a career, finding a partner and starting a family. The foundation for their future is laid, and the consequences of having a chronic disease at this time in life can be significant (Foster, Marshall, Myers, Dunkley, & Griffiths, 2003; Ostlie, Johansson, & Moller, 2009; Packham & Hall, 2002a).

Due to the complex challenges and health issues young people with chronic disease can encounter, they often have a need for multidisciplinary rehabilitation (Engen et al., 2016). The national Norwegian organization for youth with disabilities "Unge funksjonshemmede" wrote a report in 2011 regarding young patients' opinions on their possibilities and options for rehabilitation, based on several interviews and online questionnaires (Unge funksjonshemmede, 2011). They emphasized that young adults felt it was important to participate in rehabilitation with people of their own age, and that rehabilitation should focus on issues especially relevant for young adults. Overall, they concluded that the rehabilitation offered for young adults was inadequate (Unge funksjonshemmede, 2011). A report initiated by the Norwegian Directorate of Health looked at general practitioners (GP's) view on rehabilitation for young people with chronic disease and decreased functional abilities. This report revealed that only 18 % of GP's meant that the rehabilitation offer for young adults (under the age of 30) was in accordance with the need in their health region, and 16 % said it was in accordance with the need on a national level (Solli, 2010).

Inpatient rehabilitation programs often last several weeks. For young adults, it can be especially challenging to be away from home for an extended period; often due to studies, starting a career or family-life with small children (Andreassen & Eriksen, 2009). The lack of rehabilitation targeted directly towards young adults with chronic disease is a challenge affecting a wide variety of patient groups with different diagnoses (Strand & Bratli, 2012).

1.2 Inflammatory Arthritis

Musculoskeletal diseases are one of the main reasons why people seek medical care, and one of the leading causes of sick leave, rehabilitation and disability pension in Norway (Ihlebæk, Brage, Natvig, & Bruusgaard, 2010). Among the most disabling musculoskeletal diseases is inflammatory arthritis (Palazzo, Ravaud, Papelard, Ravaud, & Poiraudeau, 2014). Inflammatory arthritis (IA) is a term used to describe a heterogeneous group of chronic autoimmune musculoskeletal disorders of unknown etiology (Gran, 2008), e.g. Rheumatoid arthritis (RA), Juvenile idiopathic arthritis (JIA), Spondyloarhritis (SpA) and Psoriatic Arthritis (PsA), which are described briefly below. The severity and disease course in the various IA diagnoses differs significantly, however joint pain, stiffness and fatigue are common features, as well as a fluctuating and unpredictable disease course (Nam, Catrina, & Emery, 2015).

Rheumatoid arthritis (RA) primarily affects synovial joints (Gabay, Nissen, & van Laar, 2015). If left untreated, RA usually leads to destruction of joints due to erosion of cartilage and bones. About 40 % of patients with RA also experience extra articular manifestations during the course of their disease, such as involvement of the skin, eye, heart, lung, renal, nervous and gastrointestinal system (Gabay et al., 2015). Prevalence in developed countries is approximately 0.5-1 % of the adult population (Gabriel & Michaud, 2009).

Juvenile idiopathic arthritis is not a single disease, but rather a term used to describe a group of conditions involving joint inflammation that appears before the age of 16. Approximately 50 % of patients diagnosed with JIA continue to have active disease into adulthood (Minden et al., 2002; Packham & Hall, 2002b). A study of the Nordic countries found that the incidence was 15 per 100 000 children/year (Berntson et al., 2003).

Spondyloarthritis is a diagnostic group of inflammatory arthritic disorders, and can be differentiated into axial SpA and peripheral SpA. One of these diagnoses, Ankylosing Spondylitis (AS) is often seen as the prototypic form of axial SpA (Taurog, Chhabra, & Colbert, 2016). It involves primarily the sacroiliac joints and axial skeleton, but may also affect peripheral joints and have extra articular manifestations such as uveitis (Kiltz, Baraliakos, & Borg, 2015). Mean prevalence of AS in European countries has been estimated at 23.8/10 000 (Dean et al., 2014). The most common onset of AS is in the third decade of life (Dean et al., 2014).

Psoriatic Arthritis (PsA) is associated with psoriasis, and common symptoms are inflammation of peripheral joints, and manifestation of the spine, skin and nails (Kiltz et al., 2015). There is a substantial variability in reported incidence and prevalence in different countries. The prevalence of PsA in Europe and America varies from 0.02% to 0.42% (Liu, Yeh, Liu, & Chen, 2014).

Even though the prevalence of IA in general is higher in older adults, a significant number of young adults are also diagnosed with an IA, which can have a detrimental effect on their quality of life (Palazzo et al., 2014). The literature shows that quality of life, generic health status and functional ability in young adults with IA is influenced by their chronic disease (Foster et al., 2003; Packham & Hall, 2002b) and that young adults with arthritis are less likely to be employed than their healthy peers (Jetha, 2015).

1.3 Treatment for patients with inflammatory arthritis

A range of pharmacological and non-pharmacological treatment options are provided for persons with IA. The medical treatment for patients with IA has evolved enormously in the last decades (Lie et al., 2014). The development of disease-modifying anti-rheumatic drugs (DMARDS) and especially biologic agents, combined with early and aggressive treatment has improved patients health status significantly (Smolen et al., 2017).

However, in spite of improved medical treatment, many patients still have active disease which in a significant way impacts their quality of life. Non pharmacological interventions like patient education and exercise are therefore still considered an important adjacent treatment for this patient group (Combe et al., 2016; van der Heijde et al., 2017; Vliet Vlieland & Pattison, 2009; Zangi et al., 2015). A brief overview of the evidence for exercise and patient education for patients with IA follows, before an overview of research on rehabilitation in warm climate for patients with IA in section 1.4.

1.3.1 Exercise

A Cochrane review from 2008 stated that the effectiveness of exercise and physiotherapy interventions for patients with AS was beneficial on physical function and spinal mobility, but the level of evidence was low (Dagfinrud, Kvien, & Hagen, 2008). Another more recent review also concluded that there was moderate evidence that exercise improved physical

function, disease activity and chest expansion in AS patients (O'Dwyer, O'Shea, & Wilson, 2014). For patients with RA several systematic reviews, including a Cochrane review from 2009, have concluded that dynamic exercise is effective in improving aerobic capacity and muscle strength, and possibly functional ability, without unfavourable effect on disease activity, pain or radiological joint damage (Gaudin et al., 2008; Hurkmans, van der Giesen, Vliet Vlieland, Schoones, & Van den Ende, 2009; Stenstrom & Minor, 2003). The effects are mainly seen immediately after the intervention, and long term effects are more unclear. A newly published systematic review and meta-analysis on the effect of cardiorespiratory and strength exercises on diseases activity in patients with IA concluded that exercise had beneficial effect on disease activity in terms of inflammation, joint damage and symptoms (pain, fatigue and stiffness) (Sveaas, Smedslund, Hagen, & Dagfinrud, 2017).

Patients with IA also have a higher risk of suffering from cardiovascular disease. Exercise is well established as one of the most important behavioural interventions to decrease patients risk of suffering from cardiovascular disease and is therefore especially important for patients with IA (Mathieu, Pereira, & Soubrier, 2015; Metsios et al., 2008).

Despite the evidence of the importance of exercise for patients with IA, there is substantial research showing that they are less physically active than their healthy peers (O'Dwyer, O'Shea, & Wilson, 2015; Veldhuijzen van Zanten et al., 2015). Well-designed interventions to improve their physical capacity are therefore highly needed.

1.3.2 Patient Education

Patient education can be defined as "*a set of planned educational activities designed to improve patients' health behaviour, health status or both*" (Lorig, 2001). Many studies have investigated the effectiveness of patient education for patients with IA. The latest Cochrane was published in 2003 and found short term effects on disability, joint counts, patient global assessment, psychological status and depression for patients with RA but the evidence was graded as low (Riemsma, Kirwan, Taal, & Rasker, 2003). More recent studies on patient education with elements of behavioural, cognitive and self-management techniques have shown effects on global well-being, fatigue, coping/self-efficacy, pain, psychological status and physical activity level (Gronning, Rannestad, Skomsvoll, Rygg, & Steinsbekk, 2014; Hammond, Bryan, & Hardy, 2008; Hewlett et al., 2011; Knittle, Maes, & de Gucht, 2010).

Even though studies have shown beneficial effects of exercise and patient education, there is no consensus about the optimal mode of delivery or duration of the interventions, and there is therefore still a need for more well designed studies (Hurkmans et al., 2009).

1.4 Rehabilitation in warm climate for patients with IA

Rehabilitation in warm climate has long been an established non-pharmacological treatment for patients with IA in the Nordic countries, and in 1997 the Norwegian Parliament decided to make this a permanent therapeutic option (Forseth, Hafstrom, Husby, & Opava, 2010). The main component of this treatment is usually intensive exercise and physiotherapy in warm climate, combined with patient education (Forseth et al., 2010). The therapeutic effect of warm climate is not fully understood, however some argue that subtropic climate might contribute to less pain and stiffness, and increases the elasticity of tendons, muscles and other soft tissues, thus making it easier to perform more intensive exercise and more effective physiotherapy treatment; however the evidence is scarce (Patberg & Rasker, 2004).

Section for Climate Therapy at the Department of Rheumatology at Oslo University Hospital administers this treatment. They arrange groups for children and adolescents up to nineteen years, and groups for adults from 20 years and up. The rehabilitation programs typically lasts for four weeks, and the average age of the patients in the adult groups are often about 50 years (see table 1-1.) (Forseth et al., 2010).

Table 1-1 shows an overview of efficacy studies on rehabilitation in warm climate for patients with IA.

Table 1-1 Overview of efficacy studies on rehabilitation in warm climate for patients with IA

Author /year	Study design	Diagnosis, number (n), mean age	Location and duration	Intervention	Outcome measure and effect
Johansson & Sullivan (1975)*	RCT – Crossover	RA N= 79 Mean age= N/K	Spain vs Sweden. 6 weeks	Exercise, Individual PT Individual OT Hydrotherapy	**Between group (Sweden vs Spain)** **End of stay:** LI: p<0.05**, Grip strength : p=N/S **4 months:** LI: p= N/S, Grip strength: p<0.05**
Staalesen Strumse et al., (2009)*	RCT	RA N= 124 Mean age = 53/53 (in the two groups)	Norway vs Mediterranean, 4 weeks	Exercise, Individual PT Balneotherapy, Relaxation Patient Education	**Within group (Mediterranean)** **End of stay + 3 months:** DAS28, 6MWT, TUG, VASglobal, VASpain, VASfatigue, MHAQ: p<0.001 **6 months:**VASglobal,MHAQ,VASpain,VASfatigue:p<0.01, **Between groups (Norwegian vs Mediterranean)** **End of stay + 3months**: DAS28, VASglobal, VASpain, VASfatigue: p<0.05**; 6MWT, TUG, HAQ: p= N/S **6 months:** VASfatigue: p<0.05**, VASglobal, VASpain, MHAQ: p= N/S
Staalesen Strumse et al., (2011)	RCT	AS N = 107 Mean age = 51/48 (in the two groups)	Norway vs Mediterranean, 4 weeks	Exercise Individual PT Balneotherapy Relaxation Patient Education	**Within group (Mediterranean)** **End of stay+3 months:** BASDAI, BASFI, VASfatigue, 6MWT, TUG, Schober : p<0.001 **6 months:** BASDAI, BASFI, VASfatigue :p<0.001 **Between groups (Norwegian vs Mediterranean)** **End of stay+3months:**BASDAI, BASFI, Fatigue, Schober, ASAS20,ASAS40: p<0.05 **; 6MWT, TUG: p= N\S **6 months:** BASDAI, VASfatigue: p<0.05**; BASFI, ASAS20,ASAS40: p= N/S

Hafström (1997)*	Uncontrolled Prospective	RA and AS N= 130 Mean age = 50.4	Montenegro, Spain and Canaries 4 weeks	Exercise, Individual PT Individual OT, Hydrotherapy, Balneotherapy	**End of stay, 3 months, 6 months** : HAQ, VASGlobal: p<0.05
Hashkes (2002)*	Uncontrolled Prospective	RA, AS and PsA N= 136 Mean age = 49	Israel 4 weeks	Exercise, Individual PT Individual OT Hydrotherapy, Balneotherapy	**End of stay:** VAS pain = p <0.001, ACR20 response ACR20response: 57 %, ASAS20response: 60 %.
Cronstedt & Stenström (2002)*	Uncontrolled Prospective	SpA N= 48 Mean age =46	Canaries 3 weeks	Exercise, Individual PT Hydrotherapy, PE	**End of stay, 1 month:** BASDAI, BASFI, BASG = p<0.001, **3 months:** BASDAI, BASG-1= p<0.05, BASFI= n/s,
Hafström & Hallengren (2003) *	Uncontrolled Prospective	RA, JIA and SpA N=93 Mean age =50.7	Israel and Canaries 4 weeks	Exercise, Individual PT Individual OT, Hydrotherapy	**End of stay, 3 months and 6 months:** HAQ, VASpain, VASglobal, NHP: p<0.001,
Ajeganova et al(2016)	Uncontrolled - Prospective	RA, JIA, SpA, PsA N =161 Mean age = 53.2	Tenerife and Marbella, 4 weeks	Exercise Individual PT Patient Education	**End of stay:** HAQ, BASFI, EQ-5D, VASglobal, VASpain: p<0.01, **3 months:** HAQ, EQ-5D, VASglobal, VASpain, IPAQ : p<0.001, BASFI: p= N/S, **12 months:** HAQ, EQ-5D, VASglobal, VASpain, IPAQ: p<0.05, BASFI: p=N/S

PT: Physiotherapy, OT: Occupational therapy, LI:Lansbury Index, DAS28: Disease Activity Score 28 joint, 6MWT:6 minute walk test, TUG: Timed Up and Go, HAQ: Health Assessment Questionnaire, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASG: Bath Ankylosing Spondylitis Patient Global Score, ASAS: The Assessments in Ankylosing Spondylitis working group, ACR: American College of Rheumatology, IPAQ: International Physical Activity Questionnaire.

*** Included in the literature review from Forseth et al (2010). ** Results in favour of the Mediterranean group**

Forseth et al. (2010) conducted a systematic review to look at the evidence for the efficacy of comprehensive rehabilitation in warm climate for patients with rheumatic disease. Six studies met the inclusion criteria, two RCT's and four uncontrolled prospective studies. The quality of the studies were rated in accordance with the GRADE approach (Guyatt et al., 2008). This method grades evidence from very low to high. Five of the studies included in the systematic review were graded as low quality. One study (RCT) was graded as moderate quality (Staalesen Strumse et al., 2009). The studies were heterogeneous, and it was therefore not possible to perform a meta-analysis. For patients with RA, there was moderate to low evidence for reduction of disease activity, pain, fatigue and global disease impact. For SpA and JIA, there was low evidence for reduction in disease activity, pain, joint range of motion, activity limitation and global disease impact three months after discharge (Forseth et al, 2010). As pointed out by the author of the review, low evidence is not the same as ineffective treatment, but rather that there are too few studies of good quality to support higher evidence.

After this review was published some new studies have been conducted within the field. One randomized controlled trial, including 107 patients with ankylosing spondylitis, looked at the efficacy of four weeks of rehabilitation in both warm and cold (Norwegian) climate (Staalesen Strumse et al., 2011). They found that improvement in self-reported health status and spinal mobility were larger in the Mediterranean group, while the test of physical health status, patients global assessment and chest expansion showed comparable improvements in both groups up to three months after completion of the program (Staalesen Strumse et al., 2011). At six months all patients' assessment of health status were still significantly improved from baseline in the Mediterranean group, but not in the Norwegian group (Staalesen Strumse et al., 2011).

Another prospective observational study (Ajeganova, Wornert, & Hafstrom, 2016), including patients with peripheral arthritis and SpA, concluded that rehabilitation in warm climate had long term effect (12 months) on physical function, pain and self-reported general health. This is the only study, to the author's knowledge, on rehabilitation in warm climate with more than six months follow up time.

There have been no efficacy studies investigating the effect of rehabilitation in warm climate especially developed for young adults. However, a new rehabilitation program especially tailored towards young adults´ needs and life-situation was developed as a project at Rheuma

Sol in Spain in 2014. Fifteen young adults in the age from 18 to 35 years took part in this program. Five of the participants attended a focus group interview after the rehabilitation (Koksvik, Jakobsen, Nilssen, & Bjørngaard, 2016). The participants said that sharing knowledge and personal experience with others in similar phases in life enhanced their learning. The participants also expressed that the length of the program (17 days) was perfect due to their life situation; they would have found it more difficult to attend a traditionally four-week program. The intensity of the exercise was higher than traditionally programs and the participants felt it suited the group (Koksvik et al., 2016).

The evidence for efficacy of rehabilitation in warm climate has thus increased since the systematic review from 2010. However, there is still a need for more randomized controlled trials with long-term follow up investigating the effect of rehabilitation in warm climate, and especially studies investigating the effect of rehabilitation programs targeted especially toward young adults.

2 Aim of the study

The aim of this study was to investigate if a rehabilitation program in warm climate especially developed for young adults with IA shows indications of a long-term effect on general health status compared to usual care.

3 Methods:

3.1 Design:

This was an open randomized controlled trial, with a 2-group parallel design and a 1:1 allocation ratio. The study period lasted from June 2015 until October 2016. The protocol was registered at ClinicalTrials.gov (Study ID Number NCT02430402). The study has been conducted in accordance with the Helsinki declaration (World Medical Association, 2013).

3.2 Participants

3.2.1 Eligibility criteria

Patients were eligible to participate if they were between 20 to 35 years old, diagnosed by a rheumatologist (documented in their hospital journal) with an inflammatory arthritic rheumatic disorder (such as rheumatic arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis or polyarthritis), and having a need for rehabilitation as perceived by their treating rheumatologist or nurse.

Patients who were not independent in activities of daily living (assessed by the study nurse at inclusion through a general clinical evaluation) and patients with comorbidities leading to a substantial restriction in their ability to participate in the program (physical exercise or patient education) were excluded. This included serious cardiovascular disease, severe lung disorder, chronic open wounds, serious psychiatric disorders, substance abuse and intolerance for sun/heat.

3.2.2 Recruitment

Patients were recruited from the three different rheumatology outpatient clinics in Central Norway. Clinical Rheumatologists and nurses were encouraged to ask eligible patients during their regular outpatient appointments if the patients wanted to be included in the study. There was no registration of the number of persons asked, as this would increase the workload of the clinicians. Patients who agreed to participate were then contacted by the study nurse. An appointment at the outpatient clinic at St. Olavs Hospital was made and the patients were screened to ensure that they met the inclusion criteria. They then signed a written consent form.

3.3 Randomization and allocation

Participants were randomized after the baseline data collection, and immediately informed of the allocation (randomization outcome) by the study nurse. Randomization was performed using a web-based computerized randomization system developed and administered by the Unit of Applied Clinical Research, Institute of Cancer Research and Molecular Medicine, at the Norwegian University of Science and Technology, Trondheim, Norway. The system used block randomization and the size of the blocks was unknown to the researchers, and study nurse. There was no stratification.

3.4 Blinding

This was an open trial due to the type of intervention, and neither therapists, assessors or participants were blinded.

3.5 Intervention

Neither the intervention nor the control group had any restrictions in regards to change in medical treatment during the follow-up period.

3.5.1 Intervention group

Participants in the intervention group (rehabilitation) were divided into two groups with ten participants in each group. The intervention lasted for 17 days, and took place at Rheuma-Sol, which is a treatment centre located on the Costa-Blanca coastline in southern Spain. It is owned by the Norwegian Rheumatism Association.

The main component of this intervention was intensive individualized exercise under guidance of experienced physiotherapists. A rheumatologist, nurse and physiotherapist evaluated the participants' condition to individualize their exercise plan on the first day.

There were three exercise sessions daily on weekdays. The morning exercise (30 min) focused mainly on stretching. The midday exercise (45 – 60 min) took place in the indoor gym with varying focus, such as strengthening, cardio, balance and mobility. The afternoon exercise (60 min) was an aquatic class. The participants also had 30 minutes individual physiotherapy every weekday. These sessions were individually adjusted, were some

exercised and others got passive treatment according to their needs. There were no organized activities or exercise groups on weekends. The participants had access to exercise equipment and the pool for additional voluntary exercise.

Patient education was also a part of the intervention. Physiotherapists and nurses gave a total of five group sessions, lasting for 45 – 60 minutes each and covered the areas physical activity, coping with pain, coping with everyday stress, sleep, sleep deprivation and diet.

See appendix E for a full day to day schedule of the rehabilitation program.

The intervention took place from 9th of June to the 27th of June 2015 for the first group and the second group from 11th of August till the 29th of August 2015. The weather was mostly dry and sunny during the intervention period. Mean temperature was 24 and 28 degrees, for the two groups respectively, and the number of days with precipitation above 1.0 mm was two for the first group and zero for the second group (The Weather Company, 2017).

3.5.2 Control group

The control group received treatment as usual during the intervention and follow-up period. This could include pre-scheduled consultations at the rheumatology outpatient clinic or their GP, community based physiotherapy and relevant medication. They had no restrictions in regards to participating in other patient education, exercise or rehabilitation programs in the study period.

The mean temperature in Trondheim, Norway from 9th of June to the 27th of June 2015 was 9 degree Celsius. Number of days with precipitation above 1.0 mm was 5. In the period from the 11th of august till the 29th of august 2015 mean temperature was 18 degrees Celsius, and there were 4 days with precipitation above 1.0 mm (The Weather Company, 2017).

3.6 Data collection

Data was gathered at baseline, as well as three, six and twelve months after completed intervention. All data collection was undertaken at the department of Rheumatology at St. Olavs Hospital in Trondheim, Norway.

A nurse from the department of rheumatology at St.Olavs Hospital followed the groups thorough the whole study period. She was in charge of the study and handled all data collection, both baseline and post intervention, and stayed with the two groups at Rheuma-Sol during their rehabilitation to oversee the intervention.

Socio-demographic characteristics (age, sex, education/employment status, and exercise routines) and disease variables (diagnosis, time of diagnosis, comorbidities and medications used) were recorded at baseline.

3.7 Outcome measures

It was decided to use a new Norwegian core outcome set, which was developed to evaluate rehabilitation programs/processes and interventions for patients with rheumatic and musculoskeletal diseases (RMD). The Norwegian National Advisory Unit on Rehabilitation in Rheumatology has been in charge of a Delphi process, and together with a group of 46 experts developed this core set, which was launched in 2015. The core outcome set consists of nine simple instruments/scales which measures ten important aspects of health which have shown to be affected by rehabilitation (Klokkerud et al., 2015). This includes pain, fatigue, physical ability, mental health, activities of daily living, social participation, quality of life, coping, goal achievement and motivation. The goal of this core set is to be able to monitor the effect of rehabilitation for patients with RMD across different rehabilitation programs, patient groups and centres (Klokkerud et al., 2015). All instruments have been found valid and reliable (Klokkerud et al., 2015).

3.7.1 Primary outcome measures

In our study the following two outcome measures were chosen as the primary outcome measures.

3.7.1.1 *30-second sit to stand test (30sTs)*

This is a physical capacity test, measuring especially lower extremity strength and power. In this test individuals are required to stand up from a standard chair to a fully extended standing position with their arms folded across their chest as many times as possible within 30 seconds. The number of completed repetitions achieved in 30 seconds is then recorded (Bennell, Dobson, & Hinman, 2011). Reference values for healthy women and men between 18 – 29

years is 26 and 27 completed repetitions respectively (Tveter, Dagfinrud, Moseng, & Holm, 2014a). To see more detailed instructions on how the test was performed see appendix C.

3.7.1.2 *Effective Musculoskeletal Consumer Scale (EC17)*

EC17 is a self-administered questionnaire developed for patients with chronic rheumatic disease (Kristjansson et al., 2007). It consists of 17 questions; developed to measure the main skills and behaviours needed to effectively manage ones health and healthcare. It covers five subdomains, including "use of health information", "clarifying personal priorities", "communicating with others", negotiating roles and taking control" and "deciding and taking action". It is translated into Norwegian (Hamnes et al, 2010) and is scored from 0 -100, where 100 is the best possible score.

3.7.2 Secondary outcome measures

3.7.2.1 *Patient Specific Functional Scale (PSFS)*

PSFS is a generic instrument where patients are asked to list up to five activities that are important to them, which they have problems to carry out due to their disease. These activities are then rated on an 11-point numerical scale from 0 -10, where a score of 0 means that they are unable to perform the activity and 10 meaning that they can complete the activity without any problems (Stratford, Gill, Westaway, & Binkley, 1995). The Norwegian version has been tested and found valid, reliable and responsive (Moseng, 2013).

3.7.2.2 *Hannover Functional Scale*

Hannover Functional Scale is a self-administered instrument containing twelve questions, which measures patients perceived capability of performing activities of daily living (Magnussen, Lygren, Anderson, Breivik, & Strand, 2010). It was originally developed for people with back pain, but is also validated for use in patients with inflammatory arthritis (Oude Voshaar, ten Klooster, Taal, & van de Laar, 2011). It has been translated into Norwegian (Magnussen et al., 2010). The scale gives a score ranging from 0-24, where 0 equals best perceived physical capability.

3.7.2.3 *Hopkins Symptom Checklist*

Hopkins Symptom Checklist is a generic self-administered questionnaire developed to measure symptoms of depression and anxiety. The short version (SCL-5) consists of five questions, scored from 0-4. The average score from the five questions is then calculated. 0 equals no symptoms and 4 represent the highest possible score. The Norwegian version has been tested and validated (Strand, Dalgard, Tambs, & Rognerud, 2003). It has been estimated that a score of 2.0 in the SCL-5 is the cut off point for mental disorders (Strand et al., 2003).

3.7.2.4 *EQ5D-5L*

The EQ5D-5L is a generic standardized measure of health status, consisting of two parts. The first part consists of five questions on mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The answers given here results in a five digit code. This five digit code has then been converted into an index score which represents the patients' health state. The EQ-5D-5L Crosswalk Index Value Calculator, with the Danish values set has been used in this study (van Hout et al., 2012).

The second part of the EQ5D5L is a single VAS scale where respondents are asked to rate their overall health from 0, which represents "the worst health you can imagine" to 100, representing "The best health you can imagine" (Herdman et al., 2011).

3.7.2.5 *Coop Wonka*

The Dartmouth Coop Functional Health Assessment/ World Organization of National Colleges, Academies and Academic Association of General Practitioners (COOP/WONCA) charts is a generic self –administered instrument, which consist of 6 simple charts with ratings from 1-5. The charts have questions in the domains of physical fitness, feelings, daily activities, social activities, changes in health, and overall health. It has been translated into Norwegian (Bentsen, Natvig, & Winnem, 1997). Low score represents a favourable state in the different domains (Bentsen et al., 1997).

3.7.2.6 *NRS fatigue/pain*

A numerical scale, measuring experienced fatigue/pain within the last week was used. The scales range from 0 (no fatigue/pain is not an issue), up to 10 (fatigue/pain is a major problem) (Hawker, Mian, Kendzerska, & French, 2011).

3.8 Ethics

The study has been approved by the Regional Committees for Medical and Health Research Ethics (nr. 2015/413). All participants signed a written informed consent form (appendix C), and were informed that they could withdraw from the study at any time without stating any reason. None of the patients received treatment inferior to standard treatment.

3.9 Statistics:

No formal sample size calculation was done due to the predefined number of persons that could be included in the trial due to economical funding.

A statistician from the Section of applied clinical research at NTNU was consulted when deciding on statistical methods. Using mixed model for repeated measures was first considered, however the data did not meet the assumptions about normality distribution for this method. The approach described below was advised by the statistician.

Both intention to treat (ITT) and per protocol (PP) analysis were performed. Results from the ITT analysis are presented here. As there were no substantial differences, all PP analysis are shown in appendix D.

Due to the relatively low number of participants, descriptive baseline statistics was performed to compare the intervention group and control group. Continuous data (age and BMI) was tested with unpaired t-test. Categorical data was analysed with Pearson Chi Square test, or the Fischer's exact test when expected frequency was below five in more than 25 % of the cells.

All outcome variables were tested for normality, with formal normality test, as well as QQ plots and histograms. For the variables with indications of non-normal distribution and for outcome measures based on ordinal scales, both parametric and nonparametric tests were run. The two approaches (parametric vs non-parametric) gave no substantial differences except for

two variables; VAS pain and EQ5D5L VAS. These variables are therefore presented with the results from the non-parametric test, while all other presented results are from parametric tests.

Within group differences were tested with paired t-test, and Wilcoxon Signed Rank test as the non-parametric alternative. The within group test was conducted by comparing each outcome time-point with the baseline value. Between group differences are tested with independent t-test, and Mann Whitney U-test for non-parametric data.

To investigate if there had been any changes in self-reported medication use or work status during the study period a McNemar test was run. A Wilcoxon signed Rank test was performed to look at changes in self-reported exercise routines. BMI was also analysed with a paired t-test to see if there had been any changes at any of the time-points compared to baseline.

Cohens D effect sizes were calculated for the main outcomes (between group differences) and defined as small >0.2, medium >0.5 and large >0.8 (Cohen, 1988).

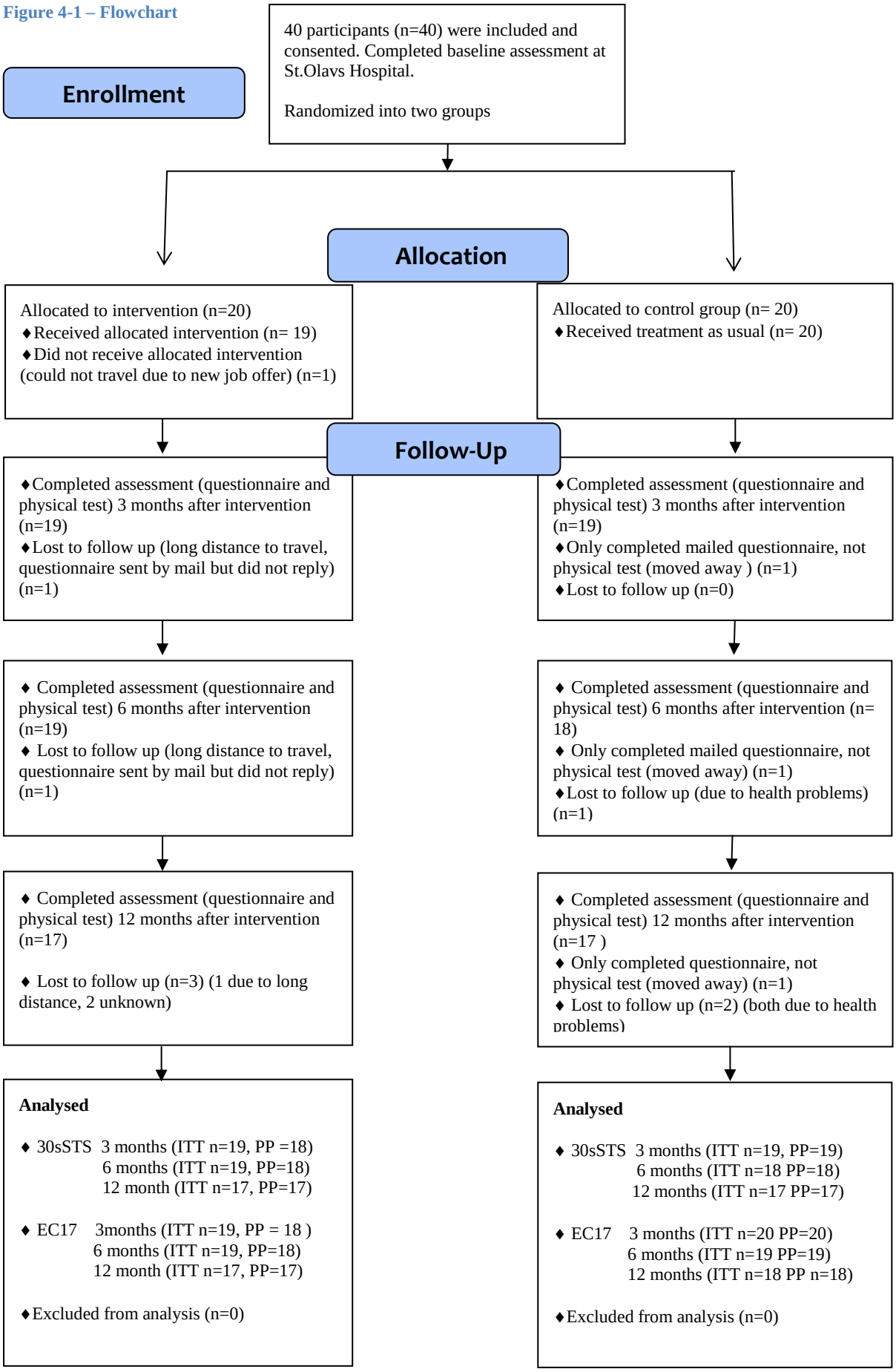
Due to unbalance in the distribution of different diagnosis between the two groups, two post hoc sensitivity analyses were run analysing within and between differences on the primary outcome measure (30sSTS) to see if this influenced the results. One analysis (paired sample t-test and independent sample t-test) was run were patients with axial SpA were excluded and in the other analysis patients with JIA were excluded.

All statistical analyses were undertaken with SPSS, version 23 for Windows. Analysis was based on available data, no imputation was done.

4 Results

A total of 40 participants were included in the study.19 out of the 20 who were randomized to the intervention group received and completed the intervention. One participant dropped out prior to the intervention due to personal reasons. At twelve months follow up, 34 out of the 40 included participants were analysed for the 30sSTStest and 35 were analysed for the EC17outcome (both ITT and PP analysis). See fig 1. for an overview of participant-flow through the study period.

Figure 4-1 – Flowchart



4.1 Baseline Characteristics:

The baseline characteristics are shown in table 4-1. The groups were similar on demographic data, and the total sample consisted of 65% females and 35 % males, with a mean age of 27.5 (SD 5). The majority (90 % in intervention group, and 80 % in control group) were using some disease-modifying antirheumatic drug (DMARD), including both biologic and synthetic DMARD's, at baseline. A large proportion in both groups had also been using either NSAIDS/COXIBs or other analgesics within the last week prior to baseline. 35 % of the participants were either unemployed, on sick leave or on disability pension.

The distributions of diagnosis in the two groups were somewhat different. 40 % of the participants in the intervention group were diagnosed with axial SpA. In the control group, juvenile idiopathic arthritis was the most frequent diagnosis (45 %).

Table 4-1 Baseline characteristics, n (%) unless otherwise stated

	Intervention (n=20)	Control (n=20)
Gender, female	12 (60)	14 (70)
Age Mean (SD)	27.0 (5.3)	28.1 (4.6)
Diagnosis		
Rheumatoid Arthritis	3 (15)	2 (10)
Juvenile Idiopathic Arthritis	3 (15)	9 (45)
Psoriatic Arthritis	4 (20)	5 (25)
Axial Spondyloarthritis	8 (40)	3 (15)
Polyarthritis	2 (10)	1 (5)
Married/cohabiting	11 (55)	11 (55)
Main daily activity		
Working ≥ 50 %	9 (45)	12 (60)
Studying	3 (15)	4 (20)
Unemployed	2 (10)	0 (0)
Sick leave	1 (5)	0 (0)
Disability pension	6 (30)	5 (25)
Self-reported hard exercise for more than 30 minutes		
≥ 3 times per week	6 (30)	5 (25)
1-2 times per week	6 (30)	8 (40)
1-3 times per month	0 (0)	1 (5)
Does not exercise regularly	8 (40)	6 (30)
BMI Mean (SD)	27.1 (6.9)	25.6 (6.4)
Self-reported medication use		
DMARD	19 (95)	16 (80)
Corticosteroids, within the last week	3 (15)	0 (0)
NSAIDS/Coxibs, within the last week	5 (25)	7 (35)
Other analgesics, within the last week	7 (35)	7 (35)

4.2 Implementation of intervention

19 out of the 20 who were randomised to the intervention group attended and completed the rehabilitation program. Participation in the various parts of the interventions was high. The

attendance rates for the various components were as follows: Morning exercise: 95 %, Midday exercise 94 %, pool exercise: 91 % and patient education: 97 %.

4.3 Main Outcomes

The results of the intention to treat outcome analysis are shown in table 4-2.

Table 4-2 Results from within and between (in italics) group ITT analysis. The values are mean (within group) or mean difference (between group) with 95% confidence interval (95%CI). Values in bold indicate a p-value below 0.05.

Outcome measures	Baseline Mean (SD)	Changes from baseline					
		3 months Mean (95 % CI)	p-value	6 months Mean (95 % CI)	p-value	12 months Mean (95 % CI)	p-value
30sSTS ↑							
Intervention group	12.75 (3.2)	**8.7 (5.7 to 11.8)**	<0.001	**8.5 (5.1 to 11.9)**	<0.001	**10.6 (7.3 to 14.0)**	<0.001
Control group	13.15 (2.7)	1.1 (-0.5 to 2.7)	0.169	**3.7 (1.2 to 6.2)**	0.006	**3.8 (0.6 to 7.1)**	0.024
Difference between group		***7.6 (4.3 to 10.9)***	*<0.001*	***4.8 (0.7 to 8.8)***	*0.024*	***6.8 (2.3 to 11.3)***	*0.004*
EC17 ↑							
Intervention group	64.5 (19.1)	0.9 (-4.0 to 5.7)	0.709	2.2 (-3.4 to 7.8)	0.427	4.0 (-3.7 to 11.7)	0.291
Control group	64.4 (10.3)	2.2 (-2.1 to 6.5)	0.295	6.8 (1.9 to 11.7)	0.009	4.2 (-1.2 to 9.5)	0.119
Difference between group		*-1.3 (-7.6 to 4.9)*	*0.670*	*-4.6 (-11.8 to 2.6)*	*0.200*	*-0.2 (-9.1 to 8.7)*	*0.966*
PSFS ↑							
Intervention group	5.0(1.7)	**1.2 (0.3 to 2)**	0.011	0.3 (-0.7 to 1.3)	0.578	0.5 (-0.5 to 1.5)	0.319
Control group	4.38 (2.2)	0.6 (-0.5 to 1.8)	0.279	1.1 (-0.3 to 2.6)	0.121	0.4 (-1.1 to 1.8)	0.598
Difference between group		*0.6 (-0.9 to 1.9)*	*0.434*	*-0.9 (-2.5 to 0.8)*	*0.315*	*0.1 (-1.6 to 1.9)*	*0.877*
EQ5D5L index ↑							
Intervention group	0.69 (0.13)	0.02 (-0.05 to 0.10)	0.498	-0.02(-0.1 to 0.06)	0.558	-0.02 (-0.12 to 0.10)	0.752
Control group	0.65 (0.13)	0.04 (-0.02 to 0.09)	0.180	0.07(-0.01to 0.10)	0.070	0.05 (-0.02 to 0.10)	0.132
Difference between group		*-0.01 (-0.1 to 0.08)*	*0.788*	*-0.09(-0.2 to 0.01)*	*0.089*	*-0.07 (-0.19 to 0.05)*	*0.255*
EQ5D5L VAS*↑							
Intervention group	67.5 (37)	**10 (15)**	0.001	5 (18)	0.233	13 (22)	0.078
Control group	70 (25)	5 (16)	0.517	5 (25)	0.175	10 (19.5)	0.200
Difference between group			*0.061*		*0.708*		*0.660*
Hannover ↓							
Intervention group	5.3 (3.5)	**-1.58 (-2.5 to -0.6)**	0.003	0.1 (-1.3 to 1.6)	0.882	0 (-1.9 to 1.9)	1.000
Control group	6.0 (4.4)	0.20 (-2.0 to 2.4)	0.848	-1.0 (-2.0 to -0.1)	0.045	0.1 (-2 to 2.2)	0.907
Difference between group		*-1.78 (-4.1 to 0.55)*	*0.131*	*1.1(-0.59 to 2.8)*	*0.195*	*-0.1 (-2.8 to 2.6)*	*0.930*
Hopkins ↓							
Intervention group	1.1 (0.8)	-0.05 (-0.4 to 0.3)	0.775	0.05 (-0.5 to 0.6)	0.842	0.10 (-0.4 to 0.6)	0.621
Control group	0.9 (0.6)	0.07 (-0.2 to 0.4)	0.619	0.02 (-0.3 to 0.3)	0.890	0.02 (-0.2 to 0.3)	0.851
Difference between group		*-0.12 (-0.6 to 0.3)*	*0.592*	*0.03 (-0.6 to 0.3)*	*0.917*	*0.1 (-0.4 to 0.6)*	*0.712*

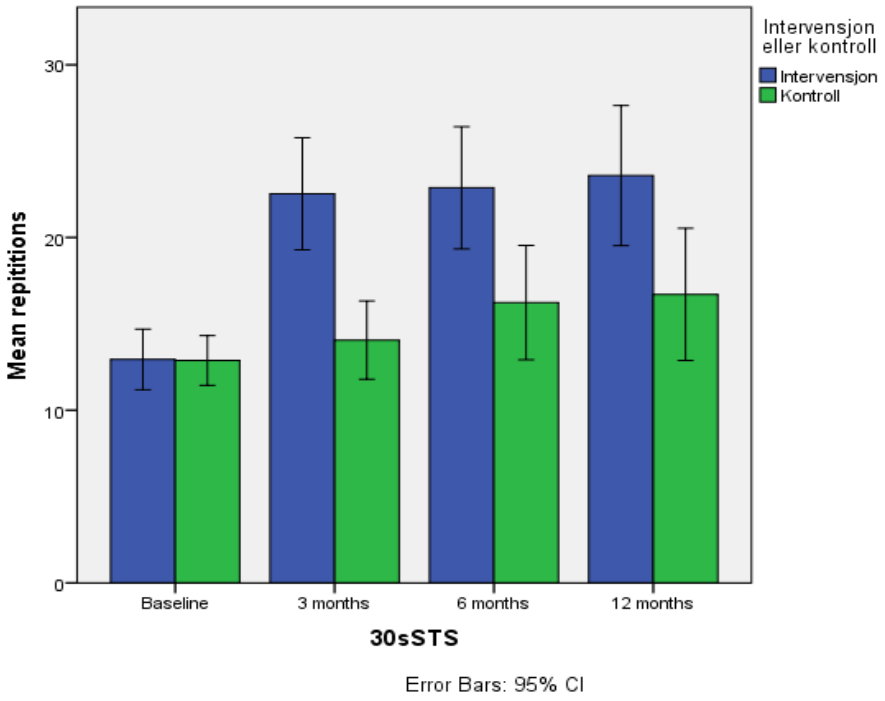
CW – Physical ↓							
Intervention	2.2 (1.0)	**-0.5 (-0.9 to -0.2)**	0.008	0.0 (-0.5 to 0.5)	1.000	-0.1 (-0.6 to 0.4)	0.580
Control group	2.2 (1.1)	0.1 (-0.5 to 0.7)	0.748	-0.1 (-0.6 to 0.4)	0.650	0.1 (-0.5 to 0.8)	0.726
Difference between group		*-0.6 (-1.4 to 0.1)*	*0.090*	*0.1 (-0.5 to 0.7)*	*0.740*	*-0.2 (-1.0 to 0.6)*	*0.542*
CW – Feelings ↓							
Intervention	2.3 (0.9)	-0.05 (-0.6 to 0.5)	0.834	0.1 (-0.8 to 0.2)	0.716	-0.3 (-0.8 to 0.2)	0.173
Control group	2.1 (0.9)	0.05 (-0.3 to 0.4)	0.789	0.1 (-0.4 to 0.6)	0.667	0 (-0.3 to 0.3)	1.000
Difference between group		*-0.1 (-0.7 to 0.5)*	*0.740*	*0.0 (-0.8 to 0.8)*	*1.000*	*-0.3(-0.8 to 0.2)*	*0.241*
CW – Daily activities ↓							
Intervention	2.3 (0.9)	-0.4 (-0.9 to 0.1)	0.057#	-0.1 (-0.5 to 0.4)	0.805	-0.2 (-0.6 to 0.3)	0.422
Control group	2.1 (1)	0.2 (-0.4 to 0.7)	0.562	-0.1 (-0.5 to 0.3)	0.607	0.2 (-0.4 to 0.7)	0.507
Difference between group		*-0.6 (-1.2 to 0.1)*	*0.092*	*0.05 (-0.6 to 0.7)*	*0.868*	*-0.3 (-1.0 to 0.3)*	*0.303*
CW –Social activities ↓							
Intervention	2.1 (1.2)	-0.4 (-0.8 to 0.1)	0.090	-0.2 (-0.6 to 0.3)	0.454	0.1 (-0.4 to 0.6)	0.608
Control group	1.9 (1.1)	-0.1 (-0.6 to 0.4)	0.681	0.0 (-0.5 to 0.5)	1.000	0.1 (-0.4 to 0.5)	0.805
Difference between group		*-0.3 (-0.9 to 0.4)*	*0.403*	*-0.2 (-0.8 to 0.5)*	*0.591*	*0.1 (-0.6 to 0.7)*	*0.845*
CW- Change in health ↓							
Intervention	2.7 (0.6)	0.0 (-0.6 to 0.6)	1.000	0.4 (-0.1 to 0.9)	0.088	0.1 (-0.5 to 0.8)	0.707
Control group	2.8 (0.8)	0.2(-0.3 to 0.7)	0.385	-0.3 (-0.7 to 0.1)	0.137	0.3 (-0.2 to 0.9)	0.210
Difference between group		*-0.2 (-0.9 to 0.5)*	*0.576*	*0.7 (0.1 to 1.4)*	*0.023*	*-0.2 (-1.0 to 0.6)*	*0.592*
CW – Overall health ↓							
Intervention	2.7 (0.9)	-0.2 (-0.7 to 0.3)	0.385	0.1 (-0.4 to 0.5)	0.826	-0.2 (-0.8 to 0.4)	0.529
Control group	2.6 (0.9)	0.1 (-0.3 to 0.5)	0.606	-0.1 (-0.5 to 0.4)	0.790	0.1 (-0.6 to 0.7)	0.859
Difference between group		*-0.3 (-0.9 to 0.3)*	*0.311*	*0.1 (-0.5 to 0.7)*	*0.732*	*-0.2 (-1.1 to 0.6)*	*0.577*
VAS fatigue↓							
Intervention	6.25 (2.2)	-1 (-2.5 to 0.5)	0.171	-0.5 (-2.1 to 1.1)	0.521	-0.6 (-2.2 to 0.9)	0.405
Control group	6 (2.6)	-0.5 (-1.7 to 0.8)	0.436	-1 (-2.3 to 0.3)	0.135	-0.6 (-1.8 to 0.7)	0.364
Difference between group		*-0.5 (-2.4 to 1.3)*	*0.570*	*0.5 (-1.5 to 2.5)*	*0.617*	*-0.1 (-2 to 1.8)*	*0.941*
VAS pain ↓*							
Intervention	5.0(3.0)	-1(2)	0.088	-0.5 (4.3)	0.658	-0.5 (2.5)	0.384
Control	5.5(3.5)	0(3)	0.924	-1.0 (2.0)	0.024	-1.0 (2)	0.177
Difference between groups			*0.418*		*0.374*		*0.574*

↑: Higher score is better ↓: Lower score is better *Analysed with non-parametric tests. Baseline values are presented with median (IQR). Change from baseline is shown as median change (IQR). # Significant different results between ITT and PP analysis.

4.3.1 Physical Function - 30-second sit to stand test (30sSTS)

The mean value of repetitions in the 30sSTS test at baseline was 12.75 in the intervention group and 13.15 in the control group. The within group analysis showed that the intervention group had a significant improvement in number of repetitions ($p < 0.001$) in the 30sSTS test at three, six and twelve months after the intervention. The control group also showed some within group improvements with significant change at six and twelve months ($p < 0.05$). The between group difference were significant at all follow up time points with the intervention group doing more repetitions (improved physical function) (3 months mean difference (95% CI): 7.6 (4.3 to 10.9), 6 months 4.7 (0.7 to 8.8) and 12 months 6.8 (2.3 to 11.3).

Figure 4-2 - 30sSTS



4.3.1.1 *Influence from diagnosis - Post Hoc sensitivity analysis on 30sSTS*

Excluding patients with axial SpA from analysis had no significant impact on either within or between group differences in the 30sSTS at three, six or twelve months (Table 4-3).

Excluding patients with JIA from the analysis had no impact on within group differences at any of the follow up points. It did however impact on between group difference at 6 and 12 months (6 months mean difference: 3.4 (-2.0 to 8.8) and 12 months mean difference 6.1 (-0.1 to 12.3), compared to the main analysis which showed a mean difference of 4.8 at 6 months and 6.8 at 12 months. This difference was due to a larger change within the control group at 6 and 12 months in the sensitivity analysis, and not due to a smaller effect within the intervention group.

Table 4-3 Post-hoc sensitivity analysis. The values are mean (within group) or mean difference (between groups) with 95% confidence interval (95%CI). Values in bold indicate a p-value below 0.

Outcome measures	Baseline values	Changes from baseline					
		3 months	p-value	6 months	p-value	12 months	p-value
	Mean (SD)	Mean (95 % CI)		Mean (95 % CI)		Mean (95 % CI)	
30sSTS ↑ ax. SpA excluded							
Intervention group	13.6 (3.4)	**8.2 (4.5 to 11.8)**	<0.001	**8.8 (5.0-12.5)**	<0.001	**10.1 (5.9-14.3)**	<0.001
Control group	13.3 (3.5)	1.6 (-0.3 to 3.4)	0.090	4.1 (1.1-7.0)	0.011	4.3 (0.3-8.3)	0.037
Difference between group		**6.6 (3.0 to 10.2)**	0.001	**4.7 (0.2 to 9.2)**	0.042	**5.8 (0.3 to 11.3)**	0.041
30sSTS ↑ JIA excluded							
Intervention group	11.9 (2.8)	**9.8 (6.5 to 13.1)**	<0.001	**8.9 (5.0 to 12.8)**	<0.001	**11.3 (7.3-15.2)**	<0.001
Control group	13.3 (3.0)	2.3 (-0.1 to 4.6)	0.058	**5.5 (1.7 to 9.1)**	0.009	5.2 (-0.3-10.7)	0.063
Difference between group		**7.5 (3.3 to 11.8)**	0.001	3.4 (-2 to 8.8)	0.202	6.1 (-0.1 to 12.3)	0.054

4.3.2 Coping - Effective Consumer Scale 17

There was no difference within the intervention group at any of the measurement points for the EC17 scale. No significant differences between the two groups were shown. The control group showed a significant within group change at six months compared to baseline (p=0.009).

4.3.3 Effect size

Cohen's d effect sizes on the between group differences were large at all time points for the 30sSTS, but not for EC17.

Table 4-4 Cohen's d effect size

Outcome measures	Cohen's d effect size, difference between groups		
	3 months	6 months	12 months
30sSTS	1.5	0.8	1.05
EC17	-0.1	-0.4	0.01

4.3.4 Within group differences from baseline on secondary outcomes

At three months the intervention group showed significant improvement in several of the secondary outcome measures (PSFS, EQ5D5L VAS, Hannover and CW physical) (Table 4-2). There were no significant within group changes in the control group at three months.

At six months no significant differences were found in the intervention group. The control group showed significant change in Hannover and VAS pain, in favourable direction.

At twelve months neither the intervention group nor the control group showed any significant within group change in any of the secondary outcome measures compared to baseline.

4.3.5 Between group differences on secondary outcomes

The only secondary outcome measure which showed a significant between group difference was CoopWonka – Change in health at six months; mean difference (95% CI) 0.7 (0.1 to 1.4), p=0.023, in favour of the control group. No other secondary outcome showed between group differences at either three, six or twelve months.

5 Discussion of findings

The aim of this study was to investigate if a 17-day rehabilitation program in warm climate especially developed for young adults with IA showed indications of long term effect on general health status, and especially physical function and coping/self-management. The main findings were that the intervention group had a significant improvement in the physical function test (30sSTS) at three months (95 % CI 4.3-10.9, p<0.001), six months (95 % CI 0.6-8.8, p=0.024) and twelve months (95 % CI 2.3-11.3, p=0.004), compared to the control group. There were no differences in coping as measured by "EC17" between the two groups at any of the follow up points. The secondary outcome measures "PSFS", "Hannover Scale" and "CoopWonka-physical" (all measuring different aspects of self-reported physical function), and "EQ5D5L VAS" , measuring self-reported overall health status, showed indications of short term effect (3 months) within the intervention group.

5.1 Physical function

The mean value of repetitions in the 30sSTS test at baseline was 12.75 in the intervention group and 13.15 in the control group. Reference values for healthy women and men between 18 – 29 years are 26 and 27 respectively (Tveter et. al., 2014a). This might indicate that the study participants had decreased physical ability and low body strength at baseline. At twelve months the intervention group had increased the mean value of repetitions to 23.6. The results of this study therefore indicates that the intervention has had an effect on performance based physical function, and especially lower extremity strength and power up to one year after the intervention, as demonstrated through significant between group change at three, six and twelve months for the 30sSTS test.

None of the other studies on rehabilitation in warm climate have used the 30sSTS as an outcome measure, making direct comparison difficult. Others (Staalesen Strumse et al. (2011); Staalesen Strumse et al. (2009)) have used different performance measures for physical function, such as the 6 Minute Walk Test (6MWT)) when comparing a 4 week rehabilitation program in warm and cold climate. They found significant improvement (p=0.001) in both groups after 16 weeks. Thus both our findings and the findings from other studies strongly indicate that rehabilitation in warm climate are effective in improving performance based physical function both in short and long term.

The results in our study did however not show a significant difference in self-reported exercise frequency. This is conflicting with the significant improvement of the 30sSTS test, as one could assume that at least the improvement in the 30sSTS after 12 months reflects a continuous increase in level of physical activity among those in the intervention group. It has been demonstrated in other studies that number of repetitions in the 30sSTS corresponds with self-reported physical activity level (Tveter, Dagfinrud, Moseng, & Holm, 2014b). Also, in the study by Ajeganova et al. (2016) on rehabilitation in warm climate patients self-assessed their physical activity using the short version of the International Physical Activity Questionnaire (IPAQ). They showed a significant increase in self-reported physical activity level up to one year follow-up assessment.

The lack of change in self-reported exercise frequency in our study may be explained by the fact that physical activity was only assessed through a single-item question about exercise frequencies based on their recall of the last month. There is a possibility that this method of assessing physical activity was not sensitive enough to pick up on actual changes. The way the question was formulated (see appendix C) in this study would for example not pick up on a change from exercising two times per week to exercising three times per week. Neither would it pick up on changes in the intensity of the exercise, making it possible that even though they did not exercise more frequently, those in the intervention group could have started to exercise in a more efficient and beneficial way as a consequence of what they had learned during their rehabilitation stay.

An interesting question to look at when considering these results is whether this apparent improvement in performance based physical function demonstrated through the 30sSTS is reflected in the outcome measures that evaluates patient's self-reported physical function. In this study self-reported physical function was measured by PSFS, Hannover Scale and CoopWonka-physical. Even though there were no significant differences between the intervention and control group in these self-reported outcomes, the intervention group showed significant within-group changes at three months, however this effect was not sustained at six and twelve months follow up.

Other studies on rehabilitation in warm climate have also looked at self-reported physical function. Staalesen Strumse et al. (2011); Staalesen Strumse et al. (2009) and Ajeganova et al. (2016) used MHAQ for RA patients and BASFI for AS patients to assess self-reported

functional status. Ajeganova et al. (2016) found significant improvement in MHAQ up to 12 months after completed intervention, while Staalesen Strumse et al. (2009) showed significant change up till 28 weeks. For AS patients Staalesen Strumse et al. (2011) showed significant change in BASFI up to 28 weeks post intervention. Ajeganova et al. (2016) however only found significant change in BASFI at the end of rehabilitation. Even though BASFI had improved also at three and twelve months this was not statistically significant.

Comparing performance based physical function with self-reported functional status is important as the purpose of rehabilitation for patients with IA is not only improvement in physical parameters such as strength and endurance, but maybe more important to help improve overall function and ability to perform tasks of everyday living (Meesters et al., 2013). Studies which have compared self-reported assessment of functional status and physical performance measures, have mostly found a moderate correlation between the two approaches (Latham et al., 2008; Ocarino et al., 2009) Many researchers therefore recommend using both self-report and performance based instruments when evaluating patient's functional profile, as they appear to give distinct, but complementary information (Latham et al., 2008; Reuben et al., 2004). It is not surprising that the correlation is only moderate as self-reported functional status depends on a variety of factors besides physical capacity, such as environmental and personal factors (Dagfinrud, Kjeken, Mowinckel, Hagen, & Kvien, 2005). This might also explain why the effects on self-reported function in our study not seem to last beyond three months, while the 30sSTS showed long term improvement. Improvement in self-reported physical function is likely more difficult to induce as it might require more complex life style changes than increased physical activity level.

Our findings of short-lived effect as measured by self-reported physical function measures also concur with what many other studies on rehabilitation for patients with IA have shown (Kjeken et al., 2013; Uhlig et al., 2016). Rehabilitation for patients with rheumatic disease often address and require life style changes of the participant in order to maintain the beneficial effect of the treatment over time. This illustrates, as other have pointed out, that some form of follow-up intervention after rehabilitation could be necessary to maintain outcome improvement (Berdal, Smedslund, Dagfinrud, Hagen, & Kjeken, 2015; Uhlig et al., 2016). The research in this area is however limited, and even though some studies have shown an improvement in long term effect, there is no consensus on what these follow up interventions should consist of (Berdal et al., 2015).

5.2 Coping and self-management

The EC-17 questionnaire is the only outcome-measure in this study that was likely to be impacted only from the patient education component of the intervention, and not from the exercise intervention. The EC-17 questionnaire was originally developed to assess self-management interventions and measures patient's skills and attributes as effective consumers who manage their healthcare (Hamnes, Garratt, Kjeken, Kristjansson, & Hagen, 2010). In our study we found no significant change either within the intervention group or between the intervention and control-group at any of the follow-up points. No other studies on rehabilitation in warm climate have used this or other directly comparable outcome-measures in their studies.

Studies which have shown an effect on the EC-17 are primarily studies on self-management programs with considerable focus on behavioural and self-management techniques (Hamnes et al., 2010; Santesso et al., 2009). The 2003 Cochrane review on patient education for patients with RA concluded that only patient education programs with behavioural treatment components showed some effect, even though small and short term, on various outcomes (Riemsma et al., 2003). Information only had no effect on the included outcome measures of the studies in this review. The EULAR recommendations for patient education for people with IA also states that the studies included in their review shows a trend towards greater inclusion of behavioural, cognitive and emotional aspects in the PE programs during the last decade (Zangi et al., 2015).

It is difficult to say why the intervention in our study showed no indications of effect on self-management/coping. It does however illustrate a need for reviewing and evaluating the patient education component of the intervention. It is possible that increasing the focus on self-management and including elements of cognitive behavioural treatment in the patient education parts of this intervention could have increased the likelihood of improving this outcome.

5.3 Other results

It should also be noted that a few of the other secondary outcome measures did not show any significant results. VAS pain and VAS fatigue showed no significant improvement neither within nor between groups, which is conflicting with results from other studies on

rehabilitation in warm climate (Ajeganova et al., 2016; Staalesen Strumse et al., 2011; Staalesen Strumse et al., 2009). At three months there was however a trend in favour of the intervention group for both VAS pain and VAS fatigue, with a mean change of 1 (on a scale of 10). This is within what has been suggested as the minimal clinical important difference for this patient group in various studies (Khanna et al., 2008; Nordin, Taft, Lundgren-Nilsson, & Dencker, 2016; Wolfe & Michaud, 2007).

Another outcome which did not show clinical important differences was the Hopkins Symptom Checklist. This was however not surprising, as the baseline values for Hopkins was 1.1 in the intervention group and 0.9 in the control group. This is well below the cut off point for mental disorders, which has been estimated to be a score of 2.0, and one could maybe therefore not expect a significant change (Strand et al., 2003).

5.4 Influence of diagnosis

To study the impact of the baseline difference between the groups in which diagnosis that were most prevalent, two post-hoc analyses were conducted. The post –hoc analysis where patients with JIA where excluded impacted on the results in the way that between group differences at six and twelve months were no longer statistical significant, but this is likely due to reduced power. When excluding 12 out of 40 patients from the analysis, the confidence interval will as a consequence become wider, and the difference between the groups needs to be even larger, as there is a bigger uncertainty of the true effect, to reach the level of significance (Sedgwick, 2014). When looking at the actual values (see table 4-2 and 4-3) they are close to similar to the main analysis, indicating that diagnosis did not have any substantial influence. The differences seen are due to a larger change within the control group and not a smaller change within the intervention group. The sensitivity analysis does in other words not change the overall findings.

6 Methodological discussion

6.1 Internal validity

Internal validity refers to the question of causality, and whether the difference between the control and intervention group can confidently be attributed to the intervention and not due to some other explanation (Higgins et al., 2011). In principle, randomized controlled trials are considered as having very high internal validity when carried out properly. One important reason for this, and a strength also in this study is the randomization procedure, which help ensure that the two groups are balanced at baseline for known and unknown confounding factors, thus reducing risk of allocation bias (Higgins et al., 2011). There are however some challenges in this study that need to be discussed in relation to internal validity.

6.1.1 Blinding

The purpose of blinding is to eliminate bias resulting from the expectations of patients, provider or researcher regarding outcome (Campbell et al., 2000). A limitation in this study is the lack of blinding. Blinding of the patients and providers of the intervention was however not seen as possible in this study as both participants and providers automatically knew which group they were in.

It would have strengthened the study if the nurse in charge of data-collection was blinded. This was however not feasible due to practical issues, as the same nurse who was in charge of data-collection also stayed at the rehabilitation centre together with the patients to oversee the intervention. This is a source of detection bias (Higgins et al., 2011), and can be a threat to the internal validity. The 30sSTS test is however an objective standardized test and the study nurse were given detailed instructions on how to perform the test, and exactly what she should say and do. The lack of blinding should therefore in theory not affect the results greatly, however it is possible that the study-nurse either consciously or unconsciously treated the patients from the two groups differently, which somehow impacted the results (Karanicolas, Farrokhyar, & Bhandari, 2010). All other outcome measures beside the 30sSTS were self-reported using validated tools where the study nurse could not influence the outcome, hence decreasing the risk of the results being affected by observer bias in a substantial way. It is also important to point out that the study-nurse had no self-interest in the study results, as she is not involved in the study in any other way.

6.2 Precision

Precision is e term used to reflect the extent to which study results are free from random error, and depends on the number of participants and events in a study (Higgins et al., 2011). Confidence intervals are important to take into account when analysing results, as it illustrates the precision of the results. The 95 % confidence intervals in this study are wide in the majority of the results (see table 4-2). The width of the confidence interval depends to a large extent on the sample size (Sedgwick, 2014). It is therefore to be expected in a study such as this with only 40 included patients. Nonetheless, it illustrates an uncertainty of the true effect.

The dropout rate in our study was however relatively low, especially at three and six months follow-up, with only one patient in each group (intervention and control) lost to follow up, strengthening the precision of our results. At 12 months there were three and two patients lost to follow up in the intervention group and control group respectively. There were however no systematic differences in losses to follow up. The data were also analysed using the intention-to-treat principle. There is therefore a low risk of attrition bias in this study (Higgins et al., 2011).

6.3 External validity

External validity refers to whether the results can be generalized to other settings and samples than used in this study. Having low external validity is one of the most common criticisms of randomized controlled trials (Rothwell, 2006). Factors which could have affected the external validity of this study are discussed below.

6.3.1 Complex intervention

Randomized controlled trials are considered as the gold standard when trying to establish causality in scientific research (Schulz, Altman, Moher, & Group, 2010). There are however some challenges when conduction a randomized controlled trial on a complex intervention (Craig et al., 2008). The intervention in this study, rehabilitation in warm climate, is highly complex with multiple interacting components. This makes it difficult to distinguish what element of the intervention has had an effect and not, and what can be explained by things such as personality of the therapists, surroundings, social support etc. It can therefore be questioned whether we would have found similar results if the same intervention had been carried out in a different setting, with different therapists. It would also be difficult for others

to replicate the exact same intervention. This limits the external validity of the results (Craig et al., 2008).

6.3.2 Intervention fidelity

Intervention fidelity refers to the extent to which an intervention is delivered as intended (Gearing et al., 2011). The participation of the various parts of the intervention in our study was very high. The attendance rates for the various components were as follows: Morning exercise: 95 %, Midday exercise 94 %, pool exercise: 91 % and patient education: 97 %.

This is important as it means that the patients received the intervention as intended. Together with the fact that the intervention was overseen by the study-nurse to ensure it was conducted as planned helps ensure high intervention fidelity and increase the external validity.

6.3.3 Choice of outcome measures

In our study, we have included patients with various rheumatic diseases, thus it was necessary for us to choose outcome measures which were generic within rheumatology. We chose to use a core-set of outcome measures developed to evaluate rehabilitation programs/processes and interventions for patients with rheumatic and musculoskeletal diseases (RMD). The objective of the core-set is to be an evidence-based set of outcome measures to be widely used for monitoring the effects of rehabilitation for patients with RMDs in Norway, across different rehabilitation programs, patient groups and centres (Klokkerud et al., 2015). This core set has been developed thorough a Delphi process and has been through thorough pilot-testing. All the outcome measures are internationally accepted instruments and have been tested for reliability and validity. Each instrument was chosen as it was considered to measure important aspects of health which can be influenced by rehabilitation. Using this core set can therefore be considered a strength in this study.

Having multiple outcome measures can however pose a statistical problem, as there is an increased risk of making a type 1 error; that is findings of "false significance" (Feise, 2002). There is disagreement in the literature on whether the use of multiple outcomes makes it necessary to make appropriate p-value adjustments to compensate. This is not done in this study. Instead two primary outcome measures were decided before the RCT was carried out. Also pointing out the uncertainty and the need to look at the magnitude of the effect and the

width of the confidence intervals, instead of purely judging based on whether a result is classified as significant or not is recommended (Feise, 2002).

6.3.4 Is the sample representative?

One important factor when assessing the external validity of a study is whether patients included in the study are a representative sample of the target population (Rothwell, 2006). This depends to a large degree on the inclusion and exclusion criteria set for the study. The exclusion criteria in this study are based on the criteria's that are used when patients apply for rehabilitation programs administered by the "Section for Climate Therapy" at the Department of Rheumatology at Oslo University Hospital. The study participants are therefore likely to be representative of patients who would normally be offered rehabilitation in warm climate, strengthening the external validity. What differ from these criteria are however of course the age restrictions in this study. These results are therefore only representative for patients between the ages of 20-35 years. Also, patients were recruited only from inpatient hospital clinics. Patients with low disease activity are sometimes only followed up by their GP. These patients were not included in our study, and the results might therefore not be representative for this patient group.

6.3.5 Was the sample large enough?

Sample size calculations are recommended prior to conducting a randomized controlled trial to ensure adequate power (Röhrig, du Prel, Wachtlin, Kwiecien, & Blettner, 2010). In this study no formal sample size calculations were done, as the number of included patients was restricted and thus predefined based on available funding. This is an important potential limitation. To explore this further, a sample size calculation has been carried out post hoc.

There have been no studies, to the author's knowledge, on the patient group young adults with IA, where the 30sSTS has been used as an outcome measure. However, the pilot-study where the core outcome set which is used in this study was developed, gave us some possible reference values, which we have used for our post hoc power calculations. It should however be noted that the patient group from this pilot study was considerably older than the patients in our study (Klokkerud, 2015).Using these reference values, power calculations were done to detect a difference of 4 repetitions in the 30sSTS, with a standard deviation of 4.7. With a significance level of 0.05, and power of 80 %., 23 patients were needed in each group.

Sample size calculations were done using SPSS SamplePower application. When looking at the values from our study at twelve month follow up, it shows a mean difference of 6.8 (between groups), and a SD of 6.8 with 17 patients analysed in each group. This gives a power of 81 %, with a chosen significance level of 0.05. The study therefore seems to be adequately powered for the main outcome.

7 Conclusion

Although this is a small study where one must be careful when drawing conclusions, the findings clearly indicate that a 17 day rehabilitation program in warm climate especially developed for young adults with IA improves patient's physical capacity in terms of improved lower extremity strength and power, at least one year post rehabilitation. There are also indications for short term improvement in patient's self-reported physical function, as well as improvement in self-reported overall health.

The intervention did not have any effect on coping or patient's ability to effectively manage their health and healthcare. Increasing the focus on self-management and including elements of cognitive behavioural treatment in the patient education parts of this intervention could maybe increase the likelihood of improving this outcome.

8 Implications for practice and research

This is the first study to look at the effect of a rehabilitation program especially targeted towards young adults with IA. To be able to make more reliable conclusions there is a definite need to follow up the results in a study with more participants.

The intervention in this study only lasted for 17 days, as opposed to the traditional 4 week rehabilitation programs. Designing a study comparing one group of young adults participating in a 17 day rehabilitation program especially developed for young adults with another group where young adults participate in the traditional 4 week programs together with patients of all ages, would be interesting. If a shorter program could show comparable effects to a longer program, this would be an important finding in many aspects.

Conducting a study where one looked at the effect of adding a follow-up intervention can also be recommended. There is evidence that follow-up interventions can improve physical functioning in patients with IA, however the evidence is low, and there is no consensus on what constitutes an optimal design of such interventions. Further high quality research is therefore most needed in this area (Berdal et al., 2015).

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23.02.2015

Forespørsel om deltagelse i forskningsprosjekt om individtilpassede behandlingsreiser for unge voksne mellom 20 og 35 år med inflammatorisk revmatisk artrittsykdom.

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie for å undersøke effekten av individtilpassede behandlingsreiser for unge voksne mellom 20 – 35 år med inflammatorisk revmatisk artrittsykdom. Du mottar denne invitasjonen fordi du har vært i kontakt med St. Olavs hospital og er i målgruppen for studien..
Behandlingsreiser til varmere strøk for revmatikere har vært brukt i en årrekke. Likevel vet vi ikke om det har effekt for personer i alderen 20 til 35 år med inflammatorisk revmatisk artrittsykdom. For å legge grunnlaget for å studere dette skal det gjennomføres en pilotstudie av effekten av alders-tilpassede behandlingsreiser.

Undersøkelsen gjennomføres av sykepleier og masterstudent ved NTNU Ingrid Nilssen. Hovedveileder er professor Aslak Steinsbekk ved Institutt for samfunnsmedisin, NTNU, og medisinsk ansvarlig er overlege Marianne Wallenius ved revmatologisk avdeling ved St. Olavs Hospital. Studien skal resultere i en mastergradsoppgave. Prosjektet er finansiert av norsk revmatologisk forening.

Hva innebærer studien?
Fordi dette er en såkalt pilotstudie med begrensede ressurser vil det bare være mulig å la 20 personer dra på behandlingsreise. For at studien skal gi de svar som trengs, må det også delta personer som får vanlig behandling i studien. Vi vil derfor rekruttere totalt 40 personer. Så vil det bli loddtrekning blant disse for å plukke ut 20 personer til hver av gruppene. Det er bare tilfeldigheter som avgjør hvem som kommer i hvilken gruppe:

- De som blir trukket ut til behandlingsreisegruppen vil delta på et tre uker langt opphold ved Reuma-Sol i Spania (man får sykemelding hvis man er i arbeid).
- De som blir trukket ut til den andre gruppen får vanlig oppfølging i Norge.

Alle som sier ja til å delta i studien må i tillegg møte til kontroll ved revmatologisk avdeling på St. Olavs Hospital 4 ganger i løpet ett år for å gjennomføre en enkel styrke og gang test og svare på spørreskjema om daglige aktiviteter, fatigue, fysisk form, livskvalitet, mestring, motivasjon, måloppnåelse, psykisk helse, smerte og sosial deltagelse.

Mulige fordeler og ulemper
Studien innebærer at du må bruke tid på å svare på spørsmål og gjennomføre enkle fysiske tester tilpasset din egen situasjon. De som trekkes ut til behandlingsreise må fly og delta i det behandlingsopplegget som tilbys, men dette vil bli individuelt tilpasset. Det er ingen andre kjente ulemper. Fordelen for den enkelte deltager er at man får ekstra oppfølging i studieperioden.

Hva skjer med informasjonen om deg?
Informasjonen som registreres skal kun brukes som beskrevet i hensikt med studien. Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Navnelisten vil bli holde innelåst. Enkeltpersoner vil ikke kunne gjenkjennes i fremtidige publikasjoner.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du denne samtykkeerklæringen.

Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte:

Ingrid Nilssen– forskningsassistent/masterstudent, Tlf: 47 66 37 21

Samtykke til deltakelse i studien

Jeg bekrefter å ha lest informasjonen og er villig til å delta i studien

---
(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Silje U. Lauvrak	22845520	15.04.2015	2015/413 REK sør-øst D
			Deres dato:	**Deres referanse:**
			24.02.2015	

Vår referanse må oppgis ved alle henvendelser

Aslak Steinsbekk
Norges teknisk-naturvitenskapelige universitet NTNU

2015/413 Individrettede behandlingsreiser for unge revmatikere i varmere klima.

Forskningsansvarlig: Norges teknisk-naturvitenskapelige universitet NTNU, St.Olavs Hospital
Prosjektleder: Aslak Steinsbekk

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst D) i møtet 25.03.2015. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikkloven § 4.

Prosjektleders prosjektbeskrivelse
Unge voksne med en inflammatorisk revmatisk artrittsykdom (IRA) er en pasientgruppe med store utfordringer. Sykdommen kan ha stor innvirkning på hverdag og livskvalitet for de som er rammet. Behandlingsreiser for revmatikere har over lang tid vært etablert som et tilbud for pasienter med IRA, men tilbudet har i liten grad vært tilpasset gruppen unge voksne. Formålet med denne studien er å gjennomføre en randomisert kontrollert pilotstudie. Intervensjonen i studien er deltagelse på ett spesialtilpasset behandlingsreisetilbud for unge voksne, fra 20 til 35 år med en IRA. Kontrollgruppen vil få ordinær oppfølgning på hjemstedet. Pilotstudie vil være med å forme fremtidige større randomiserte studier og for å skreddersy et tilbud til pasientgruppen som skal undersøkes. En viktig grunn for å gjøre en pilotstudie er for å teste hvorvidt det praktiske i studien fungerer som det skal, og gi bedre innsikt i hva som ville være det mest passende primære utkommemålet i en større skala studie.

Vurdering
Komiteen har vurdert søknaden og har ingen innvendinger til at studien gjennomføres som beskrevet i søknad og protokoll.

Vedtak
Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 01.06.2017. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 01.06.2022. Forskningsfilen skal oppbevares avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

Klageadgang
REKs vedtak kan påklages, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Finn Wisløff
Professor em. dr. med.
Leder

Silje U. Lauvrak
Rådgiver

Kopi til:
NTNU, Institutt for samfunnsmedisin: rek-ism@medisin.ntnu.no
St. Olavs Hospital ved øverste administrative ledelse: post.adm.dir@stolav.no
Siri Forsmo, Instituttleder, Institutt for Samfunnsmedisin NTNU: siri.forsmo@ntnu.no
Jan Gunnar Skogås, Klinikksjef - Klinikk for ortopedi, revmatologi og hudsykdommer St. Olavs Hospital: Jan.Gunnar.Skogas@stolav.no

Pasient nr	
Besøk nr	
Dato	

CASE REPORT FORM

Individtilpassede behandlingsreise for unge voksne revmatikere

En randomisert kontrollert pilotstudie

Baseline

Ingrid Nilssen
Mastergradstudent

Pasient nr	
Besøk nr	
Dato	

DEL 1

FYLLES UT AV STUDIEPERSONELL SAMMEN MED STUDIEDELTAGER

Pasient nr	
Besøk nr	
Dato	

SCREENING

1. **Inklusjonskriterier**
   a. Inflammatorisk revmatisk artrittsykdom Ja ☐ Nei ☐
   b. 20 -35 år Ja ☐ Nei ☐
   c. Selvhjulpen i daglige gjøremål Ja ☐ Nei ☐
   d. Har fått informasjon om prosjektet og samtykket skriftlig til å delta Ja ☐ Nei ☐

2. **Eksklusjonskriterier**
   a. Ustabil hjerte/kar sykdom Ja ☐ Nei ☐
   b. Alvorlig lungesykdom Ja ☐ Nei ☐
   c. Kroniske åpne sår Ja ☐ Nei ☐
   d. Alvorlige psykiske lidelser Ja ☐ Nei ☐
   e. Alkohol og/eller medikamentmisbruk Ja ☐ Nei ☐
   f. Intoleranse for sol og varme Ja ☐ Nei ☐

DEMOGRAFI

3. **Fødselsår:** _____
4. **Dato for skriftlig gitt informert samtykke**_____
5. **Kjønn**
   a. Mann ☐
   b. Kvinne ☐
6. **Din høyde :** _____**(cm)**
7. **Din vekt :** _____**(kg)**

Pasient nr	
Besøk nr	
Dato	

8. Er du :

a. Ugift ☐

b. Samboer ☐

c. Gift ☐

d. Skilt/separert ☐

e. Enke/enkemann ☐

9. Hvilken utdanning har du? (oppgi høyeste fullførte utdanning)

a. Grunnskole ☐

b. Videregående skole ☐

c. Høyskole ☐

d. Universitet ☐

10. Er du i inntektsgivende arbeid nå?

a) Ja ☐

Hvis ja: Heltid ☐ Deltid ☐ _____%

b) Nei ☐

Hvis nei, er du:

a) Skoleelev/student ☐

’ b) Arbeidsledig ☐

c) Uføretrygdet/ på attføring/ arbeidsavklaring ☐ _____%

d) Sykemeldt ☐ _____%

e) Foreldrepermisjon ☐

f) Annet ☐ Spesifiser _____

11. Hvor ofte trener du (økt puls og pust) i minst 30 minutter? (tenk på i løpet av siste måned)

a) 3 eller flere ganger per uke ☐

b) 1-2 ganger per uke ☐

Pasient nr	
Besøk nr	
Dato	

c) 1-3 ganger per måned ☐

d) Trener ikke regelmessig ☐

SYKDOMSKARAKTERISTIKA

12. Diagnose_____

ICD 10 kode_____

Hvilket årstall fikk du diagnosen_____

13. Andre sykdommer?

a) Ja ☐

b) Nei ☐

Hvis ja, ICD 10 koder

14. Medikamentell behandling, kryss av for de medikamenter pasienten bruker

DMARD	**Pasienten bruker disse medisinene**	**Dosering**
Adalumimab	☐	
Anakinra	☐	
Auranofin	☐	
Azatioprin	☐	
Cyclosporin	☐	
D-penicillamin	☐	
Etanercept	☐	
Gull-tiomalat	☐	
Hydroxyklorin/klorokin	☐	
Infliximab	☐	

Pasient nr	
Besøk nr	
Dato	

Leflunomid	☐		
Methotrexat (MTX)	☐		
Sulfasalazin	☐		
Reumacon	☐		
Rituximab	☐		
KORTIKOSTEROID BEHANDLING			
Prednisolon	☐		
Andre, spesifiser	☐		
NSAID/COXIBS BEHANDLING			
	☐		
	☐		
SMERTESTILLENDE MEDISINER FAST			
	☐		
	☐		
	☐		
SMERTESTILLENDE VED BEHOV			Dose og antall tatt i løpet av den siste uken
	☐		
	☐		
	☐		
	☐		
ANDRE MEDISINER			
	☐		
	☐		
	☐		
	☐		

Pasient nr	
Besøk nr	
Dato	

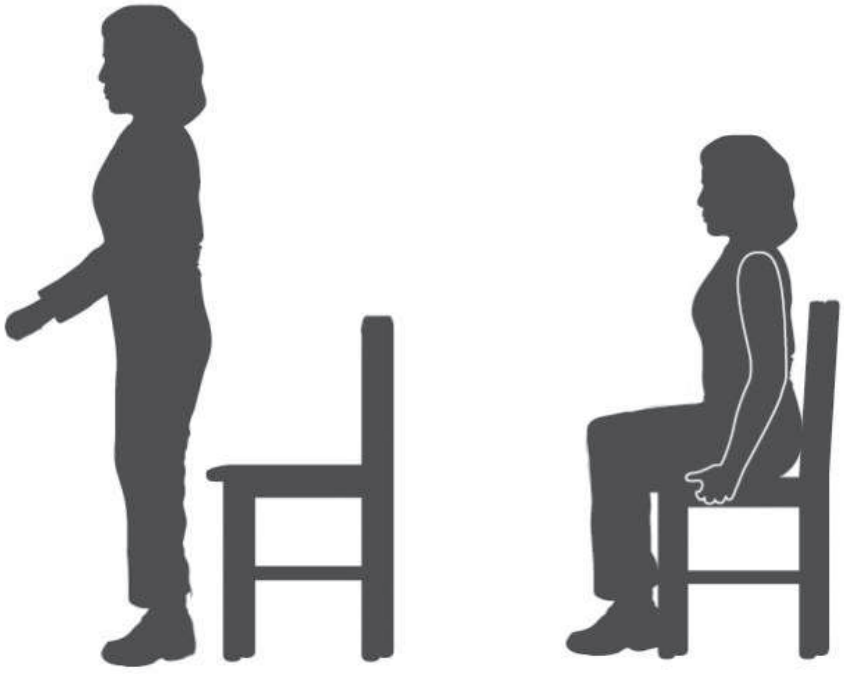
FYSISK TEST: "30 sekunder reise og sette seg"
(gjøres sammen med helsepersonell/annen person)

UTSTYR: Bruk en vanlig spisestuestol uten armlener.
Det er viktig at det er samme stol for hver gang.

INSTRUKSJON: Testpersonen skal starte i sittende stilling og reise og sette seg så mange ganger han/hun klarer i løpet av 30 sek. Hendene skal holdes i kryss over brystet. Testpersonen skal reise seg helt opp – med strake knær – og sette seg helt ned igjen. Testpersonen trenger ikke lene seg mot rygglenet, men skal sette seg helt ned for hver gang (ikke bare "touche" nedpå). Bena kan plasseres slik testpersonen selv ønsker.

Gjør gjerne et par prøveforsøk først.

Instruktør/tidtaker starter klokken og teller antall repetisjoner høyt (tell når testpersonen reiser seg opp).Husk at knærne skal strekkes helt ut og at en skal være tydelig nedpå setet for at repetisjonen skal telle. Instruktør/tidtager skal ikke gi noen form for oppmuntring underveis. Dersom testpersonen er mer enn halvveis oppe når det har gått 30 sekunder, så telles denne som en repetisjon.



ANTALL GANGER REISE OG SETTE SEG (på 30 sekunder) _____

Pasient nr	
Besøk nr	
Dato	

Pasient nr	
Besøk nr	
Dato	

15. Randomisering (utføres etter både del 1 og del 2 er ferdig utfyllt)

a) Intervensjon – Behandlingsreise ☐

b) Kontrollgruppe ☐

Alle skjemaer er sjekket og utfylt korrekt

_____

Sign. initialer

Pasient nr	
Besøk nr	
Dato	

DEL 2

FYLLES UT AV STUDIEDELTAGER SELV.

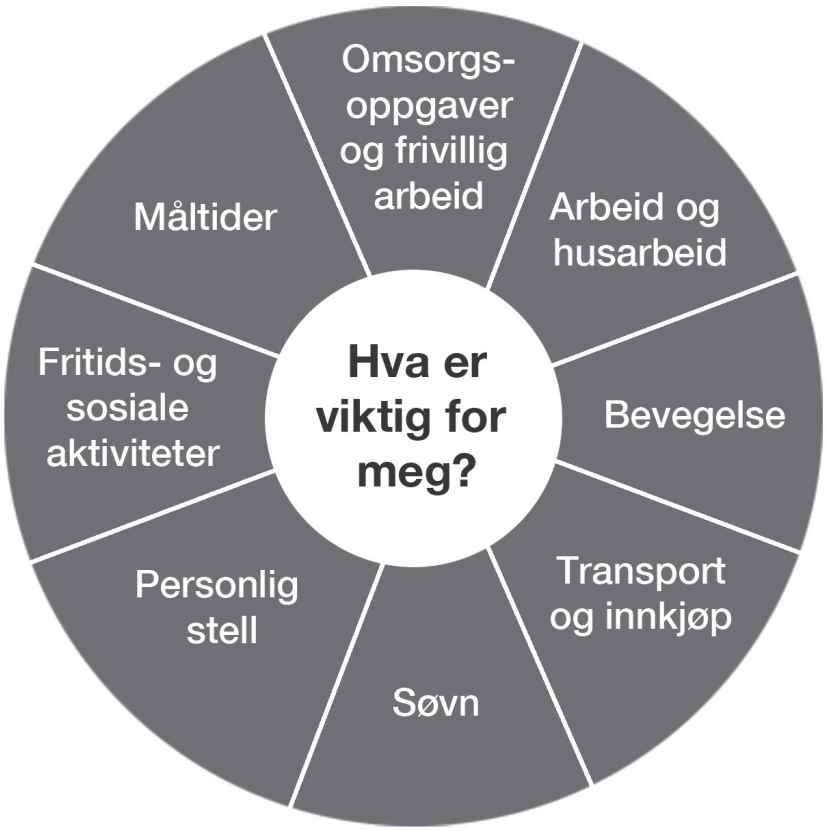
Pasient nr	
Besøk nr	
Dato	

FUNKSJON I DAGLIGE GJØREMÅL

Vi vil be deg beskrive fem viktige aktiviteter eller daglige gjøremål som du har problemer med eller ikke kan utføre i det hele tatt på grunn av din sykdom, skade eller probem.

Skriv inntil fem aktiviteter inn i tabellen på neste side (i kolonnen Aktivitet).

Aktivitetshjulet under viser ulike kategorier av aktivitet.
Tenk gjennom om det er konkrete aktiviteter fra en eller flere av kategoriene som du ønsker å jobbe med under rehabiliteringen.



Pasient nr	
Besøk nr	
Dato	

Aktivitet:
1
2
3
4
5

PASIENTSPESIFIKK FUNKSJONSSKALA og MOTIVASJON

Vi ber deg nå om å angi på skalaene, hvordan du synes du klarer å utføre hver av aktivitetene du har beskrevet.Tenk på hvordan det gikk sist gang du utførte aktiviteten, og sett en ring rundt det tallet som best passer for din vurdering i kolonnen **"Grad av vanskelighet".** 0 betyr det at du ikke kunne utføre aktiviteten ☹ og 10 betyr det at du gjorde det helt uten problemer. ☺

Angi så hvor motivert du er til å jobbe for å få til angitte aktivitet i kolonnen **"Grad av motivasjon",** hvor 0 innebærer ingen motivasjon ☹ og 10 innebærer maksimal motivasjon. ☺

Aktivitet	**Grad av vanskelighet**	**Grad av motivasjon**
1	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺
2	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺
3	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺
4	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺
5	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺	0 ☹ 1 2 3 4 5 6 7 8 9 10 ☺

Pasient nr	
Besøk nr	
Dato	

HANNOVER FUNKSJONSSPØRRESKJEMA

Følgende spørsmål dreier seg om aktiviteter i dagliglivet. Vær vennlig å svare på hvert spørsmål slik du opplever det for tiden (det vil si slik du har erfart det de siste 7 dagene).

Du har tre svaralternativer:

1	Ja	Du kan utføre oppgaven uten vanskelighet
2	Ja, men med anstrengelse	Du har vansker med å utføre oppgaven f.eks pga smerte, at det tar lenger tid enn før, eller at du må støtte deg til noe
3	Nei, eller bare med hjelp av andre	Du kan slett ikke utføre oppgaven eller bare når en annen person hjelper deg

Ring inn det tallet som passer:

Kan du strekke deg f.eks. for å hente ned ei bok fra et høyt skap eller hylle?	1	2	3
Kan du løfte opp en gjenstand som er minst 10 kg tung (f.eks. ei full bøtte vann eller en koffert) og bære den 10 meter?	1	2	3
Kan du vaske og tørke deg fra topp til tå?	1	2	3
Kan du bøye deg og plukke opp en lett gjenstand (f.eks en mynt eller en krøllete papirlapp) fra gulvet?	1	2	3
Kan du stå over en vask og vaske håret?	1	2	3
Kan du sitte på en stol som ikke er polstret i en time?	1	2	3
Kan du stå uavbrutt i 30 minutter (f.eks i kø)?	1	2	3
Kan du sette deg opp i sengen fra ryggliggende stilling?	1	2	3
Kan du ta på og av deg strømper?	1	2	3
Kan du fra sittende stilling ta opp en liten gjenstand (f.eks en mynt) som har falt ned ved siden av stolen din?	1	2	3
Kan du løfte en tung gjenstand (f.eks en full kasse mineralvann) fra gulvet og opp på bordet?	1	2	3
Kan du løpe fort (ikke gå) 100 meter f. eks. for å nå bussen?	1	2	3

Pasient nr	
Besøk nr	
Dato	

HOPKINS SYMPTOM CHECKLIST (SCL-5)

Nedenfor finner du en oppstilling av plager som man av og til har. Les nøye gjennom dem, en for en, og angi deretter hvor mye hvert enkelt problem har plaget deg eller vært til besvær i løpet av de siste 14 dagene?

	Ikke i det hele tatt	Litt	Måtelig	Ganske mye	Veldig mye
Nervøsitet eller indre uro?	☐	☐	☐	☐	☐
Stadig redd eller engstelig	☐	☐	☐	☐	☐
Følelse av håpløshet for framtida	☐	☐	☐	☐	☐
Nedfor	☐	☐	☐	☐	☐
Bekymrer deg for mye	☐	☐	☐	☐	☐

(Norsk versjon fra de Vibe 2006)

Pasient nr	
Besøk nr	
Dato	

PASIENTSKJEMA

Funksjonsmåling (COOP/WONCA)

Norsk bearbeidelse. Prof. B.G. Bentsen
Institutt for allmenmedisin og samfunnsmedisinske fag, Universitetet i Oslo

For å kunne følge din generelle helsetilstand før, under og etter en behandling trenger vi å vite "hvordan du har det". Det kan måles ved hjelp av svarene på noen enkle spørsmål.Vi ber deg derfor å svare på de seks spørsmålene på de seks skjemaene (A) til (F) nedenfor.

Du ser seks skjemaer som har som mål å angi din fysiske, psykiske og sosiale tilstand. Skjemaene besvares ved på hvert enkelt skjema **<u>å slå en ring rundt</u>** ◯ det tallet til høyre for tegningen som best beskriver din nåværende situasjon.

(A) FYSISK FORM

De siste 2 uker.....
Hva var den tyngste fysiske belastningen du greide/kunnne greid i minst 2 minutter?

MEGET TUNGT (f.eks.) å løpe fort		1
TUNGT (f.eks.) jogge i rolig tempo		2
MODERAT (f.eks.) gå i raskt tempo		3
LETT (f.eks.) gå i vanlig tempo		4
MEGET LETT (f.eks.) gå sakte - eller ikke kan gå		5

(B) FØLELSESMESSIG PROBLEM

De siste 2 uker.....
Hvor mye har du vært plaget av psykiske problemer som indre uro, angst, nedforhet eller irritabilitet?

Ikke i det hele tatt		1
Bare litt		2
Til en viss grad		3
En god del		4
Svært mye		5

Pasient nr	
Besøk nr	
Dato	

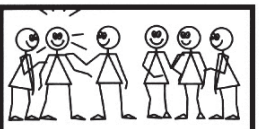
C DAGLIGE AKTIVITETER

De siste 2 uker.....
Har du hatt vansker med å utføre vanlige gjøremål eller oppgaver enten innendørs eller utendørs, p.g.a. din fysiske eller psykiske helse?

Ikke vansker i det hele tatt		1
Bare litt vansker		2
Til en viss grad		3
En god del vansker		4
Har ikke greid noe		5

D SOSIALE AKTIVITETER

De siste 2 uker.....
Har din fysiske eller psykiske helse begrenset dine sosiale aktiviteter og kontakt med familie, venner, naboer eller andre?

Ikke i det hele tatt		1
Bare litt		2
Til en viss grad		3
Ganske mye		4
I svært stor grad		5

E BEDRE ELLER DÅRLIGERE HELSE

Hvorledes vil du bedømme helsen din idag, fysisk, psykisk, sammenlignet med for 2 uker siden?

Mye bedre	++	1
Litt bedre	+	2
Omtrent uforandret	=	3
Litt verre	–	4
Mye verre	– –	5

F SAMLET HELSETILSTAND

De siste 2 uker.....
Hvorledes vil du vurdere din egen helse, fysisk, psykisk i allminnelighet?

Svært god		1
God		2
Værken god eller dårlig		3
Dårlig		4
Meget dårlig		5

Pasient nr	
Besøk nr	
Dato	

Effective Musculoskeletal Consumer Scale (EC-17)

Brukerundersøkelse
I denne spørreundersøkelsen får du spørsmål om deg selv og om hvordan du mestrer sykdommen din. Det er spørsmål om ferdigheter, holdninger og kunnskaper du kanskje har eller ikke har.

Vær så snill å krysse av for hvor ofte hver påstand stemmer for deg.

Del I Hvordan jeg bruker helseinformasjon

	aldri	sjelden	noen ganger	vanligvis	alltid
1. Jeg vet hvem som kan hjelpe meg å vurdere kvaliteten på informasjonen jeg får om sykdommen min.					
2. Jeg forstår informasjonen jeg får om sykdommen min.					
3. Jeg vet hvordan jeg kan tilpasse generell helseinformasjon til min egen situasjon.					

Del II Hvordan jeg avklarer og avveier verdier og prioriteringer

	aldri	sjelden	noen ganger	vanligvis	alltid
4. Jeg kan være tydelig på hva som er viktig i livet mitt når jeg tar avgjørelser om sykdommen min.					
5. Jeg kan vurdere fordeler og ulemper vedrørende avgjørelser om sykdommen min.					
6. Jeg kan sette realistiske mål for mestring av sykdommen min.					

Pasient nr	
Besøk nr	
Dato	

Del III Hvordan jeg kommuniserer med andre

	aldri	sjelden	noen ganger	vanligvis	alltid
7. Jeg kan tydelig uttrykke mine bekymringer til helsepersonell.					
8. Jeg vet hvordan jeg stiller gode spørsmål om helsen og sykdommen min.					
9. Jeg har bygd opp et åpent og tillits-fullt forhold, basert på gjensidig respekt, med helsepersonell jeg er i kontakt med.					

Del IV Hvordan jeg forhandler om roller og tar kontroll

	aldri	sjelden	noen ganger	vanligvis	alltid
10. Jeg tar den rollen jeg ønsker i møte med helsepersonell.					
11. Jeg vet hvem jeg kan samarbeide med for å ivareta mine helsebehov.					
12. Jeg kan være pågående for å få det jeg trenger i forhold til mine helsebehov (for eksempel informasjon og behandling).					
13. Jeg har en viss følelse av kontroll over sykdommen min					

Del V Hvordan jeg tar beslutninger og handler

	aldri	sjelden	noen ganger	vanligvis	alltid
14. Jeg føler meg sikker i forhold til å ta beslutninger om helsen min.					
15. Jeg kan forhandle med andre om hva som må gjøres for å mestre sykdommen min.					
16. Jeg kan forhandle med helse-vesenet om hva som må gjøres for å mestre sykdommen min.					
17. Jeg kan organisere livet mitt slik at jeg kan handle i forhold til beslutninger som gjelder sykdommen min.					

Pasient nr	
Besøk nr	
Dato	

EQ-5D-5L SPØRRESKJEMA OM HELSE

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

Jeg har ingen problemer med å gå omkring ❑
Jeg har litt problemer med å gå omkring ❑
Jeg har middels store problemer med å gå omkring ❑
Jeg har store problemer med å gå omkring ❑
Jeg er ute av stand til å gå omkring ❑

PERSONLIG STELL

Jeg har ingen problemer med å vaske meg eller kle meg ❑
Jeg har litt problemer med å vaske meg eller kle meg ❑
Jeg har middels store problemer med å vaske meg eller kle meg ❑
Jeg har store problemer med å vaske meg eller kle meg ❑
Jeg er ute av stand til å vaske meg eller kle meg ❑

VANLIGE GJØREMÅL *(f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

Jeg har ingen problemer med å utføre mine vanlige gjøremål ❑
Jeg har litt problemer med å utføre mine vanlige gjøremål ❑
Jeg har middels store problemer med å utføre mine vanlige gjøremål ❑
Jeg har store problemer med å utføre mine vanlige gjøremål ❑
Jeg er ute av stand til å utføre mine vanlige gjøremål ❑

SMERTER/UBEHAG

Jeg har verken smerter eller ubehag ❑
Jeg har litt smerter eller ubehag ❑
Jeg har middels sterke smerter eller ubehag ❑
Jeg har sterke smerter eller ubehag ❑
Jeg har svært sterke smerter eller ubehag ❑

ANGST/DEPRESJON

Jeg er verken engstelig eller deprimert ❑
Jeg er litt engstelig eller deprimert ❑
Jeg er middels engstelig eller deprimert ❑
Jeg er svært engstelig eller deprimert ❑
Jeg er ekstremt engstelig eller deprimert ❑

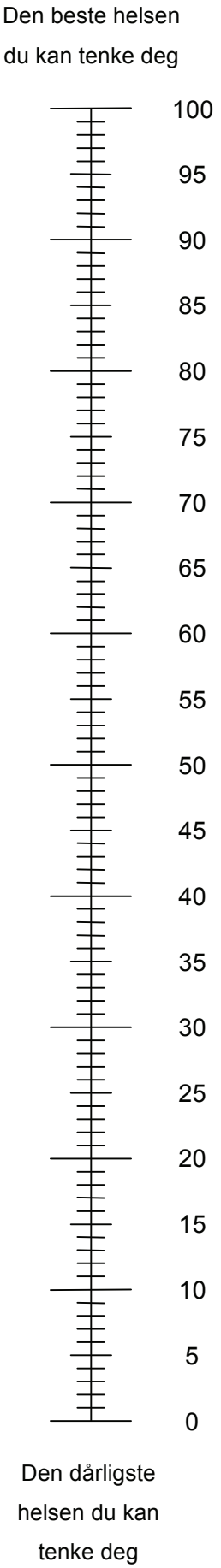
Pasient nr	
Besøk nr	
Dato	

EQ-5D-5L

SPØRRESKJEMA OM HELSE

- Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.
- Denne skalaen er nummerert fra 0 til 100.
- 100 betyr den beste helsen du kan tenke deg.
  0 betyr den dårligste helsen du kan tenke deg.
- Sett en X på skalaen for å angi hvordan helsen din er I DAG.
- Skriv deretter tallet du merket av på skalaen
  inn i boksen nedenfor.

HELSEN DIN I DAG = ☐



Pasient nr	
Besøk nr	
Dato	

NRS FATIGUE

Har du hatt problemer med følelse av fatigue (tretthet/utmattelse) den siste uken?

(Marker ditt svar ved å krysse av en rute)

0	1	2	3	4	5	6	7	8	9	10

Fatigue er ikke et problem — Fatigue er et stort problem

NRS SMERTE

Hvordan vil du gradere smertene du har hatt den siste uken?

(Marker ditt svar ved å krysse av en rute)

0	1	2	3	4	5	6	7	8	9	10

Ikke smerte i det hele tatt — Uutholdelig smerte

APPENDIX D

Table 1 - Per Protocol results

Outcome measures	Baseline Mean (SD)	Changes from baseline					
		3 months Mean (95 % CI)	p-value	6 months Mean (95 % CI)	p-value	12 months Mean (95 % CI)	p-value
30sSTS ↑							
Intervention group	12.75 (3.2)	9.2 (6.1 to 2.2)	*<0.001*	8.9 (5.5 to 12.4)	*<0.001*	**10.6 (7.3 to 14.0)**	<0.001
Control group	13.15 (2.7)	1.1 (-0.5 to 2.7)	0.169	**3.7 (1.2 to 6.2)**	0.006	**3.8 (0.6 to 7.1)**	0.024
Difference between group			*<0.001*		*0.024*	***6.8 (2.3 to 11.3)***	*0.004*
EC17 ↑							
Intervention group	64.5 (19.1)	0.1 (-4.8 to 4.7)	0.981	2.0 (-4.0 to 7.9)	0.494	4.0 (-3.7 to 11.7)	0.291
Control group	64.4 (10.3)	2.2 (-2.1 to 6.5)	0.295	6.8 (1.9 to 11.7)	0.009	4.2 (-1.2 to 9.5)	0.119
Difference between group			0.461		0.192	*-0.2 (-9.1 to 8.7)*	*0.966*
PSFS ↑							
Intervention group	5.0(1.7)	1.1 (0.2 to 2.0)	0.019	0.2 (-0.9 to 1.2)	0.704	0.5 (-0.5 to 1.5)	0.319
Control group	4.38 (2.2)	0.6 (-0.5 to 1.8)	0.279	1.1 (-0.3 to 2.6)	0.121	0.4 (-1.1 to 1.8)	0.598
Difference between group			0.485		0.285	*0.1 (-1.6 to 1.9)*	*0.877*
EQ5D5L index ↑							
Intervention group	0.69 (0.13)	0.02 (-0.05 to 0.10)	0.543	-0.02 (-0.1 to0.06)	0.568	-0.02 (-0.12 to 0.10)	0.752
Control group	0.65 (0.13)	0.04 (-0.02 to 0.09)	0.180	0.07(-0.01to 0.10)	0.070	0.05 (-0.02 to 0.10)	0.132
Difference between group			0.772		0.096	*-0.07 (-0.19 to 0.05)*	*0.255*
EQ5D5L VAS*↑							
Intervention group	67.5 (37)	10 (12)	0.001	5 (14)	0.362	13 (22)	0.078
Control group	70 (25)	5 (16)	0.517	5 (25)	0.175	10 (19.5)	0.200
Difference between group			0.099		0.499		*0.660*
Hannover ↓							
Intervention group	5.3 (3.5)	-1.31 (-2.6 to -0.6)	0.004	0.1 (-1.5 to 1.6)	0.941	0 (-1.9 to 1.9)	1.000
Control group	6.0 (4.4)	0.20 (-2.0 to 2.4)	0.848	-1.0 (-2.0 to -0.1)	0.045	0.1 (-2 to 2.2)	0.907
Difference between group			0.135		0.228	*-0.1 (-2.8 to 2.6)*	*0.930*
Hopkins ↓							
Intervention group	1.1 (0.8)	-0.00 (-0.4 to 0.4)	1.000	0.11 (-0.5 to 0.7)	0.684	0.10 (-0.4 to 0.6)	0.621
Control group	0.9 (0.6)	0.07 (-0.2 to 0.4)	0.619	0.02 (-0.3 to 0.3)	0.890	0.02 (-0.2 to 0.3)	0.851
Difference between group			0.760		0.768	*0.1 (-0.4 to 0.6)*	*0.712*
CW – Physical ↓							

APPENDIX D

Intervention	2.2 (1.0)	-0.5 (-0.9 to -0.1)	0.015	0.1 (-0.4 to 0.5)	0.805	-0.1 (-0.6 to 0.4)	0.580
Control group	2.2 (1.1)	0.1 (-0.5 to 0.7)	0.748	-0.1 (-0.6 to 0.4)	0.650	0.1 (-0.5 to 0.8)	0.726
Difference between group			0.112		0.616	*-0.2 (-1.0 to 0.6)*	*0.542*
CW – Feelings ↓							
Intervention	2.3 (0.9)	-0.05 (-0.6 to 0.5)	0.834	0.1 (-0.5 to 0.7)	0.717	-0.3 (-0.8 to 0.2)	0.173
Control group	2.1 (0.9)	0.05 (-0.3 to 0.4)	0.789	0.1 (-0.4 to 0.6)	0.667	0 (-0.3 to 0.3)	1.000
Difference between group			*0.740*	*0.0 (-0.8 to 0.8)*	*1.000*	*-0.3(-0.8 to 0.2)*	*0.241*
CW – Daily activities ↓							
Intervention	2.3 (0.9)	-0.5 (-0.9 to 0.7)	0.024#	-0.1 (-0.6 to 0.4)	0.608	-0.2 (-0.6 to 0.3)	0.422
Control group	2.1 (1)	0.2 (-0.4 to 0.7)	0.562	-0.1 (-0.5 to 0.3)	0.607	0.2 (-0.4 to 0.7)	0.507
Difference between group			0.056		0.967	*-0.3 (-1.0 to 0.3)*	*0.303*
CW –Social activities ↓							
Intervention	2.1 (1.2)	-0.4 (-0.8 to 0.1)	0.090	-0.1 (-0.6 to 0.4)	0.608	0.1 (-0.4 to 0.6)	0.608
Control group	1.9 (1.1)	-0.1 (-0.6 to 0.4)	0.681	0.0 (-0.5 to 0.5)	1.000	0.1 (-0.4 to 0.5)	0.805
Difference between group			0.380		0.709	*0.1 (-0.6 to 0.7)*	*0.845*
CW- Change in health ↓							
Intervention	2.7 (0.6)	0.0 (-0.6 to 0.6)	1.000	0.4 (-0.1 to 1.0)	0.088	0.1 (-0.5 to 0.8)	0.707
Control group	2.8 (0.8)	0.2(-0.3 to 0.7)	0.385	-0.3 (-0.7 to 0.1)	0.137	0.3 (-0.2 to 0.9)	0.210
Difference between group			0.586		*0.023*	*-0.2 (-1.0 to 0.6)*	*0.594*
CW – Overall health ↓							
Intervention	2.7 (0.9)	-0.2 (-0.7 to 0.4)	0.507	0.0 (-0.5 to 0.5)	0.826	-0.2 (-0.8 to 0.4)	0.529
Control group	2.6 (0.9)	0.1 (-0.3 to 0.5)	0.606	-0.1 (-0.5 to 0.4)	0.790	0.1 (-0.6 to 0.7)	0.859
Difference between group			0.392		0.866	*-0.2 (-1.1 to 0.6)*	*0.577*
VAS fatigue↓							
Intervention	6.25 (2.2)	-1 (-2.6 to 0.5)	0.171	-0.5 (-2.2 to 1.2)	0.522	-0.6 (-2.2 to 0.9)	0.405
Control group	6 (2.6)	-0.5 (-1.7 to 0.8)	0.436	-1 (-2.3 to 0.3)	0.135	-0.6 (-1.8 to 0.7)	0.364
Difference between group			0.541		0.648	*-0.1 (-2 to 1.8)*	*0.941*
VAS pain ↓*							
Intervention	5.0(3.0)	-1(2.8)	0.111	-1.0 (4.0)	0.492	-0.5 (2.5)	0.384
Control	5.5(3.5)	0(3)	0.924	-1.0 (2.0)	0.024	-1.0 (2)	0.177
Difference between groups			*0.418*		*0.374*		*0.574*

↑: Higher score is better ↓:Lower score is better *Analyzed with non-parametric tests. Baseline values are presented with median (IQR) .Change from baseline is shown as median change (IQR). # Significant different results between ITT and PP analysis.

Timeplan Uke 1 – Behandlingsreiser for unge voksne ved Reuma-Sol

Tid	Mandag	Tirsdag	Onsdag	Torsdag	Fredag
07:30			Frokost	Frokost	Frokost
08:00					
08:30			Innskrivningsdag Fysioterapeut 45 min Sykepleier 30 min	Morgentrening	Morgentrening
09:00					Undervisning om treningslære, ved fysioterapeut
09:30					
10:00					Samtale i gruppe om fysisk aktivitet, ved fysioterapeut
10:30					
11:00				Sal-trening Tema: Sirkeltrening (styrke)	Sal-trening Tema: Sirkeltrening basert på dagens undervisning
11:30					
12:00			Lunsj	Lunsj	Lunsj
12:30					
13:00				Individuell behandling - Fysio	Individuell behandling - Fysio
13:30			Lege 30 min		
14:00				Bassengtrening Tema: Kondisjon, styrke, bevegelse	Bassengtrening Tema: Kondisjon, styrke, bevegelse
14:30					
15:30		Ankomst	Frukt	Frukt	Frukt
18:00		Middag	Middag	Middag	Middag
19:30		Informasjonsmøte			

Alle treningssesjoner ble ledet av fysioterapeut.

Timeplan Uke 2

Tid	Mandag	Tirsdag	Onsdag	Torsdag	Fredag
07:30	Frokost	Frokost	Frokost	Frokost	Frokost
08:00					
08:30	Morgentrening	Morgentrening	Morgentrening	Morgentrening	
09:00			Undervisning om mestring, ved fysioterapeut		Stranddag med trening og aktiviteter
09:30					
10:00			Undervisning om søvn og stress, ved sykepleier		
10:30					
11:00	Sal-trening Tema: Freeletics (styrke+kondisjon)	Sal-trening Tema: Balanse	Sal-trening Tema: Bodypump	Sal-trening Tema: Zumba	
11:30					
12:00	Lunsj	Lunsj	Lunsj	Lunsj	
12:30					
13:00	Individuell behandling - Fysio	Individuell behandling - Fysio	Individuell behandling - Fysio	Individuell behandling - Fysio	
13:30					
14:00	Bassengtrening Tema: Sirkeltrening i vann	Bassengtrening Tema: Kondisjon, styrke, bevegelse	Bassengtrening Tema: Kondisjon, styrke, bevegelse	Bassengtrening Tema: Kondisjon, styrke, bevegelse	
14:30					
15:30	Frukt	Frukt	Frukt	Frukt	Frukt
18:00	Middag	Middag	Middag	Middag	Middag

Alle treningssesjoner ble ledet av fysioterapeut.

Timeplan Uke 3

Tid	Mandag	Tirsdag	Onsdag	Torsdag	Fredag
07:30	Frokost	Frokost	Frokost	Frokost	Frokost
08:00					
08:30	Morgentrening	Utflukt: Military Camp	Morgentrening	Utskrivning Fysioterapeut 45min Sykepleier 30	Morgentrening
09:00			Undervisning om kosthold, ved fysioterapeut		
09:30					
10:00			Undervisning om mestring, ved sykepleier		
10:30					
11:00	Sal-trening Tema: Sirkeltrening (styrke)		Sal-trening Tema: Stafetter		Sal-trening
11:30					
12:00	Lunsj	Lunsj	Lunsj	Lunsj	Lunsj
12:30					
13:00	Individuell behandling - Fysio	Individuell behandling - Fysio	Individuell behandling - Fysio	Utskrivning fortsetter	
13:30					
14:00	Bassengtrening Tema: Kondisjon, styrke, bevegelse	Bassengtrening Tema: Sirkeltrening	Bassengtrening Tema: Kondisjon		Bassengtrening
14:30					
15:30	Frukt	Frukt	Frukt	Frukt	Frukt
18:00	Middag	Middag	Middag	Middag	Avslutningsmiddag

Alle treningssesjoner ble ledet av fysioterapeut.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.