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# The effect of a supervised exercise intervention on physical activity level in patients with Spondyloarthritis (SpA )

12-months follow-up of a multicenter randomized controlled trial

**Master thesis in**

**Department of**

**Norwegian School of Sport Sciences, 2018**

## ACKNOWLEDGEMENT

This thesis was made possible thanks to the support from the Norwegian School of Sport Science and Norwegian Rheumatism association. The Norwegian Rheumatism Association contributed with many work hours within office hours. I would also like to thank all the help I got from NKRR and Hanne Dagfinrud, her knowledge and facilitating all my questions, access to all the data and needs. I have greatly benefited from Diakonhjemmet Hospital, and the expertise within this place. NKRR close connection to the patient group and studies conducted at the hospital, and the academic environment for my thesis.

First of all, a warm and huge thank to my main supervisor, Silje Sveaas, for introducing me to this exciting research field of rheumatic diseases, physical activity and axial Spondyloarthritis. I feel privileged to have you as my supervisor. You have put in a lot of work and not at least patience. Thank you for your involvement and time. I would also like to thank my co-supervisor Yngvar Ommundsen. Thank you for your positivity and guidance for this thesis during the whole period and for your understanding of my life situation. I am also grateful to my boss, Anna Fryxelius. Thank you for giving me the chance to write this master thesis at work and for always giving me your smart input and alterations. I really appreciate your guidance throughout my tough time discovering my own chronic disease. I would like to thank Kaya S. Kristiansen, my girlfriend and cohabitant, who was in charge of the work and planning at home with our foster daughter and dog. I really admire your effort at home, patience with me, encouragement, your passion and willingness to give me extra time to write. You have given me tremendously support throughout these past years. I also need to thank my near family and friends for their support and kindness, a little talk always seems to help.

Oslo, October 2018

Ole-Martin Wold

# ABSTRACT

**Background:** Exercise is an important part of the treatment for patients with axial spondyloarthritis (axSpA), both to limit the consequences of the disease and the risk of morbidities. Without proper treatment, the disease may have a great reduction on spinal stiffness together with physical function. Most studies investigating the physical activity level on patients with axSpA implies that they are less active compared to healthy controls.

**Purpose:** To investigate if there is a long-term effect of a twelve-week supervised exercise program with regard to physical activity level in patients with axSpA. Further, to examine which factors that may influence the level of physical activity.

**Method:** Patients diagnosed with axSpA was included in a randomized controlled trial. The exercise group participated in a 40-60 minutes exercise program three times a week for 12 weeks. Two of the sessions were supervised by a physiotherapist and one was home based. 12 months after the baseline assessment, physical activity level was assessed by using the self-administered International Physical Activity Questionnaire-Short form (IPAQ-short). Differences between the groups at 12-months follow-up were analyzed with Mann Whitney U-test (non-parametric) for continuous variables, and chi-square for categorical variables. A logistic regression analysis was used to analyze factors associated with regular participation in cardiorespiratory and strength exercises at 12-months follow-up.

**Results:** The results showed there were no statistical differences in the total amount of physical activity (METs) between the two groups at 12-months follow-up ($p=0.81$). The exercise group reported significantly more physical activity (METs) on a vigorous intensity level compared to the control group ($p<0.03$) while the control group reported significantly more MET minutes per week spent on walking than the exercise group ($p<0.02$). Significantly more patients in the exercise group compared to the control group reported they performed cardiorespiratory exercises ($<0.001$) and muscular strength exercises ($p<0.001$) at 12-months follow-up. Univariate analyses showed that participation in regular cardiorespiratory and strength exercises at 12-months follow-up were significantly associated with younger age, having received the intervention ($p=0.01$) and experience with cardiorespiratory and strength exercises before the baseline assessment ($p<0.001$). The logistic regression analysis showed that exercise experience before the baseline assessment was the strongest predictor of exercise participation at 12-months follow-up.

**Conclusion:** The results from this study suggest that a 12-week supervised exercise program may have a long-term effect on exercise habits in patients with axSpA. A beneficial effect on participation in regular cardiorespiratory- and strength exercises and physical activity at a vigorous intensity level at 12-months follow-up were seen. Hence, more patients may take advantages of the health benefits associated with regular cardiorespiratory and strength exercises at a high intensity if they attend a 12-week supervised exercise program. However, there was no effect of the exercise intervention on total amount of physical activity and exercise experience before the baseline assessment was the strongest predictor of regular participation in cardiorespiratory and strength exercises at 12-months follow-up.

# ABBRIVATIONS

| | | |
|---|---|---|
| SpA | - | Spondyloarthritis |
| axSpA | - | Axial Spondyloarthritis |
| AS | - | Ankylosing Spondylitis |
| ACSM | - | American College of Sports Medicine |
| ASAS | - | Assessment of Spondyloarthritis International Society |
| ASDAS | - | Ankylosing Spondylitis Disease Activity Score |
| BASFI | - | Bath Ankylosing Spondylitis Functional Index |
| BASDAI | - | Bath Ankylosing Spondylitis Disease Activity Index |
| BASMI | - | Bath Ankylosing Spondylitis Metrology Index |
| BMI | - | Body Mass Index |
| CVD | - | Cardiovascular Diseases |
| EULAR | - | European League Against Rheumatism |
| NSAIDs | - | Non-Steroidal Anti-Inflammatory Drugs |
| RA | - | Rheumatoid Arthritis |
| RCT | - | Randomized Controlled Trial |
| SD | - | Standard Deviation |
| TNF-R | - | Tumor Necrosis factor receptor |
| TNF | - | Tumor necrosis factor |
| VO2max | - | Maximal oxygen uptake |

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## 1.0 INTRODUCTION

Spondyloarthritis (SpA) is an inflammatory rheumatic disease which mainly attacks the spinal column and may lead to reduced physical function and in worst-case lead to total stiffening of the spine (Dougados & Baeten, 2011). SpA is divided into two main categories based on the two main clinical features: axial symptoms (axSpA) and peripheral involvement (Dougados & Baeten, 2011). Ankylosing Spondylitis (AS) is a subtype of SpA and the prototype (Dougados & Baeten, 2011). Together with reduction of physical function and spinal stiffness (Dougados & Baeten, 2011), the patients often report fatigue (Sveaas, 2017), and SpA may lead structural impairment, loss of dynamic function, resulting in problems with daily activities (Fongen, Halvorsen & Dagfinrud, 2013). Furthermore, patients with axSpA have a higher risk of developing cardiovascular disease compared with the general population (Mathieu & Soubrier, 2018).

Besides pharmacological treatment, non-pharmacological treatment is recommended as a very important part of the management of axSpA, including the elements of patient education and supervised physical therapy exercise (Braun et al., 2011). Patients with axSpA are recommended to engage in physical activity and exercise (van der Heijde et al., 2017), and inflammatory back pain can decrease with physical activity (Dougados & Baeten, 2011). A recent meta-analysis concluded that high intensity cardio- and strength exercise may have beneficial effects on disease activity in terms of stiffness, pain, flexibility, fatigue and inflammation in patients with inflammatory rheumatic diseases including axSpA (Sveaas, Smedslund, Hagen & Dagfinrud, 2017). High-intensity interval exercise is a typical exercise type to increase $VO_{2max}$, and $VO_{2max}$ is one of the best indicators of cardiorespiratory fitness (Serna et al., 2016). $VO_{2max}$ is considered one of the most important predictors or the cardiovascular disease (CVD) mortality, and $VO2_{max}$ is directly related to cardiovascular health. An improvement in $VO2_{max}$ has been linked to decrease the risk of death from cardiovascular disease (Serna et al., 2016).

Most studies investigating the physical activity level on patients with axSpA implies that they are less active compared to healthy controls (Swinnen et al., 2014; O`Dwyer et al., 2015b; Jacquemin et al., 2018; Haglund et al, 2012; Jacquemin et al., 2018). Exercise as medicine is a well-documented treatment alternative for most chronic diseases, however it is reported that 50-80 % of patients are discharged exercise programs within a year after rehabilitation (Brubaker et al., 1996; Moore, Charvat, Gordon, Pashkow, Ribisl, Roberts & Rocco, 2006; Moore, Dolansky, Ruland, Pashkow & Blackburn 2003). To the best of our knowledge, an intervention study with the purpose to change or/and increase the physical activity level in patients with axSpA has not been performed.

There is a combination of barriers and facilitators that influences the patient's adherence to participate in physical activity and exercise over time. Hence, these factors are important to map, it is also important to identify why this patient group exercise or not. What can we do to get the axSpA patients to be more physical active, and may a 12-week supervised exercise intervention enhance physical activity level after 12 months? Therefore, the aim of this thesis is to investigate the level of physical activity after a 12-week intervention and what factors that may influence the level of physical activity.

## 2.0 PURPOSE OG RESEARCH QUESTION

### 2.1 Purpose

The main aim was to investigate if there is a long-term effect of a twelve-week supervised exercise program with regard to physical activity level. Further, the aim was to examine which factors that may influence the level of physical activity. The findings will hopefully give us an answer on whether practical training in an exercise program may increase the physical activity level in the long-term.

### 2.2 Main Thesis

In people with axial Spondyloarthritis (axSpA); is there a long-term effect of a twelve-week supervised exercise program with regard to physical activity level? Comparison with a control group and identification of factors of importance for sustained physical activity.

### 2.3 Explorations of terms

*Physical Activity:* includes all types of muscle activity that significantly increase energy consumption (Caspersen, Powell, & Christenson, 1985).

*Physical Fitness:* is a set of attributes that you have or acquire, and which are related to the ability to perform physical activity (Nerhus, Anderssen, Lerkelund & Kolle, 2011).

*Axial Spondyloarthritis (axSpA):* An inflammatory rheumatic disease. Is a subgroup of Spondyloarhritis (SpA) (Dougados & Baeten, 2011).

# 3.0 THEORY

## 3.1 Inflammatory Rheumatic Disease

Rheumatic disease is a collective term and there are over 200 different diseases. A third of people of all ages are affected at some point during a lifetime, and untreated rheumatic disease may reduce life expectancy. Inflammatory rheumatic disease refers to various painful medical conditions that affects bones, cartilage, tendons, joints, ligaments and muscles (European League against Rheumatism (EULAR), 2018). Globally, inflammatory rheumatic disease is an enormously economic burden, and in Europe, the cost is estimated to be over 200 billion euros per year. Rheumatic disease has a significant impact on people's everyday life and is a huge contributor to cause of sick leave and even premature retirement (EULAR, 2018). People today live longer because of the development of new medicine; however, many people are living with reduced function, especially people with rheumatic disease. Therefore, it is important to have a focus to increase the level of physical function within this patient group (Lim et al., 2012).

## 3.2 Spondyloarthritis

Spondyloarthritis (SpA) is a collective name for several chronic inflammatory rheumatic diseases, and Ankylosing Spondylitis (AS) is the most studied form of Spondyloarthritis (Dougados & Baeten, 2011). In addition, SpA consists of psoriatic arthritis, reactive arthritis, arthritis related to inflammatory bowel disease, a subgroup of juvenile idiopathic arthritis. The prevalence of SpA is reported to be between 0.3– 0.45% in the adult population (Haglund, Bergman, Petersson, Jacobsson, Strombeck & Bremander, 2012). There are several clinical forms of SpA and they include peripheral arthritis, spinal (axial) features, enthesopathy and additional article features such as uveitis, psoriasis and bowel disease (Assessment of SpondyloArthritis International Society (ASAS), 2003; Dougados & Baeten, 2011) (Figure

1). Axial SpA (axSpA; symptoms in the spine) can be divided into two main categories, radiographic axSpA and non-radiographic axSpA (Dougados & Baeten, 2011).

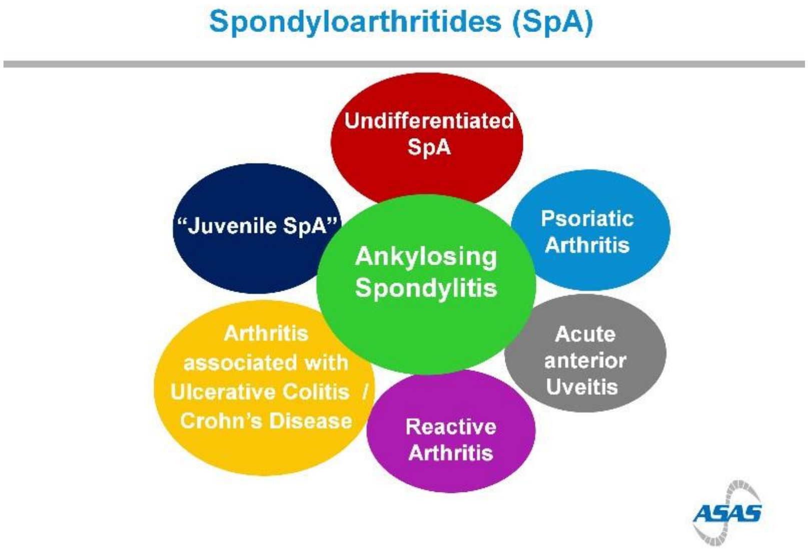


***Figure 1*** *Subgroup of SpA (reprinted with permission of the ASAS-group) (Assessment of SpondyloArthritis International Society (ASAS), 2003).*

Normally axSpA occurs before the age of thirty, and less often after the age of 45, and affects the patient's social and professional life (Dougados & Baeten, 2011. AxSpA is often initiated by inflammatory back pain (Dougados & Baeten, 2011; Rudwaleit et al., 2009). By radiographic examination, disease changes in axSpA can be seen, affecting primarily the spinal column and iliosacral joints (Braun & Sieper, 2007). The inflammation of the sacroiliac joint, spine and entheses is the main characteristics of axSpA, and may eventually lead to abnormal stiffening and immobility of joint due to fusion of the bones (Lee et al., 2015).

### *3.2.1 Classification criteria*

The terminology of axSpA was introduced in 2009 and includes both radiographic and non-radiographic axSpA (Rudwaleit et al., 2009). The term radiographic refers to radiological changes in the sacroiliac joints. Hence, as shown in Figure 2, if a patient changes in the sacroiliac joints that are show on imaging (MRI or radiograph) and at least one SpA features the patient will receive a radiographic axSpA diagnosis (Rudwaleit et al., 2009) (Figure 3). In addition, a patient with inflammatory pain for more than 3 months and a positive Human leukocyte antigen (HLA)-B27 test (genotype), in addition to two or more associated features can also fulfill criteria for axSpA (non-radiographic) (Figure 2).

A meta-analysis by Mathieu et al (2011) of eight studies concluded that patients with AS appear to have a higher risk of cardiovascular disease (CVD) (Mathieu, Gossec, Dougados & Soubrier, 2011). The risk of CVD appears to be increased by the prevalence of traditional CV risk factors (dyslipidemia, hypertension and smoking) and systemic inflammation (Peters et al., 2010).

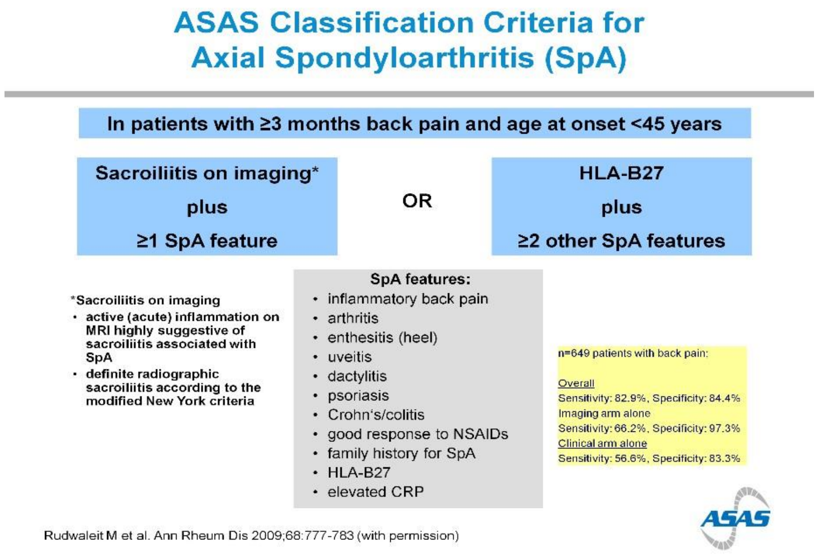


***Figure 2*** *Classification criteria for axial SpA (reprinted with permission from ASAS-group) (Assessment of SpondyloArthritis International Society (ASAS), 2003).*

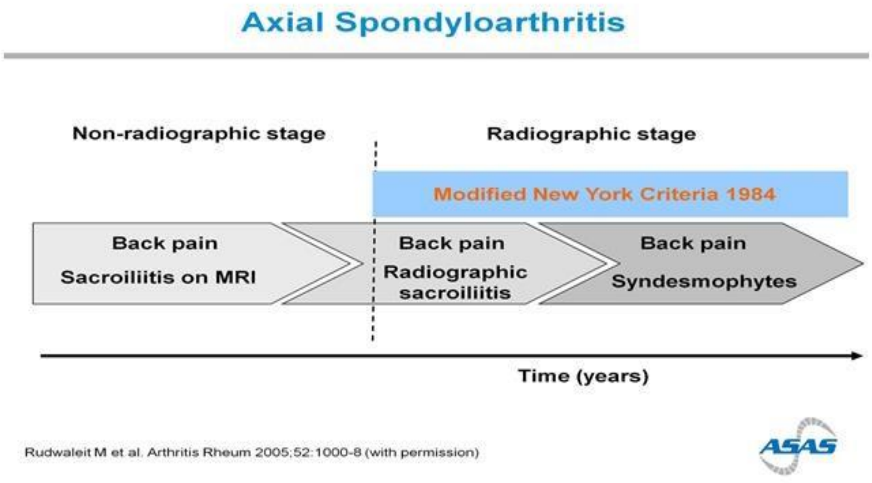


***Figure 3*** *Development of axial SpA from a non-radiographic stage to a radiographic stage (reprinted with permission from ASAS-group) (Assessment of SpondyloArthritis International Society (ASAS), 2003).*

### *3.2.2 Consequences of axSpA*

In a cross-sectional study of 152 patients with AS, the results showed that everyday activities as for example driving a car, energy to social activities, sleep or go grocery shopping were problematic because it affected them in a serious degree of some kind (Dagfinrud, Kjeken, Mowinckel, Hagen & Kvien, 2005). The problems of the daily activities were partly associated with reduced mobility, pain, fatigue and deformities (Dagfinrud et al., 2005). In addition to the negative impact on physical health, patients with axSpA also have a higher prevalence of depression mental health are in patients with axSpA (Zhao et al. 2018).

### *3.2.2 Management of axial Spondyloarthritis*

International recommendations indicate that the optimal management of axSpA consists of both pharmacological and non-pharmacological treatment throughout the course of the disease (Braun et al., 2011).

#### *3.2.2.1 Pharmacological treatment*

Of pharmacological treatment of AS, non-steroidal anti-inflammatory drugs (NSAIDs) are the most used intervention and has shown a significant beneficial effect on symptoms of the disease (Dougados & Baeten, 2011). In addition, observational studies have shown that a high use of NSAIDs are associated with lower rate of radiographic spinal progression, and NSAIDs are recommended as the first-line pharmacological therapy for AS (Poddubnyy, 2013). As a second line therapy, TNF-inhibitors (immunosuppressive drugs) are recommended for patients with a persistently high disease activity (Poddubnyy, 2013).

#### *3.2.2.2 Non-pharmacological treatment*

Non-pharmacological treatment is highly recommended in the management of axSpA and includes patient education and supervised exercise (Braun et al., 2011). Regular exercise is therefore recommended as a first-line therapy for the treatment of axSpA (Poddubnyy, 2013), and supervised exercise is reported to be more effective than home exercises (Dagfinrud et al., 2008).

#### *3.2.2.3 Physiotherapy treatment of axSpA*

According to international recommendations, physiotherapy with exercises is regarded as a part of the overall treatment program for this patient group (van der Heijde et al., 2017). Physiotherapy includes several modalities, in which exercise is one of the main approaches.

The role of the physiotherapist is to ensure safety, optimal benefit and individual adjustments to an exercise program (Dagfinrud et al., 2008). For this patient group, low intensity exercises, flexibility exercises and pool exercises have been mostly used. This is emphasized by research in the field that shows that most of the exercise studies have investigated the effect of flexibility exercises (Dagfinrud, Halvorsen, Vollestad, Niedermann, Kvien, Hagen, 2011; Regel et al., 2017).

## 3.3 Physical activity and physical function

### *3.3.1 Definition of physical activity*

Physical activity, exercise, physical function and physical fitness are all close related terms that can relate to another. Physical activity is defined as “any bodily movement produced by skeletal muscles that result in energy expenditure” (Caspersen et al., 1985). The term physical activity embraces many types of activities and include sports, household tasks (yardwork, cleaning and home repair as example), cardiorespiratory exercises and other activities. The term exercise is a subgroup of physical activity and is defines as planned, structured and repetitive with a purpose to improve or maintain one or more components of physical fitness (Caspersen et al., 1985).

«Physical fitness is defined as a set of characteristics that you have or acquire, and which are related to the ability to perform physical activity» (Caspersen et al., 1985; Nerhus et al., 2011). The components that constitutes the physical fitness is divided into two subgroups; skill-related fitness that have a more focus on performance (agility, balance, coordination, speed, power, reaction time) and health-related fitness that is “the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies"(Caspersen et al., 1985), and includes cardiorespiratory fitness, muscular endurance, muscular strength, body composition and flexibility.

The total energy expenditure of physical activity is determined by the result of intensity, duration (time) and frequency (how often) (Caspersen et al., 1985). The intensity of the physical activity is especially important because physical activity with high intensity can enhance the effects on the physical fitness (and $VO_{2max}$) rather than activities with low intensity (Caspersen et al., 1985; Garber, Blissmer, Deschenes, Franklin, Lamonte, Lee & Swain, 2011; Kurtze, Rangul, Hustvedt & Flanders, 2008).

The best indicator for cardiorespiratory fitness is the $VO_{2max}$ level and this is also an important predictor of CVD in men and woman (Serna, Velez, Arias & Feito, 2016). Cardiorespiratory exercises at moderate intensity over a prolonged time as well as high-intensity interval training are exercise types reported to increase $VO_{2max}$ (Serna et al., 2016). High intensity are typically short intervals with intensities near maximum (80-100% peak heart rate, whereas moderate- continuous training programs typically have a peak heart rate between 60-75%. A meta-analysis have shown a slightly higher improvement in $VO_{2max}$ with high intensity interval training compared to moderate- continuous intensity training (Serna et al., 2016). $VO_{2max}$ is directly related to cardiovascular health, and an improvement in $VO2_{max}$ has been linked to decrease the risk of death from cardiovascular disease (Serna et al., 2016). For every metabolic equivalent gained in $VO_{2max}$, mortality rates have been shown to decrease about 8-17% (Serna et al., 2016).

### *3.3.2 General recommendations of physical activity*

To promote and maintain health in adults, the American College of Sports Medicine (ACSM) recommend all healthy adults to be physically active (aerobic activities) on a moderate intensity level for a minimum of 30 minutes on five days per week (Haskell et al., 2007). The alternative is to be physical active in a minimum of 20 minutes on a vigorous intensity level for 3 days each week. There can also be a combination of moderate- and vigorous intensity activity to meet the recommendations. This can for example be a briskly walk for 30 minutes twice a week followed by 20 minutes of jogging two other days. Brisk walking, which is a form of moderate-intensity activity, increase the pulse enough to perform continuously for a minimum of 10 minutes corresponding to the 30 recommended minutes. Vigorous intensity can be jogging that leads to a significant pulse increase (Haskell et al., 2007).

It is important to specify that the recommended 30 minutes of physical activity comes as an addition to the routines and daily activities (Journal of the American heart association. P 1083-1084; Haskell et al., 2007). The ACSM recommends muscle strength activities to maintain or promote good health and physical independence. Adults will benefit from performing activities that maintain or increase muscle strength and endurance for minimum of two days each week (Journal of the American heart association. p. 1084; Haskell et al., 2007). There is a dose-response relationship between amount of physical activity and health benefits.

#### *3.3.2.1 Metabolic Equivalent of Task*

An effective and much used way to measure physical activity is the metabolic equivalent of task (MET). This is a shorthand way to measure energy expenditure of the moderate- and vigorous-intensity activities combined. One MET represents an individual`s energy expenditure while sitting quietly. If an adult walk on a flat and hard surface in 3 mph (approximately 4.8 km/h), their energy expenditure is about 3.3 MET`s, and whilst jogging/running on a similar surface at 5 mph (approximately 8 km/h), will use approximately 8 MET`s (Journal of the American heart association. p. 1086; Haskell et al., 2007).

Potentially, this means that activities on a vigorous-intensity level will generate greater energy expenditure than moderate-intensity activities. For example, activities like walking around at home or work equals <3 MET`s, 3-6 MET equals physical activity at moderate intensity (brisk walking) and ≥ 6 MET equals high-intensity physical activity (running or bicycling) (Journal of the American heart association. p. 1086; Haskell et al., 2007).

## 3.4 Physical function, physical activity and physical fitness in patients with axial Spondyloarthritis

### *3.4.1 New recommendations for Physical Activity in patients with rheumatic diseases*

Physical activity is promoted for people with rheumatic disease as well as the general population (Rausch Osthoff et al., 2018). European League against Rheumatism (EULAR) gathered a panel of experts to promote health benefits of physical activity and develop guidelines for physical activity in patients with SpA. The panel consisted of 22 European physical activity experts and four overarching principles and ten recommendations for physical activity were developed.

The overarching principles were that cardiorespiratory fitness, muscle strength, flexibility and neuromotor performance are applicable (feasible and safe) for people with SpA, and planning of physical activity requires a shared decision between healthcare providers and patients with SpA (Rausch Osthoff et al., 2018). The ten recommendations for physical activity contains cardiorespiratory fitness-, muscular strength-, flexibility- and neuromotor muscular exercise. As in the recommendations for the general population, a combination of moderate and vigorous intensity exercise is suggested to meet the recommendations. Because of the dose-response relationship between physical activity and health, adults who wants to improve further fitness, reduce risk of chronic disease and disabilities and prevent unhealthy weight gain, may benefit by exceeding the minimum recommended amount of physical activity (Rausch Osthoff et al., 2018).

*3.4.2 Physical function in patients with SpA*

Physical function can reflect the challenges or difficulties in executing both daily- and physical activities, and self-reported Bath Ankylosing Spondylitis Functional Index (BASFI) is one of the recommended ways to measure physical function in patients with axSpA. For patients with axSpA it has been reported that impairments in cervical rotation, lateral thoracolumbar flexion, chest expansion, hip-range of motion, along with more tender entheses, swollen joints and tender joints are associated with a higher score on BASFI, indicating a lower physical function (Bethi et al., 2014). Similarly, limitation of spinal movement is negatively related to physical function and health-related quality of life (Stolwijk, Ramiro, Vosse, Landewè, van der Heijde & Tubergen, 2014).

The reduced function of the patients with axSpA consists of non-reversible and reversible components (Landewe, Dougados, Mielants, van der Tempel & van der Heijde., 2008). The non-reversible consequences cannot be treated compared with the reversible (Landewe et al., 2008).

*3.4.3 Physical activity in patients with axSpA*

***Table 1*** *Shows an overview of studies that have investigated the physical activity level in patients with axSpA*

| Author | N | Sample / Participants | Method | Results |
|---|---|---|---|---|
| Plasqui, Boonen, Geusens, Kroot, Starmans & van der Linden, 2011 | 50 | 25 patients with AS and 25 healthy controls (adults matched for age, sex, and body mass index) | The aim of the study was to investigate body composition and objectively assessed physical activity in patients with AS. The physical activity was assessed using a triaxial accelerometer and physical fitness was tested with a maximal workload test. | The results showed that there was no difference in physical activity level comparing the two groups. |
| Haglund et al, 2012 | 2167 | Patients with SpA. | A cross-sectional study of patients with SpA. Questionnaire about physical activity habits. | The results showed that 68% met the WHO recommendations for physical activity. When they divided the physical activity into moderate and vigorous intensity, only 57% were exercising in a moderate intensity (≥30 minutes ≥5 days per week). Furthermore, even fewer were physically active at vigorous intensity, were only 32% meet the recommended amount (exercising at a more vigorous intensity for ≥30 minutes 2-3 times per week) |
| Swinnen, Scheers, Lefevre, Dankaerts, Westhovens & de Vlam, 2014 | 80 | 40 patients with axSpA and 40 healthy controls | A cross-sectional study that compared physical activity level in 40 patients with axSpA with 40 controls.<br>Physical activity was measured during five consecutive days using ambulatory monitoring (SenseWear Armband). | The results showed that the physical activity level and energy expenditure were significantly lower in patients with axSpA. |

| | | | | |
|---|---|---|---|---|
| van Gendersen, S., van den Borne, C., Geusens, P., van der Linden, S., Boonen, A & Plasqui, G, 2014 | 48 | 24 patients with AS and 24 healthy controls. | A case-control study of 48 participants (matched for age, gender, and body mass index), completed the BASFI and Baecke questionnaire and wore a triaxial accelerometer. | The results showed that there was no difference in physical activity level comparing the patient group and healthy controls. The physical activity assessed by Baecke and the accelerometer did not differ between groups |
| O`Dwyer, O'Shea & Wilson, 2015b | 2972 | Nine studies with axSpA patients. | A systematic review of nine studies (RCT`s and observational studies was included) | The results were that patients with axSpA have a lower physical activity level than the general population. Higher disease activity was associated with lower self-reported physical activity levels. |
| van Genderen, Boonen, van der Heijde, Heuft, Luime, Spoorenberg & Plasqui, 2015 | 234 | Patients with ankylosing spondylitis (n= 135) and healthy controls (n= 99). | Cross sectional study. The participants were asked to wear a triaxial accelerometer for 7 days and to complete a series of questionnaires. | There were no differences in the total amount of physical activity comparing the patients with the control group. However, the patient group avoided engagement in higher intensities of physical activity. |
| Jacquemin et al., 2018 | 157 | Patients with RA or axSpA | A multicentric prospective observational study. Physical activity was assessed over three months using a mobile activity tracker (smartphone), recording the number of steps per minute. | Only 27.4 % of the patients reached the recommended amount of physical activity per week. |

To summarize, a minority of the studies shows that patients are equally active, however, most of the studies showing that patients with axSpA are less physically active than healthy controls.

*3.5 High Intensity exercise in patients with axial Spondyloarthritis*

A study by Swinnen et al (2014) showed that patients with axSpA were significantly less physically active on a vigorous, very vigorous and moderate/very vigorous intensity level compared to healthy controls (Swinnen et al., 2014)

*3.5.1 Overview of studies conducted on high intensity exercise in patients with rheumatic disease*

***Table 2*** *Studies conducted on cardiorespiratory and muscular strength exercise in patients with rheumatic disease*

| Author | N | Sample / Participants | Method | Results |
|---|---|---|---|---|
| Sveaas, Berg, Provan, Semb, Hagen, Vøllestad… Dagfinrud, 2014 & Sveaas, Berg, Fongen, Provan, Dagfinrud, 2018 | 28 | 28 axSpA patients | A single blinded randomized controlled pilot study. The exercise group performed 12 weeks of endurance and strength exercise while the control group received treatment as usual. | Treatment effect was seen in disease activity score. There were also observed treatment effects in secondary outcomes of fatigue, physical function, arterial stiffness and VO2max. The exercise group had a statistically significant beneficial effect on emotional distress (p=0.01), fatigue (p= 0.02], and ability to do a full day's work (p= 0.02] compared to the control group. |
| Sandstad, Stensvold, Hoff, Nes, Arbo & Bye, 2015. | 18 | 7 women with RA and 11 with adult-JIA, 20-50 years | Cross-over study.<br>A high intensity interval training study conducted on patients with Rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA). The patients exercised twice a week for 10 weeks with an intensity of 85-98% of maximum heart rate on spinning bikes. | The patients increased their VO2 max, 2.9 % improvement in heart rate recovery (p= 0,05). Positive effects on BMI, body fat, and waist circumference muscle mass and CRP. |
| Sveaas, Smedslund, Hagen & Dagfinrud, 2017 | 1286 | Patients with inflammatory rheumatic disease | A systematic review with a meta-analysis. | The authors concluded that the cardiorespiratory and strength exercises had a beneficial effect on disease activity in terms of flexibility, pain, stiffness, inflammation and fatigue. |

## 3.6 Factors associated with participation in physical activity

Despite the evidence for the benefits of physical activity on disease activity (Sveaas, 2017), activities and participation, people with rheumatic disease are in general less active compared to healthy controls (Garber et al., 2011; Walsh et al., 2011; Fedewa, Hathaway, Ward-Ritacco, 2016). The possible underlying reasons could be that healthcare providers and patients may be reluctant towards participating in physical activity, fearing the flare-up or joint damage caused by exercising (Metsios, Stavropoulos-Kalinoglou, Panoulas, Wilson, Nevill, Koutedakis & Kitas, 2009). Brophy et al (2013) reported that AS patients with a high disease activity had a lower physical activity level compared to those with moderate and mild disease activity (Brophy, Cooksey, Davies, Dennis, Zhou & Siebert, 2013). In line of these founding's, Fongen et al (2013) reported that patients with high disease activity reported less physical activity compared to patients with low disease activity and population controls (Fongen, Halvorsen & Dagfinrud, 2013).

On the other hand, Falkenbach (2003) evaluated patients with AS, where the aim was to investigate if patients who performed disease specific exercise had fewer functional limitations and disability compared to those who exercise more often (Falkenbach, 2003). A large sample of 1500 patient with AS were grouped by how many times per week they performed disease-specific exercises for at least five minutes. The conclusion was that the patients with less disability exercised less than their more disabled counterparts (Falkenbach, 2003). The authors suggested that the reason for this was that patients that were most disabled was most motivated to perform exercises (Falkenbach, 2003).

### *3.6.1 Factors related to physical activity level in patients with axSpA*

Passalent et al (2010) used an exercise questionnaire to identify perceived benefits and barriers to exercise in patients with AS (Passalent, Soever, O'Shea & Inman, 2010). The study reported that the most frequently barrier to exercise were “exercise tires me” (71.4%), “exercise is hard work” (60.7%), and “I am fatigued by exercise” (57.1%) (Passalent et al., 2010). A study by Sundström et al (2002) evaluated exercise habits among patients with ankylosing spondylitis. The main obstacle for these 189 patients in the study was “lack of time” and “fatigue” (Sundström, Ekergård & Sundelin, 2002). Fongen et al (2014) conducted a study on a group of patients with AS, where the aim was to explore their barriers and facilitators for being physical active (Fongen, Sveaas & Dagfinrud, 2014). A total of 281 patients and controls were included and underwent structured interviews regrading barriers, facilitators and perceived health benefits. The patients were significantly more likely to report barriers for being physical active compared to the control group ($p \leq 0.001$) (Fongen et al., 2014). The most common reported barriers to physical activity was pain, stiffness, fatigue, disability, time, quality of sleep and motivation. The disease related barriers were more frequently reported than regular barriers (Fongen et al., 2014). Lack of time and motivation were reported equally among the patients and controls (Fongen et al., 2014). Fongen et al (2014) reported that about 60% of both patients and controls had the potential to increase their physical activity level, and having more time was the most frequently reported facilitator for both patients and controls (28 % versus 29%) (Fongen et al., 2014).

Haglund et al (2012) found in a cross-sectional study (2167 patients with SpA) that it was less likely that patients with reduced physical function achieved the recommendations for physical activity (Haglund et al., 2012). Madsen et al (2015) also reported in a study based on interviews with 12 men that sport activities were one of several activities that was limited due to reduced physical function in AS (Madsen, Jensen & Esbensen, 2015).

To summarize these studies shows that disease related barriers are the main factors for physical activity level in patients with axSpA. High disease activity and fatigue are two of the most reported barriers to physical activity among patients with axSpA. Furthermore, patients are also reporting more barriers to physical activity than healthy controls. The most reported facilitators to participate in physical activity were having more time.

*3.6.2 Interventions aiming to enhance physical activity level*

In 2003 the Center of Medical Method-assessment conducted a review of literature of articles which among other things assessed the effect of facilitators to influence the patients living habits (Bahr, 2008). Some of their conclusion was that it was possible to change the patient's behavior if they got advice from their doctor, and the effect was stronger if the information was given oral and written. Furthermore, the authors stated that a change in habits trough physical activity and nutrition could be cost-effective (Bahr, 2008).

Furthermore, a systematic review with the aim to investigate effects of different methods to enhance physical activity has been published (Bahr, 2008). All the included studies had a follow-up period of six months, a control group and enhanced physical activity levels as an ending point. The results showed that consultation counseling, supervised training in a group, theory-based behavior intervention and individually adapted training programs was effective methods to enhance physical activity (Bahr, 2008). The authors concluded that a consultation with patients at the doctor leaded to 12-50% increased activity level six months after consultation, enhanced intensity and frequency with more contacts, if the consultation included physical activity on prescription, activity diary, pedometer or information material enhanced physical activity (Bahr, 2008). The patients with cardiovascular disease who got supervised in a training group enhanced their activity level, and the patients with peripheral vascular disease also enhanced their physical fitness with supervised group-based training (Bahr, 2008). The theory based behavioral intervention enhanced physical activity 10-15 % more than regular consultation (Bahr, 2008).

Several theoretical models to understand, explain and change behavior on health-related areas have been used. Theories and models have been used to conduct research on physical activity within due to behavior change; the model of behavior change, social cognitive theory, theory of planned behavior, classic learning theory, self-determination theory and the social-ecological perspective of physical activity are all examples (Bahr, 2008). The theories seem to affect behavior change in the direction to increase the level of physical activity. It has been observed improvement in physical activity level in patients with diseases (cardiovascular) when a program for behavioral change is used in the treatment (Bahr, 2008). An important part of the message presented in the association with regular physical activity, is the assumptions that physical activity is not the same for people with diseases. There are many reasons and preconditions to base everything on. Some of these assumptions cannot be changed if there is a disease (chronic disease) and will affect the prerequisites for participation in regular physical activity (Bahr, 2008). Hence, physical activity must be adapted if a person has a chronic condition, and there will always be a person who will experience participation in physical activity in another way. Behavior change can be a common goal, however, the way towards this goal are not identical for all, and it requires time (Bahr, 2008).

#### *3.6.2.1 Interventions aiming at enhancing physical activity level in patients with rheumatic diseases*

Thomsen et al (2017) investigated the efficacy of an individually tailored theory-based behavioral intervention to reduce sitting time, pain and fatigue, and to improve health-related quality of life and physical function in patients with rheumatoid arthritis (RA) (Thomsen et al., 2017). A total of 150 patients with RA were included in this RCT. The intervention group received three individual motivational counselling sessions and short message service, or text messages aimed at reduction of sedentary behavior during the 16-week intervention period.

The results showed a mean reduction of 1.61 hours/day in sitting time in the intervention group compared to the control group (0.59 hours/day) ($p<0.0001$) (Thomsen et al., 2017). In addition to the effect on reduced sitting time, this individually based intervention improved patient-reported outcomes and cholesterol levels (Thomsen et al., 2017).

A long-term follow-up of a RCT conducted on patient's hip osteoarthritis (OA), investigated the efficacy of a supervised exercise program (Svege, Nordsletten, Fernandes & Risberg, 2013). A total of 109 patients were included and physical activity level was assessed with the physical activity scale for the elderly (PASE). The PASE is a self-administered questionnaire that is a 7-days recall of activities divided into 24 questions to assess physical activity in elderly (Svege et al., 2013). The exercise therapy program was designed for OA and consisted of functional, strengthening and flexibility exercises. The exercise group performed exercise two to three times per week for 12-weeks, whilst they were supervised by a physical therapist at least once a week. The control group only attended a follow-up visit at the physiotherapist clinic as part of the education program in the intervention period. The data of training sessions per week were collected at baseline and four months, strength and flexibility training were collected at 16 and 29 months. The number of self-reported exercise sessions per week was similar in both groups. There was no significant difference in PASE scores between the exercise therapy group and the control group over the 29-month follow-up period ($p=0.39$) (Svege et al., 2013).

In this context, an intervention study with the purpose to change or/and increase the physical activity level in patients with axSpA is not been performed. A question to be asked is: what can we do to get the axSpA patients to be more physical active, and may a 12-week supervised exercise intervention enhance physical activity level after 12 months?

### 3.7 Research questions

- Is there a difference in physical activity level between the exercise group and the control group at 12-months follow-up?
- Is there an overall difference between the groups in exercise frequency at 12-months follow-up?
- Is there an overall difference between the groups in exercise intensity at 12-months follow-up?
- Is there an overall difference between the groups in duration of exercise session at 12-months follow-up?
- Is there a difference in exercise modalities between the groups at 12-months follow-up?
- Is there an effect of a supervised exercise program on participation in cardiorespiratory and strength exercises at 12-months follow-up?
- Which factors are associated with participation in cardiorespiratory and strength exercise at 12-months follow-up?

# 4.0 METHOD

## 4.1 Description of the study

This master`s thesis is a part of a multicenter randomized controlled trial (RCT) which has been conducted under the auspices of the National Agency for Rheumatological Rehabilitation (NKRR), Diakonhjemmet Hospital; «Exercise for SpondyloArthritis (SpA) - the ESpA study». The background data and analysis were collected from the EspA study. The study was designed to compare the effects of a 12-weeks of high intensity exercises with standard care (no intervention). The main purpose was to investigate the effect of high-intensity cardiorespiratory- and strength exercise on disease activity and risk factors of cardiovascular disease in patients with ankylosing spondylitis. This master thesis is a secondary analysis of the RCT and includes only the Norwegian study centers.
The trial was conducted at outpatient rheumatology departments at four hospitals in Norway (Diakonhjemmet Hospital, Martina Hansen Hospital and the University Hospital of North Norway).

## 4.2 Study design

The study was designed as a multicenter RCT comparing the exercise group and control group at 12-months follow-up. The study protocol is registered at clinicalTrials.gov. (NCT01436942)

## 4.3 Participants

The participants were recruited via rheumatologists and physiotherapists from the outpatient rheumatology departments at Diakonhjemmet Hospital, Martina Hansen Hospital and the University Hospital of North Norway. They were also recruited trough advertisement at social media-channels (Facebook and websites for patients).

### 4.4 Inclusion & Exclusion criteria

The inclusion and exclusion criteria from participation in the main study are presented in table 3.

***Table 3*** *Inclusion and exclusion criteria from the ESpA-study*

| Inclusion criteria | Exclusion criteria |
|---|---|
| • Diagnosis of axial SpA (ASAS classification criteria (Rudwaleit et al., 2009) confirmed by a rheumatologist<br>• Age, 18-70 -years<br>• Steady medication for ≥3 months<br>• Moderate disease activity defined as a BASDAI score of ≥3.5 or a patient global score ≥3.5<br>• Not participated in a structured cardiorespiratory and strength exercise program during the last 6 months (>1 hour/week) | • Severe co-morbidity which involves reduced exercise capacity and/or contraindications for physical activity as per American College of Sport Medicine guidelines<br>• Not able to participate in weekly exercise sessions<br>• Pregnancy |
| ASAS: Assessment of Spondyloarthritis International Society, BASDAI: Bath Ankylosing Spondylitis<br>Activity Index, ACSM: American College of Sports Medicine | |

### 4.5 Randomization and blinding

A statistician that was not involved in other aspects of the study assigned the participants numbers to either the exercise group or the control group following a computerized randomization program. Block randomization with a block size of four was used. The group alignment was concealed in envelopes that were opened after the baseline testing. The recruiting investigator was unaware of the next participant allocation. The assessor was blinded for group assignment and participants were instructed not to reveal any information regarding group belonging to the assessors.

*4.5.1 Description of the exercise intervention*

The intervention consisted of a 40-60 minutes exercise program were the patients exercised for three times a week for 12 weeks. Two of the sessions were supervised by a physiotherapist and included 40 minutes of cardiorespiratory exercise performed on a treadmill or cycle ergometer at high intensity. Followed by 20 minutes of strength exercises for major muscle groups with external weight loads. These exercises were individually adapted (leg press, deadlifts, squats, row to chest, pulldowns, sit-ups, bench press and shoulder press), with eight to ten repetitions with two or three sets. In addition, patients in the exercise group were encouraged to perform on their own consisting of cardiorespiratory exercise for minimum 40 minutes. The exercise adherence at home was recorded in a training diary, whereas the physiotherapist will record the attendance at the supervision sessions. (Table 4).

***Table 4*** *Shows the three-months exercise intervention program*

| Exercise program (exercise period: 3 months) | |
|---|---|
| **Cardiorespiratory exercises** (3 days a week) ($HR_{max}$ was determined at the end of a maximal treadmill test) | |
| **High Intensity interval exercise** | |
| Delivery | Supervised by a physiotherapist at a gym in a hospital or a fitness centre |
| Type | Walking or running on a treadmill/cycle ergometer |
| Frequency | 2 days per week |
| Intensity | 10 min warm up at 70% of $HR_{max}$. 4 x 4 min interval exercise at 90-95% of $HR_{max}$ with 3 min of active resting period at 70% of $HR_{max}$ between each interval. 3 min cool down at 70%. The intensity was controlled by a Polar puls watch during each session. |
| Time | 38 minutes |
| **Home Session** | |
| Delivery | Unsupervised individual training |
| Type | Walking/running/cycling outdoor or at fitness center |
| Frequency | 1 day per week |
| Intensity | ≥70% of $HR_{max}$. The intensity was controlled by a Polar pulse watch. |
| Time | ≥40 minutes |
| **Muscular strength exercises** (2 days a week)- Started with 2-3 weeks with gradually adaption before the work load was set to 8-10 repetitions maximum | |
| Delivery | Supervised by a physiotherapist (performed after the high intensity interval exercise) |
| Type | Six exercises for major muscle groups, individually adapted. Preferably with external load. Examples of exercises: Squat, leg press, deadlifts, rows to chest, bench press, shoulder press, pull downs and sit-ups |
| Frequency | 2 days per week |

| | |
|---|---|
| Intensity | Circle of exercises or switching between two exercises (no rest-intervals). |
| Time | 20 minutes |
| Repetitions | 8-10 repetitions |
| Sets | 2-3 sets |
| Progression | If the patient could perform more than 10 repetitions per sets, the workload was increased |
| The exercise program followed the American College of Sports Medicine exercise recommendations.<br>HR; Heart rate | |

## 4.6 Data Collection procedure

Data presented in this master thesis was collected at baseline and at 12-months follow-up. At baseline the data were collected at Diakonhjemmet Hospital and the University Hospital of North Norway by self-reported questionnaires and a clinical examination. There was one test leader (Silje Halvorsen Sveaas) who conducted all the clinical examinations at both study centers. After 12-months, patients were sent a questionnaire together with a reply-paid envelope by post. If the questionnaire was not returned during two week, participants were contacted by telephone and reminded to return the questionnaire.

## 4.7 Outcome measures

### *4.7.1 Background variable*

Information about gender, age, marital status and works status was collected from questionnaires.

### *4.7.2 Physical function (The Bath Ankylosing Spondylitis Functional Index (BASFI))*

The BASFI is a self-assessed instrument that consists of eight specific questions regarding function in AS, and two questions regarding the patient`s ability to cope with everyday life (Calin, Garret, Whitelock, Kennedy, O`Hea, Mallorie & Jenkinson, 1994). The questions are answered in a horizontal scale, which gives a BASFI score 0-10 (0=lowest, 10=highest) (Calin et al., 1994).

*4.7.3 Disease activity Bath Ankylosing Spondylitis Disease Activity Index*

The Bath Ankylosing Spondyloarthritis Disease Activity Index (BASDAI) - was used to assess global disease activity, and in this case specific towards fatigue (van der Heijde, Kvien, Sieper, Van der Bosch, Listing, Braun & Landewe, 2009). It is based on six questions related to fatigue, enthesitis, peripheral arthritis, spinal pain and morning stiffness (both severity and duration). The questions were answered in a numeric rating scale (NRS) and gives a BASDAI score from 0-10 (10=worst) (Mattey et al., 2012).

*4.7.4 Flexibility (The Bath Ankylosing Spondylitis Functional Index (BASMI))*

The Bath Ankylosing Spondyloarthritis Metrology Index as used to assess spinal mobility. BASMI is a combined index comprising of five assessments of spinal mobility. It includes assessments of lumbar flexion, lateral lumbar flexion, intermalleolar distance, tragus-to-wall distance and cervical rotation. Each measurement is scored from 0-10 and the mean of the scores gives a BASMI score 0-10 (10=worst) (van der Heijde, Landewe & Feldtkeller, 2008).

*4.7.5 Physical activity level and exercise habits*

*Physical activity was measured by two self-reported questionnaires:* International Physical Activity Questionnaire-Short form (IPAQ-sf) and a questionnaire about exercise habits.

*4.7.6.1 Physical activity*

Physical activity level was measured with a short form of the "International Physical Activity Questionnaire" IPAQ-sf, a self-reported questionnaire. The IPAQ-sf searches for the time the patient has used on physical activity the last 7 days (www.ipaq.ki.se, 2004). The questionnaire consists of six questions, divided into three activity levels; high exertion (activity who requires that you`ll breath heavily and mush more than you normally do), moderate exertion (activity that requires a moderate effort and makes u breath more than usual) and walking (light exertion) (attachment 3). In addition, there is a question about the patients last seven days and sitting time. Every question gives good examples on activities the patient can recognize as daily activities. Only ten minutes of continuous activity should be reported. For every activity level the IPAQ measures the duration (time spent in activity in one of those days, measured in time/day) frequency (how many days spent on activity the last 7 days).

Validity and reliability of IPAQ-sf

A study by Arends et al (2013) showed that the correlation between the IPAQ total score and accelerometer activity counts was 0.38 ($P < 0.05$), hence they concluded with a modest validity for the IPAQ (Arends et al., 2013). In a similar study of patients with lower back pain the validity of IPAQ was tested and showed a fair relationship between self-reported and objective measures showed (Carvalho et al., 2016). Kurtze et al (2008) evaluated the reliability and validity of the IPAQ short version in a Health study. The validity was tested by comparing results with $VO_{2max}$ and ActiReg (instrument that measures physical activity and energy expenditure). The validity suggested that the total IPAQ vigorous physical activity was a moderate good measure of vigorous activity, having a moderately strong significant correlation with $VO_{2max}$ ($p \leq 0.01$), however, it correlated not with activities measured at MET values of 6 or more, measured with AciReg. The total IPAQ of walking was the only one that correlated with MET`s at 1-3 and 3-6 ($p \leq 0.05$) (Kurtze, Rangul, Hustvedt & Flanders, 2008).

A study conducted by Craig et al in 2003 used a test-retest repeatability of the same IPAQ forms administered at two various times, not more than 8 days apart. The short version of IPAQ showed an acceptable level, with 75% of correlation coefficient 0.65, ranging between 0.88 to 0.32 from the various short forms (Craig et al., 2003). Another study showed significantly correlation with the energy expenditure and Metabolic equivalents (MET`s) minutes spent moderately to vigorously active following the activity diary and accelerometer (Meeus, Van Eupen, Willems, Kos & Nijs, 2010).

*4.7.6.2 Exercise habits*

The patients exercise habits was measured by questions about exercise habits, derived from the Health Survey in Nord-Trøndelag (HUNT) (Kurtze et al., 2008).

In this form the patients reported their frequency, intensity and duration of exercise. For exercise frequency there was five options; “never”, “less than once a week”, “once a week”, 2-3 times a week”, “approximately every day”. For intensity there was three options; easy (take it easy without breathing heavily or sweating), moderate (taking it so hard that I get tired and sweaty) and hard (I almost take it all out). Duration four options; “less than 15 minutes”, “16-30 minutes”, “30 minutes to 1 hour” and “1 hour and more”.

*Validity and reliability of questions about exercise habits*

The questionnaires showed a good reliability (weighted kappa for frequency, r=0.80, intensity, r=0.82, and duration, r=0.69). The HUNT was tested on 108 men whereas they answered the same questions a week apart (Kurtze et al., 2008).

*4.7.6.3 Different exercise- and activity categories*

The patients reported their several types of activities they participated in at 12-months follow up. Based on the type of activities the patients reported, a categorization in relation to whether they reported cardiorespiratory exercise, muscular strength exercise, walking, pool-exercises and cardiorespiratory- and muscular strength combined exercise. The patients were also asked to fill out the question: “What exercise and training activities have you been active in during the past year?” specified by number of times. (Attachment 5).

*4.7.7 Processing of variables*

Questions that were not answered, were treated as "blank".

*4.7.7.1 Physical activity level: Self-reported physical activity (frequency, intensity, duration)*

To present the patients frequency, intensity and duration of exercise, frequency was first divided into two, where the first of frequency included four categories; “never/less than 1 time per week”, “1 time per week”, “two to three times per week” and “about everyday”. These four categories were merged into two; “never/less than 1 hour per week”, “1 hour per week” and “1 hour per week or more”. Then second presentation of frequency were; “does not exercise 2-3 times per week” and “exercises 2-3 times per week”. Duration was categorized in three; “16-30 minutes”, 30 minutes - 1 hour” and “more than 1 hour”. The categories were merged into two main categories; “less than 30 minutes” and “30 minutes or more”. Intensity were divided into three categories; “Takes it easy without getting anxious or sweating”, “Taking it so hard I get breathless and sweaty” and “Almost take me all out”. These three categories were merged into two categories; “Takes it easy without getting anxious or sweating” and “Taking it so hard I get breathless and sweaty/Almost take me all out”. The number and amount of patient’s physical activity by intensity, frequency and duration was calculated in SPSS.

*4.7.7.2 Physical activity level: Physical activity (converted to metabolic equivalent)*

First the calculation for MET was converted from hours to minutes (www.ipaq.ki.se, 2004). The MET minutes/week was calculated by multiplying the amount of days with time spent on daily activities for the various levels ("walking" (all types of walking is included), "moderate" and "vigorous"). For walking the MET-minutes/week were multiplied with 3.3, and activities in "moderate" level the MET-minutes/week was multiplied with 4.0, and on the "vigorous" level MET-minutes/week was multiplied by 8.0. This were the formula that calculated the three different intensity levels (www.ipaq.ki.se, 2004).

*4.7.7.3 The patients different exercise- and activity categories*

The patients reported several physical activities that they were active in at baseline and 12-months follow-up. All of the reported activities were gathered and categorized within five categories and distributed as; "cardiorespiratory exercises", "pool-exercise", "strength exercises", "walking" and "cardiorespiratory and muscular strength". There were used a crosstabulation to place the patient's different activities. There were only registered activities for those patients who reported to exercise once per week or more. SPSS was used to assess the variables.

**4.8 Statistical analysis**

The background variables are presented as mean and standard deviation for continuous variables (median and minimum-maximum values were presented if the data was not normal distributed). Mann Whitney U-test (non-parametric) were used for the independent groups for continuous variables. For categorical variables, differences between the groups were analyzed with cross-tabs (Chi-Square). A logistic regression analysis was used to analyze factors associated with regular participation in cardiorespiratory and strength exercises at 12-months follow-up (dependent variable). Variables that were thought to be associated with participation in regular exercise were explored (gender, age, exercise experience and if they had received the exercise intervention) and were included in the final model if they were significantly associated with the dependent variable in simple analyses.

The level of statistical significance was set at $p < 0.05$. All statistical analyses were performed in SPSS for Windows, version 21.

### 4.9 Ethics

The study was approved by the Regional Medical Ethics Committee (REK South East 2015/86) in Norway. All the procedures followed the Declaration of Helsinki and all participants gave written and oral informed consent before entering. All the participants gave their written consent to participate in the study. Data was registered as a code per participant and were saved in the hospitals research-server in order to secure the patient information. In our opinion the exercise intervention and testing did not cause any risks or disadvantage for the participants. For patients in the exercise group, the exercise sessions were supervised by a physiotherapist, hence the physiotherapists monitoring also contributed to the safety and comfort for the patients. Further, participation in the study may also lead to a higher participation in physical activity and might therefore be healthful. All the procedures were carried out in accordance with the World Medical Association Declaration of Helsinki. The study has received an approval by the National Committee for Medical Research Ethics, Southern Norway (2015/86). (Attachment 6)

## 4.10 Search of literature

The databases PUBMed, Medline and Google were used to search for literature. A systematic search of literature has not been performed. The words used to search for literature was: "Rheumatic disease, axial Spondyloarthritis, Ankylosing Spondylitis, axSpA, AS, disease activity, intervention and physical activity, exercise, physical activity, participation in physical activity, MET, physical function, physical inactivity, high intensity, high intensity exercise, HIIT, effect of physical activity, effects of exercise, effects of high intensity exercise, rheumatic, rheumatism, physical activity and SpA, physical activity and axSpA, physical activity in patients with AS". There has also been a manual searching from the reference list from earlier research, and research that have been presented in association with the studies found in the manual search. This search was last updated 29.10.2018.

# 5.0 RESULTS

## 5.1 Description of the patients

A total of 67 of the patients from three different hospitals; Diakonhjemmet Hospital (n=35), Martina Hansens Hospital (n=9) and the University Hospital in North-Norway (n=23) are included in this thesis. The total group varied in age from 18 years of age until 70, and the gender distribution was in favor of women with 36 women (55%), and 31 men. At baseline the self-reported disease activity (BASDAI) ranged from 2 to 8 on a scale from 0-10 (10=worst), the patients reported as an average; 4.9 (SD 1.4). There were no differences in physical activity level between the exercise group and the control group at baseline. (Table 5)

***Table 5*** *Shows the patients baseline data*

| Characteristics | Controls group (n= 34) | Exercise group (n= 33) | Total (n=67) |
|---|---|---|---|
| Age (year), mean (SD) | 48.4 (9.3) | 43.7 | 46.1 (9.8) |
| Woman, n (%) | 18 (53%) | 18 (55%) | 36 (55 %) |
| Disease activity (BASDAI, 1-10, 10=worst) mean (SD) | 5.0 (1.4) (2.3-7.8) | 4.8 (1.4) | 4.9 (1.4) |
| Physical function (BASFI, 1-10, 10=worst), median (min-max) | 2.8 (0.6-8.5) | 2.4 (0.2-6.7) | 2.7 (0.2-8.5) |
| Spinal mobility (BASMI, 1-10, 10=worst) median (min-max) | 2.4 (0.6-7.1) | 2.7 (0.4-4.3) | 2.6 (0.4-7.1) |
| Height (cm), mean (SD) | 172 (11) | 170 (11) | 172 (10) |
| Weight (kg), mean (SD) | 82.9 | 82.1 | 82.5 (16.2) |
| BMI, mean (SD) | 27.9 (4.9) | 28.0 (5.3) | 27.9 (5.1) |
| > 12-year education, n (%) | 24 (70%) | 23 (70%) | 47 (70%) |
| Total level of physical activity (MET), median (min-max) | 784 (0-5280) | 671 (0-14868) | 693 (0-14 868) |
| Total MET in walking intensity, median (min-max) | 99 (0-2772) | 346 (0-4158) | 198 (0-4158) |
| Total MET in moderate intensity, median (min-max) | 170 (0-2160) | 0,0 (0/5040) | 80 (0-5040) |
| Total MET in high intensity, median (min-max) | 0 (0-4320) | 0 0/8640 | 0 (0-8640) |
| $VO_2$max, mean (SD) | 36.1 (6.0) | 36 (1.1) | 36.1 (6.2) |

ASDAS: «The Ankylosing Spondylitis Disease Activity Score,[a] <1.3: not an active disease, 1.3-2.1: moderate disease activity, 2.1-3.5: high disease activity, >3.5 very high disease activity (Assessment of SpondyloArthritis international Society). BASDAI: Bath Ankylosing Spondylitis Disease Activity Index (attachment 3), BASFI: «The Bath Ankylosing Spondylitis Functional Index» (Attachment 1), BASMI: «The Bath Ankylosing Spondylitis Metrology Index (Attachment 2), SD: Standard deviation.

### 5.2 Flow of participants

At baseline there was a total of 67 patients, and at 12 months follow-up; 57 of 67 patients (88%) completed the questionnaire. Hence, there was a drop-out of ten patients (exercise group; n=5, control group; n=5) from baseline and 12 months of collection (figure 4).

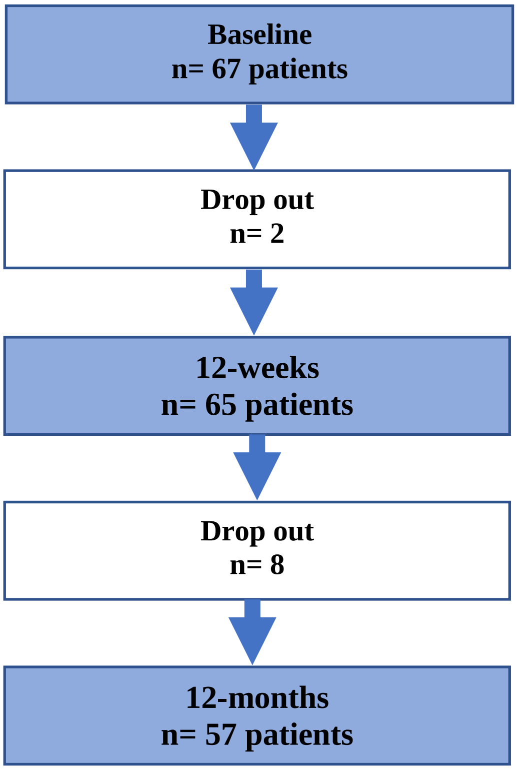


***Figure 4*** *The figure represents the flow of participants through the trial.*

### 5.3 Total amount of physical activity at 12-months follow-up

In the following, the patients total physical activity level and reported time spent with vigorous, moderate and walking intensity after 12 months follow-up are shown. A total of 57 of 67 patients answered the IPAQ questionnaire at 12 months follow-up and are included in the analysis. There was no significant difference between the two groups in total amount of MET`s after 12 months ($p<0.81$). (Table 7)

***Table 6*** *Total physical activity level in the control group and the exercise group at 12-months follow-up measured in MET`s*

| Total MET by groups | n | Median | Min/max | p-value |
|---|---|---|---|---|
| Control group | 29 | 1053 | 00-7710 | |
| Exercise group | 28 | 1419 | 00-9918 | |
| Total | 57 | | | 0.81 |
| (*MET: Metabolic equivalent of task) | | | | |

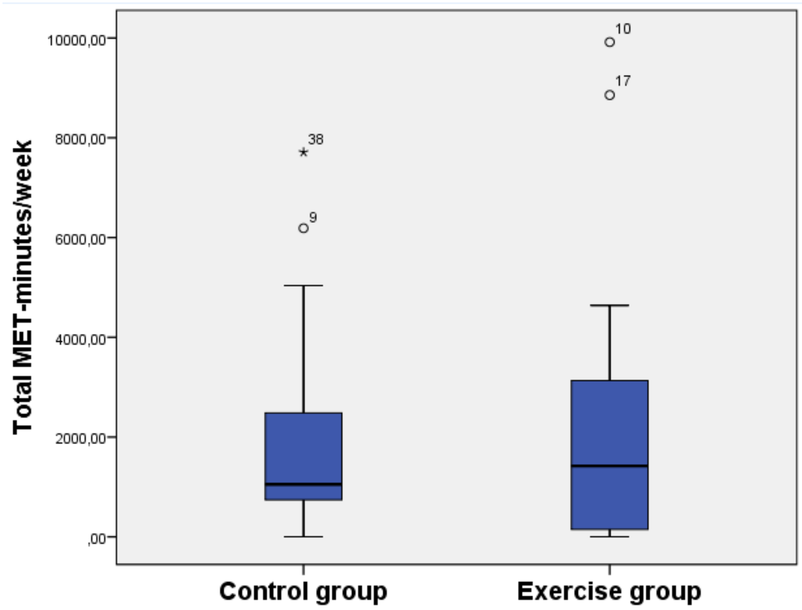


***Figure 5*** *Shows a box-plot of the total MET minutes per week in the control group and the exercise group. Median, quartiles, range and outliers are shown.*

**5.4 Total physical activity at different intensity levels at 12-months follow-up**

*5.4.1 Total physical activity at vigorous intensity*

The exercise group reported significantly more MET on vigorous intensity compared to the control group at 12-month follow-up ($p<0.03$). (Table 7)

***Table 7** Comparison of vigorous intensity activity at 12-months follow-up measured in* MET`s *between the control group and the exercise group*

| **Total MET Vigorous intensity** | **n** | **Median** | **Min-max** | **p-value** |
|---|---|---|---|---|
| Control group | 29 | .00 | 00-4320 | |
| Exercise group | 28 | 680.00 | 00-2880 | |
| Total | 57 | | | 0.03 |
| (*MET: Metabolic equivalent of task) | | | | |

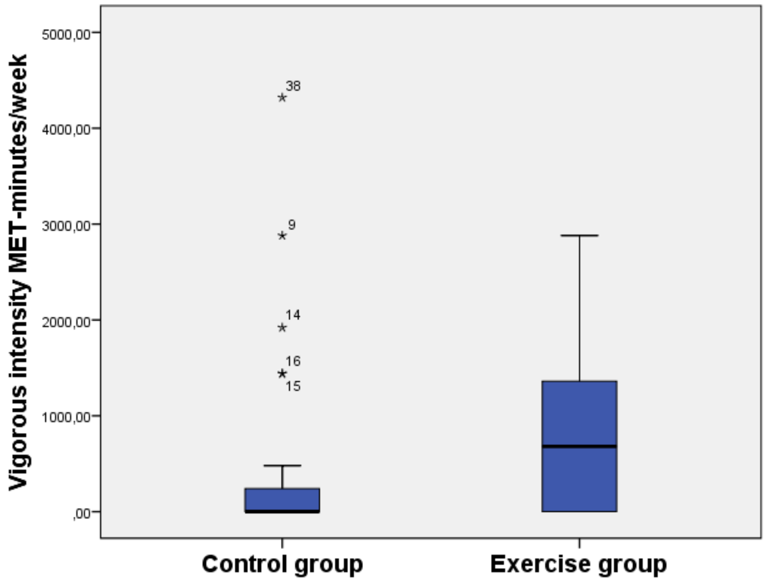


***Figure 6**: Box-plot of the vigorous intensity between the two groups in total MET minutes per week. Median, quartiles, range and outliers are shown.*

*5.4.2 Physical activity at moderate intensity*

There was no difference between the two groups regarding time spent on moderate intensity (Table 8)

**Table 8** *The patients moderate intensity activity at 12-months follow-up measured in MET`s.*

| Total MET Moderate intensity | n | Median | Min/max | p-value |
|---|---|---|---|---|
| Control group | 29 | 240.00 | 00-2400 | |
| Exercise group | 28 | .00 | 00-5040 | |
| Total | 57 | | | 0.53 |
| (*MET: Metabolic equivalent of task) | | | | |

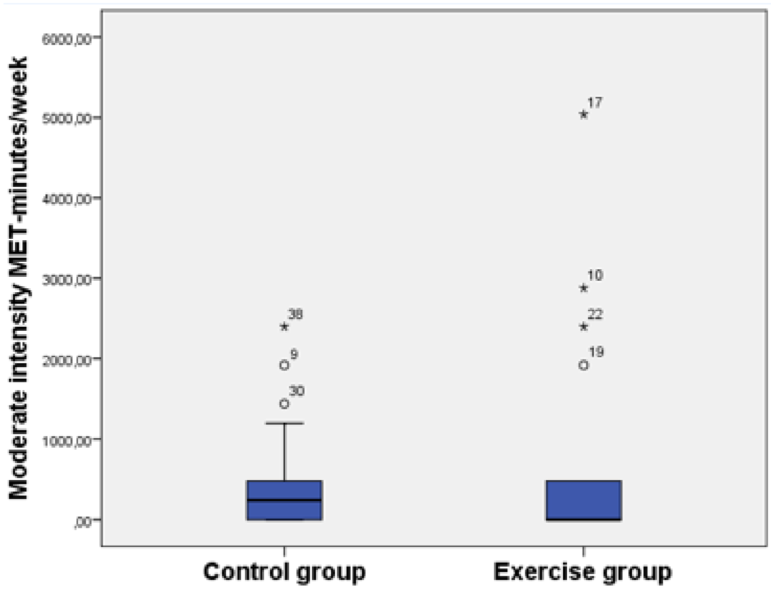


***Figure 7:*** *Shows a box-plot of total MET minutes per week at moderate intensity in the exercise group and the control group. Median, quartiles, range and outliers are shown.*

*5.4.3 Total amount of walking at 12-months follow-up*

The control group reported significantly more MET minutes per week spent on walking compared to the exercise group ($p<0.02$) (Table 9).

***Table 9*** *Comparison of walking activity at 12-months follow-up measured in MET`s in the exercise group and the control group.*

| Total MET Walking | n | Median | Min/max MET | p-value |
|---|---|---|---|---|
| Control group | 29 | 742.50 | 00-4158 | |
| Exercise group | 28 | 222.75 | 00-4158 | |
| Total | 57 | | | 0.02 |
| (*MET: Metabolic equivalent of task) | | | | |

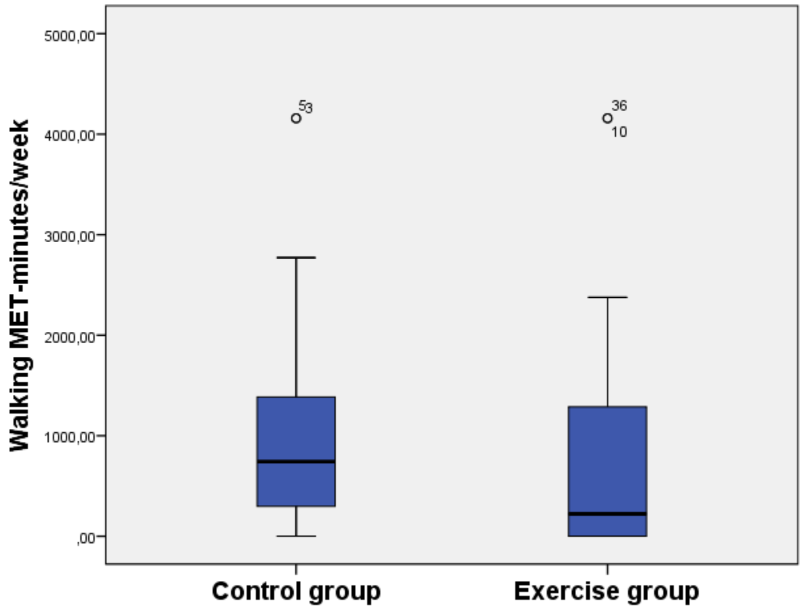


***Figure 8*** *Box-plot of total METs minutes per week spent on walking in the exercise and the control group between the two groups in total MET minutes per week. Median, quartiles, range and outliers are shown.*

**5.5 The patient's intensity, frequency and duration of exercise at 12-months follow-up**

There weas no difference in exercise frequency between the exercise and control group at 12 months follow-up (p=0.21). However, significantly more patients in the exercise group compared to the control group who reported to exercise 2-3 times per week at 12-months follow-up (p=0.04).

If the patients reported that they were exercising at least once a week (n=49), they were also asked about the exercise intensity, duration and type. Significantly more patients in the control group reported that the intensity was low during exercises (takes it easy without …) compared to the exercise group (exercise group; n=2, control group; n=14, $p<0.003$). (Table 10). There were no differences between the exercise group and the control group in the duration of exercise sessions at 12-months follow-up.

***Table 10*** *Shows an overview of the patient`s frequency, intensity and duration of reported exercise habits at 12-months follow-up.*

| **Group** | **Frequency** | | | | | | **Intensity** | | | | **Duration** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | <1/week | 1/week | 2-3/week | Almost every day | Total** | p-value | Low | High | Total** | p-value | <30 min | >30 min | Total | p-value |
| **Control, n (%)** | 5 (17%) | 7(24%) | 11 (38%) | 6 (21%) | 29 | | 11(45%) | 13 (55%) | 24 | | 5 (20%) | 19 (80%) | 24 | |
| **Exercise, n (%)** | 3 (11%) | 5 (18%) | 18 (62%) | 2 (7%) | 28 | | 2(8%) | 23 (92%) | 25 | | 1 (4%) | 24 (96%) | 25 | |
| | | | | | 57 | 0.21 | | | 49 | 0.003 | | | 49 | 0.72 |

Low; Easy without heavy breathing/ sweating
High; I breath heavily and sweat/ Almost all out
** 57 (total response-rate to questions about frequency)
** 49 (total response-rate to questions about intensity and duration)

### 5.6 Type of exercise activities at 12-months follow-up

Type of exercise activities for patients who reported to exercise ≥1 time per week are shown in table 11.

*5.6.1 Comparison of exercise types*

Significantly more patients in the exercise group compared to the control group reported they performed cardiorespiratory exercises (<0.001) and muscular strength exercises (p<0.001) at 12 months follow-up. More patients in the control group reported to perform pool exercises (p=0.02) and walking (p=0.01) compared to the exercise group. Furthermore, significantly more patients in the exercise group than in the control group reported to perform a combination of cardiorespiratory and muscular strength exercises (p=0.006) (table 11).

***Table 11** Represents different exercise types in the control- and exercise group at 12-months follow-up.*

| Exercise mode | Control group n= 24 | Exercise group n= 25 | p-value |
|---|---|---|---|
| Cardiorespiratory exercise | 3 (13%) | 12 (48%) | <0.001 |
| Strength exercise | 2 (8%) | 13 (52%) | <0.001 |
| Combination of cardiorespiratory and muscular strength exercises | 1 (4%) | 9 (36%) | 0.006 |
| Walking | 20 (83%) | 5 (20%) | 0.01 |
| Pool exercises | 12 (45%) | 14 (56%) | 0.02 |
| p-values analyzed with Chi-Square | | | |

**5.7 Factors associated with participation in cardiorespiratory and muscular strength exercises at 12-months follow-up**

The table shows a comparison of all the patients who performed cardiorespiratory and strength exercises ≥2 times per week at 12 months follow-up (n=17) and those who did not (n=40). Patients who performed cardiorespiratory and strength exercises ≥2 times per week were significantly younger than those who did not (p=0.03), significantly more patients had received the intervention (p=0.007) and had experience with cardiorespiratory and strength exercises before the baseline assessment (p<0.001). There were no differences in gender between patients that exercised regularly at 12-months follow-up and those who did not (Table 12).

***Table 13*** *Factors associated with participation in cardiorespiratory and strength exercises ≥2 per week at 12-months follow-up (followed the exercise intervention).*

| | **Regular cardiorespiratory and strength exercises[1] (n=17)** | **Not regular cardiorespiratory and strength exercises[2] (n=40)** | **p-value[2]** |
|---|---|---|---|
| Age, mean (SD) | 41.8 (9.1) | 48.3 (10.3) | 0.03 |
| Males, n (%) | 6 (35%) | 20 (50%) | 0.31 |
| Exercise experience[1] | 12 (71%) | 3 (8%) | <0.001 |
| Received intervention | 13 (77%) | 15 (38%) | 0.007 |

[1]Had performed cardiorespiratory and strength exercises during the last year before the baseline assessment
[2]Categorical variables: Chi square, continuous variables: independent sample t-test
**[1]≥2 per week cardiorespiratory and strength exercises (n=17)**
**[2] <2 per week with cardiorespiratory and strength exercises (n=40)**

Table 13 shows the result of a multiple logistic regression analysis of factors associated with participation in cardiorespiratory and strength exercises ≥2 times a week at 12 months follow-up. Univariate analysis showed that for each year the patient grows older, the odds of participating in regular was reduced (p=0.04). Further, univariate analyses showed that exercise experience before the baseline assessment (<0.001) and if the patients had been in the exercise group (p=0.01) was significantly associated with a higher OR for participation in regular cardiorespiratory and strength exercises at 12 months. The adjusted estimates, shows that the strongest impact on the odds of performing exercise was exercise experience before the baseline assessment. Adjusted for age and if patients had received the exercise intervention, the odds for participation in regular cardiorespiratory and strength exercise was 25 (95%CI 4.2, 148.6) if the patients had exercise experience before the baseline assessment (p<0.001).

***Table 13*** *Factors associated with participation in regular cardiorespiratory and muscular strength exercises at 12-months follow-up.*

| | **Crude estimates Odds ratio (95% CI)** | **p-value** | **Adjusted estimates[3] Odds ratio (95% CI)** | **p-value** |
|---|---|---|---|---|
| **Age** | | | | |
| Continuous | 0.93 (0.88, 0.99) | 0.04 | 0.94 (0.86, 1.02) | 0.14 |
| **Exercise experience[1]** | | | | |
| No experience | Reference | <0.001 | Reference | <0.001 |
| Experience | 29.6 (6.1, 142.6) | | 25 (4.2, 148.6) | |
| **Exercise intervention** | | | | |
| Control group | Reference | 0.01 | Reference | 0.75 |
| Exercise group | 5.4 (1.5, 19.7) | | 1.3 (0.2, 7.8) | |

[1]Had participated in cardiorespiratory and/or strength exercises during the year before the baseline assessment

# 6.0 Discussion

## 6.1 Discussion of main findings

The purpose of this master thesis was to investigate the long-term effect of a supervised exercise intervention on physical activity level in patients with axSpA, and to assess which factors that may affect the physical activity level at 12 months follow-up. The results showed that there were no statistical differences in the total amount of physical activity level between the exercise group and the control group at 12-months follow-up. However, the exercise group reported significantly more MET on vigorous intensity compared to the control group while the control group reported significantly more MET minutes per week spent on walking compared to the exercise group.

When it comes to exercise habits, significantly more patients in the exercise group compared to the control group reported that they performed cardiorespiratory exercises and muscular strength exercises at 12-months follow-up, and they reported also to exercise at a higher intensity level. Furthermore, participation in regular cardiorespiratory and strength exercises (≥2 times per week) were significantly associated with younger age, having received the intervention and experience with cardiorespiratory and strength exercises before the baseline assessment.  The strongest predictor of exercise participation at 12-months follow-up was exercise experience.

### *6.1.2 The significance of the findings*

Globally, inflammatory rheumatic disease is an enormously economic burden, and rheumatic disease has a significant impact on people’s everyday life and is a huge contributor to cause of sick leave and even premature retirement (EULAR, 2018). Today people live longer due to the development of new medicine, however, a large amount of people is living with reduced function, especially people with rheumatic disease. Patients with axSpA is affected in both social and professional life (Dougados & Baeten, 2011), suffering pain (Dougados & Baeten, 2011; Rudwaleit et al., 2009), have a higher risk of developing cardiovascular disease (Mathieu et al., 2011), problems of the daily activities partly associated with reduced mobility, pain, fatigue and deformities (Dagfinrud et al., 2005), fatigue (Passalent et al., 2010) and may eventually lead to abnormal stiffening and immobility of joint due to fusion of the bones (Lee et al., 2015). Therefore, it is important to have a focus to increase the level of function within this patient group (Lim et al., 2012).

There seems to be an effect of a supervised exercise program regarding participation in cardiorespiratory and strength exercises 12-months after engaging the study. A period of 12-weeks of high intensity exercise seems to increase the knowledge due to exercise, physical activity and the intensity domains. The intervention group were more active compared to the control group when the total amount of physical activity was investigated, and the vigorous intensity was significantly higher in the exercise group, with a positive correlation to cardiovascular health and potentially reduces the risk of cardiovascular disease and other comorbidities. There were also significantly more patients in the control group reported that the intensity was low during exercises. Increased knowledge through supervised exercise combined with education seems to have an increased level of physical activity in the intervention group. The society today and following infrastructure presents less challenges due to daily physical activity and not so challenging physical activity domains (occupational, domestic, transportation, and leisure time). The results from this study can initiate enhanced physical activity and exercise because the patient who were included in the study had a moderate to high disease activity during the whole intervention period.

The exercise intervention in the present study consisted of high intensity supervised exercise two times per week with cardiorespiratory- and strength exercise, and one home-based exercise with the same type of exercise. The findings in this study, showing increased physical activity at a high intensity level should be seen in the light of the general management recommendations stating that besides pharmacological treatment, non-pharmacological treatment is recommended as a very important part of the management of axSpA (Braun et al., 2011). Hence, a 12-week exercise program may increase participation in health promoting physical activity in the long term. Together with the benefits of decreased inflammatory back pain with physical activity (Dougados & Baeten, 2011), high intensity cardio- and strength exercise may have beneficial effects on disease activity in terms of stiffness, pain, flexibility, fatigue and inflammation in patients with inflammatory rheumatic diseases including axSpA (Sveaas, Smedslund, Hagen & Dagfinrud, 2017). The high intensity exercise is a typical exercise type to increase $VO_{2max,}$ and $VO_{2max}$ is one of the best indicators of cardiorespiratory fitness (Serna et al., 2016). As high cardiorespiratory fitness can have protentional protective effect against CVD, and axSpA patients have a higher risk of developing cardiovascular disease (Mathieu & Soubrier, 2018) it is probably crucial to improve cardiorespiratory fitness for this patient group.

Most studies investigating the physical activity level on patients with axSpA implies that they are less active compared to healthy controls (Swinnen et al., 2014; O`Dwyer et al., 2015b; Haglund et al, 2012; Jacquemin et al., 2018), however, this study indicates that the intervention group exercised more and participated more in vigorous exercise compared to the control group, something that has been shown to be a general challenge for this patient group (Haglund et al., 2012; van Genderen et al., 2015; Jacquemin et al., 2018).

## 6.2 Main findings compared to studies investigating physical activity level and patients with axSpA

Studies have shown that patients with axSpA in general are less active than healthy controls and does not fulfill the general recommended physical activity from the ACSM (Swinnen et al., 2014 & O`Dwyer et al., 2015b & Jacquemin et al., 2018). However, some studies suggest that they are equally physical active as healthy controls, but nevertheless only a few percentage meets the recommended physical activity level (Haglund et al, 2012; Jacquemin et al., 2018). This 12-week intervention of cardiorespiratory- strength exercises has shown that if a patient group participate in cardiorespiratory- and strength exercises consistently over a 12-week period, they will learn about high intensity exercise, and potentially use this by themselves. The high intensity exercise weas supervised by a physiotherapist. The supervised exercise might have given the participants in the exercise group a feeling of comfort and trust and they overcome the potential barrier to high intensity exercise that can be intimidating. Exercising for 12-weeks under supervision, may give the patients a feeling of confident to conduct this exercise type alone, and developed a basis knowledge about how and why this type of exercise is safe.

The exercise group reported significant more exercise at vigorous intensity. Differences in the exercise intensity between the groups to be further confirmed when the patients reported the exercise intensity as significantly more patients in the control group reported that the intensity was low during exercises compared to the exercise group.

Furthermore, significantly more patients in the exercise group compared to the control group reported they performed cardiorespiratory exercises and muscular strength exercises, and the significant more with a combination of cardiorespiratory and muscular strength exercises. Summarizing these findings, the exercise group participates in more exercise and activity in vigorous intensity.

Comparing this thesis, Haglund et al (2012) cross sectional study, reported 68% of the SpA patients met the WHO recommendations of physical activity (Haglund et al., 2012). The study shows strong validation with a large sample size (n=2851). However, the questionnaire in the survey consisted only three questions about physical. Only 32% (n=697) of the 68%

who meet the recommendations of physical activity, met the recommended amount of vigorous intensity (30 min/2-3 week (Haglund et al., 2012).

The study of van Genderen et al (2015) showed that patients with axSpA and healthy controls were equal physical active, however, patients with axSpA spent fewer minutes per day in moderate to vigorous physical activity (van Genderen et al., 2015). Hence, underlines the importance of increase physical activity at a high intensity level for this patient group.

The study of Swinnen et al (2014) showed that patients with axSpA were less active than healthy controls and the level of weekly average physical activity of vigorous, very vigorous and moderate/(very) vigorous combined were significantly lower in patients with axSpA (Swinnen et al., 2014). The study used SenseWear pro 3 Armband (an accelerometer) and was the first study to use technology-based physical activity assessment for this patients group. A challenge due to lack of comparison to other studies using these measurement methods. A potential bias it that the patients were not to use the armband during water-based activities which is a very popular activity for rheumatic patients in general.

Jacquemin et al., 2018 showed that only 27% met the recommended amount of physical activity in patients with AS (Jacquemin et al., 2018). This observational study used smartphone as an activity tracker, recording the number of steps per minute. A potential weakness could be to wear the activity tracker for three months and might affect the participant’s activity level. Being in a study who tracks your steps everyday might influence the activities and the level of the activity for the participant, either less or more activity due to increase or decrease in motivation. Wearing an activity tracker might also influence the participant, who might be more motivated to be more active. The activity tracker counted a number of steps per minute, and this determined if the activity was moderate intensity or vigorous intensity. The WHO recommendations were defined as at least 10.000 steps per week, and only 9.6% of the patients walked a mean of 10.000 steps per week (Jacquemin et al., 2018). However, the activity tracker might underestimate the activities during cycling (i.e spinning) or participating in muscular exercise/strength exercise.

To summarize, many observational studies have shown that patients with axSpA are participating less in vigorous physical activity than the general population. Hence, as the present study showed that a supervised exercise intervention increased participation in a vigorous physical activity, these studies underlines the importance of implementing supervised exercise programs for this patient group.

### *6.2.1 Studies conducted on axSpA patients without differences in physical activity*

Plasqui et al (2011) showed the patients in their study were equally active as healthy controls and used accelerometers to measure physical activity (Plasqui et al., 2011). However, the participants were instructed to not use the accelerometer during water activities (Plasqui et al., 2011). Walking, stretching and pool exercises was one of the most common and reported exercises (Fongen et al., 2013). This means that the accelerometer might underestimate the exercise in Plasqui et al (2012) study. However, there is a lack of studies and literature showing beneficial effects of exercise in water and significant effect on health-related fitness in patients with rheumatic disease (Wong & Scudds, 2009).

The risk of bias might be high due to the small sample size (n=25) and the recruitment was of first degree relatives as controls (about half of the sample) and did not investigate the different intensity domains of physical exercise, and the accelerometer was not used in water activities (Plasqui et al., 2013). In addition, the comparison to the general population and recommended physical activity could be a challenging point, whereas the general population does not meet the general recommended physical activity (www.folkehelseinsituttet.no, 2017 & www.who.com, 2018).

Van Genderen et al (2015) presented similar results regarding patients (n= 135) with AS and healthy controls (n= 99) who used triaxial accelerometer for seven days and to complete a series of questionnaires, showed no difference in total physical activity between patients with AS and healthy controls (van Genderen et al., 2015). However, the patients spent fewer minutes per day in moderate to vigorous physical activity, 23 minutes with physical activity in the patients group versus 30 minutes in the exercise group. Additionally, the patient minutes with physical activity was negatively influenced by BMI, physical function (BASFI) and disease duration, ant the authors concluded that the patients may avoid activities in higher intensities (van Genderen et al., 2015).

To summarize, many observational studies have shown that patients with axSpA are less physical activity than the general population. However, the methods did not include water exercises, a very popular activity in patients with rheumatic disease.

The Norwegian institute of public health reports that within the general population in Norway, only one out of three meet the recommended amount of physical activity (www.folkehelseinsituttet.no, 2017). Additionally, the WHO (2018) reports globally that one out of four adults are not active enough, and more than 80% of the world`s adolescent population is insufficiently physical active (www.who.com, 2018). Hence, comparing patients with axSpA with healthy controls will raise some questions since the general population does not meet the recommended amount of physical activity. Comparing patients and healthy population, it is crucial to be critical to the research method and what kind of physical activity standard the study has included compared to the general recommended physical activity.

The control group in the present study reported significantly more time spent walking compared to the exercise group at twelve months follow-up. In line with these results, Passalent et al (2010) reported walking as one of the most specific types of exercise most frequently reported by respondents (Passalent et al., 2010), hence it is reasonable to believe that the control group continued with their usual physical activities. There is a possibility that the control group overestimated their exercise and physical activity level, by reporting walking as an exercise. Another reason could be that the control group does not understand exercise is not the same as physical activity, and a challenge due to distinguish between moderate and vigorous activity. Within the intervention, the control group did not receive the same education as the exercise group and may not have the right basic knowledge about how physical activity is measured.

### *6.2.2 Factors associated with participation in cardiorespiratory and strength exercise at 12-months follow-up*

Regular participation in cardiorespiratory and strength exercises at 12-months follow-up indicated that for each year the patient grows older, the odds of participating in exercise regularly was reduced. The combination of barriers and facilitators that influences the patient’s adherence to participate in physical activity and exercise over time seems to be affected by age, participating in the intervention group and exercise experience earlier in life. Studies shows a different result on whether age are limiting or an enhancing factor for participants in physical activity, but in the present study younger age was associated with regular participation in cardiorespiratory and strength exercise. However, in contrast to the present result, Haglund et al (2012) results showed the youngest age group (18-29 years) met the WHO recommendations to the lowest degree, compared to the oldest age group (65-85 years), suggesting the older participants were more active than the younger patients (Haglund et al, 2012). However, Falckeback (2003) suggested the younger patients were less active than the older patients, and, patients with highest disability exercised more than those with lower disability. Summarized, age seems to have a divided result due to participation in physical activity and disease specific activity.

The adjusted estimates, shows that the strongest impact on the odds of performing exercise was exercise experience before the baseline assessment. Adjusted for age and if patients had received the exercise intervention, participation in regular cardiorespiratory and strength exercise was strong if the patients had exercise experience before the baseline assessment.

There is evidence that physical activity works as a prevention of lifestyle diseases, both mental and physical well-being. There are also many psychological theories how to start, enhance and continue with physical activity. Health behavior needs a conscious effort by the individuals in a set of ways either passive or active maintain their own health and lifestyle. This can and will be a very challenging field for promotion of health. The benefits of physical activity do not exist without continued, regular participation. For the general population can be difficult to initiate physical activity and to maintain regular physical activity, especially amongst sedentary individuals. For patients with axSpA the participation in physical activity challenges might be enhanced.

A population survey indicated that the person with self-reported doctor-diagnosed arthritis were less likely to meet physical activity guidelines for moderate and vigorous activities compared to persons without arthritis (Shih, Hootman, Kruger & Helmick, 2006). However, Swinnen et al (2014) found that disease activity did not affect the physical activity level between patients and controls (Swinnen et al., 2014). Haglund et al (2012) suggested through their results that patients with a higher reduced function physical function were less likely to meet the recommended moderate activity (Haglund et al., 2012). They also found negative association with older age, worse function, higher self-reported disease activity and smokers/previous smokers in physical activity with vigorous intensity (Haglund et al., 2012). Van Genderen et al (2015) additional analyses showed that the patients showed that time spent with physical activity was negatively influenced by BMI, physical function (BASFI), and disease duration (van Genderen et al., 2015).

To summarize, patients with axSpA might experience enhanced barriers to participate exercise, however, can change with the knowledge about physical activity and the perceived benefits, both physically and mentally.

### 6.3 Factors that potentially affect the findings in the study

Li`s study in 1996 talks about why people start participating in physical activity to begin with. The reason for this could be both extrinsic and intrinsic in nature. Research indicates that the motives for getting individuals involved in exercise activity vary depending on personal needs and social reinforcement (Li, 1996). Exercising with other might be a positive reinforcement for the exercise group, however, not for the control group who exercised by themselves.

The pharmacological treatment, non-steroidal anti-inflammatory drugs (NSAIDs) are the most used intervention and has shown a significant beneficial effect on symptoms of the disease (Dougados & Baeten, 2011). The patient group and the exercise group were equal with regards to disease activity at baseline, however, the disease activity might change to better or worse. Studies implies that disease related factors can reduce the level of physical activity in patients with axSpA (Fongen et al., 2014), and patients has shown more likely to report barriers for being physical active compared to population controls (Fongen et al., 2014). The participant may change their medication due to change of medication type, enhanced intake or stop of the usage, or a very high/low disease activity. There can be an enhanced barrier to physical activity if the patient experiences a higher occurrence of pain, fatigue, stiffness, enhanced stress and less sleep due to the negative effects from an increased disease activity.

The axSpA everyday life might have an enhanced challenge due to disease related barriers to participate in physical activity. Many of these factors can be influenced by the positive effects shown in this study.

Exercise experience was the strongest predictor for participating in cardiorespiratory- and muscular strength exercises two times or more per week at 12-months follow-up. However, the target group of patients with axSpA who are not physically active or have no experience of exercised and had experienced benefits of physical activity nor high intensity exercise, this patient should also be included as the main focus in the future. Another challenge is the time of year may affect the general physical activity participation, especially the activity level conducted outdoors. In general, rheumatic patients can react to cold weather, and can avoid certain activities if the weather is cold. Weather could potentially be a barrier to physical activity whereas patients with rheumatic disease reports in general a lot of exercise in water. For this patient group, low intensity exercises, flexibility exercises and pool exercises have been mostly used. This is emphasized by research in the field that shows that most of the exercise studies have investigated the effect of flexibility exercises (Dagfinrud et al., 2011; Regel et al., 2017). Fongen et al (2013) reported that one of the most reported exercises was pool exercises (Fongen et al., 2013). In this thesis, there were more patients in the control group reported to perform pool exercises and walking compared to the exercise group. The warm temperature of the water (hydrotherapy) may decrease pain and stiffness, as well as promote relaxation in patients with Arthritis (Bartels, Lund, Hagen, Dagfinrud, Christensen, Danneskiold-Samsøe, 2007; Bartels, Lund, Hagen, Dagfinrud, Christensen, Danneskiold-Samsøe, 2009). The buoyancy of the water reduces the amount of load going through the joint, which enables patients to perform functional closed-chain exercises that may not be possible on land (Hinman, Heywood & Day, 2007).

However, the patients may not know that there are limited studies showing clinical benefits of water exercise on disease symptoms and cardiovascular health, hence, patients often refer to pool activities as water exercise. The knowledge about this type of activity or exercise in water might influence the self-reported physical activity and the level of intensities. A study conducted by Wong et al (2009) showed repeated measure analysis of variance showed a statistical difference in pain, six domains of SF-36 questionnaire: general health, physical function, role-physical, role-emotional, vitality and bodily pain (Wong & Scudds, 2009). An improvement in confidence in performing exercise and exercise participation (Wong & Scudds, 2009). However, these factors are highly associated with quality of life, and not improvement in physical or mental health (Wong & Scudds, 2009). The challenge may be that the patients misinterpret these feeling of an enhanced quality of life during and short time after water exercise. The patients could then report water exercise as a quality exercise in the self-reported questionnaire and questions about exercise habits. The water properties of the water can affect the body to get a slightly different picture of self-exerted effort compared to on land.

Summarized, water and pool exercises are a very popular choice of exercise in patients with rheumatic disease due to the relief of several disease related challenges, however, the quality of the health-related benefits is insufficient.

## 6.4 Strengths and limitations

### *6.4.1 Study design*

In this thesis the effect of a supervised exercise intervention on physical activity level and exercise habits in patients with axSpA are investigated. Within methods to investigate the effect of the exercise intervention, it is important to have a control group to compare the intervention. A randomized controlled trial does always have a control group and is one of the best methods to controls the participant exposure (Laake, Olsen & Benestad, 2008). The background variables as gender, age, weight, BMI and other factors may influence the outcome, so the conditions should be as equal as possible due to the possible and wanted effect of the intervention, and the groups were selected via randomization (Laake et al., 2008). The testing of the patients at baseline was carried out before the randomization, therefore the patients were blinded for groups, so the distribution of patients resulted in no statistical differences at baseline between the control and exercise group.

Internal and external validity may affect the validity of the study results (Laake et al., 2008). The internal validity in most cases in a RCT study, is good because of the randomized selection of participants, almost equal groups that can reduce the systematic bias (population and information bias). This is a good method to detect factors that may affect the results from outside, and there is a higher chance to draw conclusions from the intervention and effect (Laake et al., 2008). The external validity assesses how the results in this study are generalizable to other people, situations and contexts (Thomas, Silverman & Nelson, 2011). It is important that the study has enough participants and that they present the population who is investigated. A RCT external validity might be low due to the strict inclusion and exclusion criteria and the purpose is to investigate a special effect on a specific population. The participants is a highly selected group of people of this patient group, like in this study got a specific treatment (intervention), and is not obvious that the results from this intervention group is representative to all axSpA patients (Laake et al., 2008).

### *6.4.2 Participants*

Before initiating a study, it is important to estimate the number of participants to be included to draw strong conclusions about the effect (Laake et al., 2008). The selected patients given an opportunity to investigate factors to look closer to, and we draw conclusions about the population on the basis of these observations (Laake et al., 2008). The sample size of the participants and selection of characteristics to be measured will determine what conclusions (Laake et al., 2008). The bigger the sample is in the study, the more accurate the result will be for the population. There were 67 patients at baseline and 57 in total who returned the self-reported questionnaires. The mean age was 46.1 years, the gender was about equal distribution was in favor of women with 36 women (55%), and 31 men. At baseline there were no statistical differences in self-reported disease activity (BASDAI), physical function (BASFI), Spinal mobility (BASMI), BMI and no differences in physical activity level between the exercise group and the control group at baseline.

If the patients group in this study reflects the population of general patients group with axSpA, the study generates a strong external validity. External validity is an important measurement of which the findings in the study can be generalized to common situations in society (Grønmo, 2017). The participants in the study were volunteers, and those patients who volunteer for an exercise intervention study may differ from non-participants in motivation for the experimental task and setting (Thomas, Nelson & Silverman, 2005). The participants in the study may have been affected of the recruitment method because the recruitment was voluntary though the hospitals via oral and writing information. This might have given an opportunity for the patients to initiate exercise by the assistance from the supervision of a physiotherapist and maybe easier to maintain the exercise whilst not by themselves. The patients who wanted to participate may not have the same motivation to exercise as the ones who did not participate. The participants may have been more interested in physical activity and exercise and could interfere and present a selection bias compared to the general axSpA patients.

All the patients might have joined the study deliberately or with a wish to be in the exercise group. The tough exercise sessions could also influence those who were thinking of joining the study. Without any prior experience to high intensity exercise and no knowledge, the sessions might be intimidating, and studies have shown that the axSpA patients seems to avoid vigorous intensity (Haglund et al, 2012; van Genderen et al., 2015; Jacquemin et al., 2018). The patients were recruited through the rheumatology departments at the four hospitals by various social media channels (hospital web pages and Facebook). The patient inclusion criteria were strict were a diagnosis of axSpA, aged between 18-70, steady medicated for three months, without established CVD and high disease activity and more or less inactive. The potential participant was excluded if the patient had severe co-morbidity (contraindications for physical activity), pregnancy or not able to participate in weekly exercise sessions.

These strict inclusion criteria may have affected the external validity of this study. This means that the results may be generalized to patients with less or no regular exercise with moderate disease activity outside the study. Furthermore, the results of the study may be generalized to an untrained group of patients with axSpA who are motivated to start exercising. The participants were recruited from Oslo, Tromsø (North-Norway) and Bergen. These are large cities with that likely offers a larger activity offer compared to small places There was an approximately equal distribution of patient dropout from each group (n=5 in the exercise group and n=4 in the control group. Dropout is a threat to the validity of a study, as the dropout problem is an extraordinary challenge for longer periods of time, and in the trial scheme there may be various conditions related to the dropout in the two groups that are compared (Laake et al., 2008).

Adherence to the exercise protocol can affect the strengths of the findings, where there were nine participants who did not follow 80% of the exercise protocol, and of these, there were three participants who was registered as drop-out because they did not like the exercise intervention. 24 of the participants in the exercise group completed a minimum of 80% of the exercise protocol (a minimum of 29 of 39 sessions). In addition, there were four participants in the control group who started to exercise cardiovascular exercise or muscular strength exercise two or more times per week. The three participants who retired from the program might could reduce their conception of intensive exercise and the results from the exercise group might be affected by those three patients could report more time spent walking or moderate. There was a patient in the exercise group who had to moderate the high intensity exercise to moderate intensity, due to a heart condition. This patient might also affect the results, due to not able to exercise in high intensity. There was a total of 57 patients who completed the 12-moths follow-up, showing a reduced external validity due to small size of investigated axSpA patients.

#### *6.4.3 Statistical analysis*

As a treat to the validity of the statistical analyses conducted in this study and thesis, the statistical validity refers to the extent to which the statistical analyses are appropriate (Polit & Beek, 2004).

#### *6.4.4 Measurement*

To have a strong and valid study, it is important that there is an internal validity. The internal validity in this study is based on the quality of the intervention was completed in a satisfying way, whereas the conclusion of the causation is valid under the examination conditions (Grønmo, 2017). This means that we must trust the researchers responsible for the tests protocols, data-collection protocols and the statistical analyzed data and reduce the chance og bias. The implementation of the research project may affect participants or groups as "studied". This can lead to the fact that those who are being studied, change their behavior during the study itself as compared to what they normally would do (Grønmo, 2017).

Wong et al (2003) suggested that the sample size of participants in the study will affect the outcome, together with the use of quality measurements (Wong, Day, Luan, Chan & Wareham, 2003). If there were used poor measurements of the exposure, the study size of 150 989 people would be required to detect an interaction with 95% power at a significant level (Wong et al., 2003). The study suggests that the smaller the sample size, there must be a higher quality of measurements used in the study.

In this context this study had 67 patients and finished with 57. There was a low dropout, however, the size of the sample in the study can affect the external validity. The larger the group, the higher the probability is that it represents the general population. Additionally, the exercises in the intervention should be applicable to the general population, without a supervision from physiotherapist two out of three exercise sessions.

We can also estimate that people join in on exercise and physical activity interventions and studies, they already have a motivation for joining and to be more active. It might be harder to include those we cannot reach, with less motivation and does not have any motivation towards physical activity.Yet another limitation concerns the validity of patient-reported physical activity versus observed physical activity (i.e., with accelerometry), and it is well known that there are difficulties comparing these two methods even if none of the measures are proposed as the gold standard (Haglund et al., 2012)

The patients in this study were investigated three times; baseline, three months and 12-months follow-up after baseline. There was only one therapist conducting and supervising the test`s in the study, so as a potential consequence, the results may not be generalized to an intervention led by other therapists.

*6.4.5 IPAQ*

Physical activity is difficult and complex behavior to measure. IPAQ is a subjective methodology and rely on the individual to record activities as they occur or to recall previous activities (Strat et al., 2013). Studies of questionnaires shows s strong correlation with other construct criteria for vigorous-intensity physical activity, however, they are less accurate for light- to moderate-intensity activities (Strat et al., 2013). Self-reported questionnaires can collect data from a large number of people, at a low cost. The recall does not alter the behavior under study, and it is possible to assess all the dimensions of physical activity, so the pattern may be examined (Sallis & Sealens, 2000). It successfully ranks the categories in high and low, is assesses structured physical activity and low burden for the participants (Strat et al., 2013).

Wareham et al (2003) assessed the validity and repeatability of energy expenditure estimated by self-report and objectively measures of energy expenditure (Wareham, Jakes, Rennie, Schuit, Mitchell, Hennings & Day, 2003). The repeatability of the physical activity index was high and there were positive association between physical activity index from questionnaires and objective measures of daytime energy expenditure to resting metabolic rate and cardiorespiratory fitness. The indirect validity showed a positive association between the physical activity index and the ratio of energy intake, assessed by 7-days intake (Wareham et al., 2003).

Another strength that normally occurs as a potential bias is the social and cultural specifics in this study are not normally presentable, however, in this study they only use patients who has an active disease (inclusion and exclusion criteria) with axSpA. One of the purposes in this study is to investigate the physical activity level in patients with axSpA, and what kind in factors that influence their activity level. A strength of IPAQ is that it has been tested in both developed and developing countries, and demonstrated acceptable reliability and validity properties across both, especially in the urban samples (Craig et al., 2003). Self-report questionnaires are significantly more reliable at the group than the individual level (Sylvia et al., 2014).

The challenges with the IPAQ is that there are possibilities for recall and social desirability bias, and the low validity for assessing incidental or lifestyle physical activity (Strat et al., 2013). Social desirability is something that sees as positive in the social context, can be exercise, physical activity, healthy lifestyle, nutrition, sex and so on. This might affect the reports and the participant can overestimate their physical activity level and habits. The social but not desirable can influence the participants to report less of “sensitive information” or negative associated information; alcohol, drugs, weight/BMI, unhealthy food and physiological problems.

The self-reported methods have several limitations tin terms of reliability and validity (Prince, Adamo, Hamel, Hardt, Connor Gorber & Tremblay, 2008), whereas the direct measurements of physical activity are more commonly used to increase the accuracy and precision (Prince et al., 2008). The direct measures could offer more precise estimates of energy expenditure and removes many of the protentional bias (Prince et al., 2008). Physiologic markers (biomarkers, cardiorespiratory fitness), indirect calorimetry (double labeled water, indirect, direct), motion sensors and monitors (accelerometers, pedometer and heart rate monitor) and direct observation are examples of direct measures. Using these methods also gives some challenges where they often demand specialized training, often use time and are expensive (Prince et al., 2008). Prince et al (2008) conducted one of the largest review of literature to attempt to examine the self-reported and direct measures og physical activity (Prince et al., 2008). Their conclusion was that the risk of bias in one third of all the research because of the studies had a lower quality based on their description of methods and external and internal validity (Prince et al., 2008).

A study from Brenner & DeLamater (2016) suggested that self-reported surveys can give an inaccurate answer to the questions, especially those about normative behavior (Brenner & DeLamater, 2016). How the persons who is asked to interpret the questions and can transform to whether what identity the person has to the identity the person aspires to be (Brenner & DeLamater, 2016). The person who answers the self-reported questionnaires may reflect the person they want to be in the survey rather than honestly to themselves and question, especially compared to the social desirable questions.

Recalling physical activity is a highly complex cognitive task (Sallis & Sealens, 2000). Very old adult may have difficulties remembering and recall skill limitations (Sallis & Sealens, 2000). The participants in this study variated between 18-70 years with a mean of 46 years, where the oldest were 69 years old. The participants may not be included as a "very old adult". The participants must understand the terms "physical activity", "low intensity", "moderate intensity" and "vigorous intensity" (Sallis & Sealens, 2000). At 12-months follow-up, the patients in the intervention group educational exercise compared to the control group, giving them more knowledge about moderate and vigorous exercise. If the questionnaire forms are easy, important information may be lost, and if the questionnaire is to be complicated, the participant find it difficult or may not answer.

Telephone, mail or face to face are some examples to administer the questionnaire and can determine the quality. There is normally a protocol of how the questionnaires are administered, and a protocol of how and what kind of guidance they get, and how to answer and understanding of the questions. There was used three different hospitals to conduct the IPAQ short version, however, under supervision of physiotherapist. The patients answered the questionnaire at baseline with supervision, so the physiotherapist could assist or ask if the participants have fulfilled the whole questionnaire. At 12-months follow-up, the questionnaire was answered without guidance, because they were send by mail. There has to a challenge to the participant who might not remember how to answer properly. These questionnaires are also affected in the way of how data are obtained (e.g., paper and pencil assessment, computerized questionnaire, interview) (Sylvia et al., 2014).

*6.4.6 IPAQ Short version*

The short-version of IPAQ was used in this RCT study. Lee et al (2011) conducted a systematic review of studies validating the IPAQ-SF (Lee, Macfarlane, Lam, Stewart, 2011). There were included twenty-three validation studies in the review. The correlation between the total physical activity level measured by the IPAQ-SF and objective standards ranged from 0.09 to 0.39. None of the studies reached the minimal acceptable standard in the literature (Lee et al., 2011). As for vigorous activity or moderate activity level/walking and an objective standard, their conclusion was that they showed even greater variability (-0.18 to 0.76), however, several reached the minimal acceptable standard. Most of the studies the IPAQ-SF overestimated physical activity level, and only one study underestimated (Lee et al., 2011). However, Kurtze et al (2008) conducted a study to evaluate the reliability and validity of IPAQ, short-version (Kurtze, Rangul, Hustvedt, & Flanders, 2008). The questionnaire showed a good reliability for vigorous activities and fair for moderate activities. The intraclass correlations ranged from 0.30 for moderate activity hours and 0.80 for sitting hours (Kurtze et al., 2008). The validity suggested that the total IPAQ vigorous physical activity was moderate good measure, with a moderately strong, significant correlation with $VO_{2max}$, however, correlated not with MET`s valued six or more measured with ActiReg (Kurtze et al., 2008).

Meeus et al (2011) evaluated the criterion validity and internal consistency of the IPAQ-short form (IPAW-sf) in chronic fatigue syndrome patients (Meeus, Van Eupen, Willems, Kos & Nijs, 2010). The patients completed the IPAQ-sf after they used tri-axial accelerometer and filled out activity diaries. The IPAQ-sf correlated significantly with energy expenditure and Metabolic Equivalents (METs) minutes spent moderately to vigorously active following the activity diary and accelerometer (Meeus et al., 2010). However, the patients hardly reached moderate or vigorous activity levels, so on the contrary, this study shows that the IPAQ-sf did not seem to be appropriate tool to assess physical activity in patients with chronic fatigue syndrome (Meeus et al., 2010).

### 6.5 Future research

The results from this study shows that there is an increased physical activity in patients who participated in a high intensity exercise study. These interesting findings can build a higher understanding and further investigation about how patients with axSpA can reduce their CVD risk and other lifestyle related diseases to meet the recommended amount of physical activity. Patients with axSpA is shown to be less active compared to both healthy controls and does not meet the general recommended physical activity. The main aim should be focused to health-related fitness and should be the main concern for patients with rheumatic disease and axSpA. The information about high intensity cardiorespiratory- and muscular strength exercise, potential benefits and the patients educational level must be risen in this patient group.

## 7.0 CONCLUTION

The results from this study suggest that a 12-week supervised exercise program may have a long-term effect on exercise habits in patients with axSpA. A beneficial effect on participation in regular cardiorespiratory- and strength exercises and physical activity at a vigorous intensity level at 12-months follow-up were seen. Hence, more patients may take advantages of the health benefits associated with regular cardiorespiratory and strength exercises at a high intensity if they attend a 12-week supervised exercise program. However, there was no effect of the exercise intervention on total amount of physical activity and exercise experience before the baseline assessment was the strongest predictor of regular participation in cardiorespiratory and strength exercises at 12-months follow-up.

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**OVERVIEW OF APPENDIX**

## BASFI-SPØRSMÅL OM FYSISK FUNKSJON

Spørsmålene nedenfor gjelder hvordan du følte deg den siste uken. Marker ditt svar med å krysse i en rute ☒.

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1.** | **Ta på strømper eller strømpebukser uten assistanse eller ved bruk av hjelpemidler (for eksempel strømpepåtrekker)** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **2.** | **Bøye deg fremover fra midjen for å plukke opp en penn fra gulvet uten å bruke et hjelpemiddel** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **3.** | **Nå opp til en høythengende hylle uten bruk av hjelpemidler (feks gripetang)** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **4.** | **Reise deg fra en spisebordsstol uten armlener eller annen hjelp?** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **5.** | **Reise deg opp fra liggende stilling på gulvet uten hjelp** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **6.** | **Stå oppreist uten støtte i 10 min. uten å få ubehag** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **7.** | **Gå opp 12-15 trappetrinn uten å bruke rekkverk eller gåstøtte. En fot på hvert trinn** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **8.** | **Se deg over skulderen uten å vri kroppen** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **9.** | **Utføre fysisk krevende aktiviteter (feks fysioterapiøvelser, hagearbeid eller sport)** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |
| **10.** | **Utføre en hel dags aktiviteter enten hjemme eller på arbeid** | | | | | | | | | | | | |
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| | Lett | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Umulig |

**BASMI- BEVEGELIGHET**

| | | | | |
|---|---|---|---|---|
| **Brystkassebevegelighet**<br>Måles med armene i nakken. Mål anteriort ved 4.intercostal. | | | | |
| 1 | | Utpust<br>☐☐☐.☐ | Innpust<br>☐☐☐.☐ | **Forskjell**<br>☐☐.☐ |
| **BASMI** | | | | |
| | Mål angis i 0.5 cm eller nærmeste 5° | | | |
| 1 | **Tragus (øregang) til vegg (cm)**<br>Hæl inntil veggen, strake knær, skuldre tilbake, nøytral stilling med hodet. Rett opp mest mulig. | Hø ☐☐.☐ | | Ve ☐☐.☐ |
| 2 | **Lumbal fleksjon (cm)**<br>Sett et merke mellom SIPS og 10 cm ovenfor. Mål avstand mellom merkene når pasienten er maksimalt fremoverbøyd. | ☐☐.☐ | | |
| 3 | **Lumbal sidebøy (cm)**<br>Hæl og rygg inntil vegg, uten å bøye seg forover eller i knær. Merk ved miderste finger og mål avstand mellom stående og full sidebøy. | Hø ☐☐.☐ | | Ve ☐☐.☐ |
| 4 | **Cervikal rotasjon (grader)**<br>Pasient sitter på stol, hendene i fanget, nøytral stilling med hodet. Med myrionometer måles forskjellen i antall grader mellom nøytral stilling og maksimal rotasjon. | Hø ☐☐° | | Ve ☐☐° |
| 5 | **Intermalleolær avstand (cm)**<br>Måles ryggliggende, strake knær, tær opp. Mål avstand mellom malleolene ved maksimal abduksjon. | ☐☐☐. ☐ | | |

## BASDAI- SPØRSMÅL OM SYKDOMSPÅVIRKNING

Spørsmålene nedenfor gjelder hvordan du følte deg den siste uken. Marker ditt svar med å krysse i en rute ☒.

**1.** **Hvordan vil du beskrive den generelle graden av utmattelse/tretthet du har erfart?**

| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ingen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Svært høy |

**2.** **Hvordan vil du beskrive den generelle graden av smerter i nakke-, rygg eller hofter i forbindelse med Bekhterevs sykdom (spondyloartritt)?**

| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ingen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Svært høy |

**3.** **Hvordan vil du beskrive det generelle nivået av smerter/hevelse du har hatt i andre ledd enn nakken- ryggen eller hoftene?**

| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ingen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Svært høy |

**4.** **Hvordan vil du beskrive den generelle graden av ubehag du har hatt på eventuelle steder som gjør vondt ved berøring eller trykk?**

| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ingen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Svært høy |

**5.** **Hvordan vil du beskrive den generelle graden av stivhet du har opplevd om morgenen fra det tidspunktet du våkner?**

| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ingen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | Svært høy |

**6.** **Hvor lenge varer morgenstivheten fra det tidspunktet du våkner?**

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 0 timer | | | | | 1 time | | | | | 2 timer eller mer |

# INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

# SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

## FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

***Background on IPAQ***

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

***Using IPAQ***

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

***Translation from English and Cultural Adaptation***

Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

***Further Developments of IPAQ***

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

***More Information***

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

# INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

**This is the end of the questionnaire, thank you for participating.**

## Questions about exercise habits

**1. Hvor ofte driver du mosjon?** (ta et gjennomsnitt)

- ☐ Aldri
- ☐ Sjeldnere enn en gang i uken
- ☐ En gang i uka
- ☐ 2-3 ganger i uka
- ☐ Omtrent hver dag

**2. Dersom du driver slik mosjon så ofte som en eller flere ganger i uka: Hvor hardt mosjonerer du?**
(ta et gjennomsnitt)

- ☐ Tar det rolig uten å bli andpusten eller svett
- ☐ Tar det så hardt at jeg blir andpusten og svett
- ☐ Tar meg nesten helt ut

**3. Hvor lenge holder du på hver gang?** (ta et gjennomsnitt)

- ☐ Mindre enn 15 minutter
- ☐ 16-30 minutter
- ☐ 30 minutter – 1 time
- ☐ Mer enn 1 time

# Questions about exercise habits

| | |
|---|---|
| **4.** | **Hvilke mosjons- og treningsaktiviteter har du vært aktiv i i løpet av det siste året?** |
| | Aktivitet: Angi antall ganger per uke i ruten |
| a) | |
| b) | |
| c) | |
| d) | |
| e) | |
| f) | |
| g) | |
| h) | |

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK



| Region: | Saksbehandler: | Telefon: | Vår dato: | Vår referanse: |
|---|---|---|---|---|
| REK sør-øst | Gjøril Bergva | 22845529 | 10.04.2015 | 2015/86/REK sør-øst D |
| | | | Deres dato: | Deres referanse: |
| | | | 23.03.2015 | |

Vår referanse må oppgis ved alle henvendelser

Hanne Dagfinrud

Diakonhjemmet Sykehus


**2015/86 Trening ved SpA**

**Forskningsansvarlig:** Diakonhjemmet Sykehus, Haukeland Universitetssykehus, Martina Hansens
Hospital, Universitetssykehuset i Nord-Norge

**Prosjektleder:** Hanne Dagfinrud

Vi viser til tilbakemelding fra prosjektleder, mottatt 23.03.2015, i forbindelse med ovennevnte søknad. Tilbakemeldingen er behandlet av komiteens leder på delegert fullmakt.

**Prosjektomtale**

*Spondyloartritt er en kronisk inflammatorisk revmatisk sykdom som rammer unge mennesker. Sykdommen kan forårsake redusert fysisk funksjon og en økt risiko for hjerte- og karsykdom som følge av den systemiske inflammasjonen. Formålet med denne studien er å undersøke effekten av høyintensiv trening på sykdomsaktivitet og risikofaktorer for hjerte- og karsykdom hos pasienter med spondyloartritt. Studien vil bli gjennomført som en multisenter randomisert kontrollert studie hvor 128 deltakere tilfeldig fordeles til treningsgruppe og kontrollgruppe. Resultatene av studien vil kunne føre til en bedre og mer målrettet behandling for pasienter med spondyloartritt.*

**Saksgang**

Søknaden ble første gang behandlet i møtet møtet 25.02.2015, hvor komiteen utsatte å fatte vedtak. Komiteen ba prosjektleder besvare følgende merknader:

1) *Etter komiteens syn er dette et omfattende prosjekt der deltagerne skal bruke mye tid på en rekkeundersøkelser og trening. Det skal gjøres EKG, MR-undersøkelse av rygg, iliosacralledd og lår, ultralydundersøkelse av halsens blodkar, blodtrykksmåling, og det skal tas blodprøver. Det skal også tas muskelbiopsier fra et utvalg av pasientene, noe som kan medføre ubehag og en viss infeksjonsfare.*

*Komiteen kan ikke se at det er redegjort for at muskelbiopsi er relevant for hovedmålsettingen med studien. Komiteen ber derfor prosjektleder begrunne behovet for muskelbiopsi. Hva er hypotesen, og hvordan skal de 20-30 deltagerne velges ut? Komiteen spør seg om deltagerne burde kunne reservere seg mot muskelbiopsi, men likevel delta i studien.*

*2) Det opplyses om at biologisk materiale (blod og muskelbiopsi) som samles inn i forbindelse medprosjektet, skal oppbevares i tidligere godkjente biobanker: «Konsekvenser av Bekhterevs sykdom» (REK-referanse 2011/1468) og «Muskelvev hos pasienter med spondyloartritt» (REK-referanse 2014/893).*
*Disse biobankene er spesifikke forskningsbiobanker knyttet til konkrete forskningsstudier. Komiteen kan ikke*

**Besøksadresse:** Gullhaugveien 1-3, 0484 Oslo
**Telefon:** 22845511
**E-post:** post@helseforskning.etikkom.no
**Web:** http://helseforskning.etikkom.no/
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*se at det er naturlig at materiale fra den aktuelle studien inngår i disse, da dette er en ny selvstendig studie. Komiteen anbefaler derfor at det opprettes en ny spesifikk forskningsbank for prosjektet. Komiteen ber om at navn på biobanken og navn på ansvarshavende for biobanken sendes komiteen.*

*3) Prosjektslutt for studien er 31.12.2018. Det oppgis i søknad at innsamlede data vil bli anonymisert senest8 år etter at sluttrapport fra studien er skrevet, og at alle innsamlede data (inkludert blodprøver og muskelvev) vil slettes etter 15 år. Etter komiteens syn er den planlagte oppbevaringen av innsamlet biologisk materiale i 15 år etter prosjektslutt, uforholdsmessig lang. Komiteen forutsetter at biologisk materiale og opplysninger oppbevares i kun 5 år etter prosjektslutt, jf. helseforskningsloven § 38.*

**Vurdering**

I tilbakemeldingen opplyser prosjektleder om at man likevel ikke vil belaste deltakerne med å ta muskelbiopsier. Det skal opprettes en ny spesifikk biobank for dette prosjektet med navnet «Trening ved spondyloartritt-ESpA-studien». Ansvarshavende er Professor dr.med. Tore K. Kvien ved Revmatologisk avdeling på Diakonhjemmet Sykehus. Det opplyses også om at alle innsamlede data vil slettes eller destrueres 5 år etter prosjektslutt.

Komiteen finner tilbakemeldingen tilfredsstillende, og har ingen innvendinger mot at prosjektet gjennomføres som beskrevet i prosjektleders tilbakemelding.

**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, protokoll og tilbakemelding fra prosjektleder, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Komiteen godkjenner opprettelse av en spesifikk forskningsbiobank, i tråd med det som er oppgitt i tilbakemeldingen. Biobankregisteret vil få kopi av dette brev. Hvis forskningsbiobanken opphører, nedlegges eller overtas av andre, skal det søkes REK om tillatelse, jf. helseforskningsloven § 30.

Tillatelsen gjelder til 31.12.2018. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil
31.12.2023. 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.

REKs vedtak kan påklages, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst, 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

Gjøril Bergva
Rådgiver

**Kopi til:**s.h.sveaas@medisin.uio.no; irene.lillebo@helse-bergen.no; bente.slungaard@mhh.no; Elisabeth.Pedersen2@unn.no

Diakonhjemmet Sykehus ved øverste administrative ledelse:
postmottak@diakonsyk.no Helse Bergen HF - Haukeland universitetssjukehus
ved øverste administrative ledelse: postmottak@helse-bergen.no
Martina Hansens Hospital ved øverste administrative ledelse: postmottak@mhh.no
Universitetssykehuset Nord-Norge ved øverste administrative ledelse: post@unn.no
Biobankregisteret ved Nina Hovland: nina.hovland@fhi.no

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

| Region: | Saksbehandler: | Telefon: | Vår dato: | Vår referanse: |
|---|---|---|---|---|
| REK sør-øst | Gjøril Bergva | 22845529 | 29.12.2015 | 2015/86/REK sør-øst D |
| | | | Deres dato: | Deres referanse: |
| | | | 21.12.2015 | |

Vår referanse må oppgis ved alle henvendelser

Hanne Dagfinrud

Diakonhjemmet Sykehus

**2015/86 Trening ved SpA**

**Forskningsansvarlig:** Diakonhjemmet Sykehus, Martina Hansens Hospital, Universitetssykehuset i Nord-Norge, Gøteborgs Universitet

**Prosjektleder:** Hanne Dagfinrud

Vi viser til søknad om prosjektendring datert 21.12.2015 for ovennevnte forskningsprosjekt. Søknaden er behandlet av leder for REK sør-øst D på fullmakt, med hjemmel i helseforskningsloven § 11.

**Endringene innebærer:**

-Haukeland Universitetssykehus utgår som forskningsansvarlig institusjon

- Gøteborgs Universitet inngår som ny forskningsansvarlig institusjon

-Innhenting av nye data fra samme utvalgsgrupper: Langtidsoppfølging gjennomføres ved at kontroll- og intervensjonsgruppe får tilsendt spørreskjema (som ved baseline) 12 måneder etter avsluttet intervensjonsperiode. Deltakere som ikke allerede har samtykket til dette ved inklusjon i studien vil bli forespurt om å delta i 12-måneders oppfølgingen.

**Vurdering**

Komiteen har vurdert endringssøknaden og har ingen innvendinger mot endringen av prosjektet. Komiteen forutsetter at den svenske delen av studien godkjennes av REK i Sverige.

**Vedtak**

REK godkjenner prosjektet slik det nå foreligger, jfr. helseforskningsloven § 11, annet ledd.

Tillatelsen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden, endringssøknad, oppdatert protokoll og de bestemmelser som følger av helseforskningsloven med forskrifter.

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

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Med vennlig hilsen

Finn Wisløff
Professor em. dr. med.
Leder

Gjøril Bergva
Rådgiver

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