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Beneficial long-term effect on leisure time physical activity level in individuals with axial spondyloarthritis: secondary analysis of a randomized controlled trial

Silje Halvorsen Sveaas, Hanne Dagfinrud, Melissa Woll Johansen, Elisabeth Pedersen, Ole-Martin Wold and Annelie Bilberg

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From the National Advisory Unit on Rehabilitation in Rheumatology, Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; the Department of physiotherapy, Martina Hansens Hospital, Bærum, Norway; the Department of physiotherapy, University Hospital of North Norway, Tromsø, Norway; Department of Coaching and Psychology, Norwegian School of Sport Sciences; The Norwegian Rheumatology Association, Norway and the Institute of Neuroscience and Physiology, Section of Health and Rehabilitation, Physiotherapy, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

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S.H. Sveaas, PhD, National Advisory Unit on Rehabilitation in Rheumatology, Diakonhjemmet hospital; H. Dagfinrud PhD, National Advisory Unit on Rehabilitation in Rheumatology, Diakonhjemmet hospital; M.W. Johansen, MSc, the Department of physiotherapy, Martina Hansens Hospital, E. Pedersen, PT, the Department of physiotherapy, University Hospital of North Norway, O.M. Wold, MSc, Department of Coaching and Psychology, Norwegian School of Sport Sciences; The Norwegian Rheumatology Association, Norway; A. Bilberg, and the Institute of Neuroscience and Physiology, Section of Health and Rehabilitation, Physiotherapy, Sahlgrenska Academy, University of Gothenburg.

Corresponding author:

Silje Halvorsen Sveaas, National Advisory Unit on Rehabilitation in Rheumatology, Department of Rheumatology, Diakonhjemmet Hospital, PO BOX 23 Vinderen,0319 Oslo, Norway. Tel: +4799648102, e-mail address: <u>s.h.sveaas@medisin.uio.no</u>.

Running head: Exercise in spondyloarthritis

## Abstract

*Objective*. To explore long-term effect of a 3-month exercise programme on leisure time physical activity level in individuals with axial spondyloarthritis (axSpA).

**Methods.** A secondary analysis was performed on data from 100 individuals with axSpA who were included in a randomized controlled trial. The exercise group (EG) participated in a 3-month exercise programme while the control group (CG) received no intervention. Physical activity during leisure time was measured with a questionnaire (physically active =  $\geq 1$  hour/week with moderate/vigorous intensity physical activity). Disease activity was measured with the Ankylosing Spondylitis Disease Activity Scale (ASDAS, higher score=worst). Statistical analyses were performed on an intention to treat basis using chi-square tests, logistic regression and mixed models. Clinical Trials.gov (NCT02356874).

**Results.** At 12-month follow-up, significantly more individuals in the EG than in the CG were physically active (29 [67%] vs. 13 [30%], p<0.001) and exercised 2-3/week (25 [58%] vs. 15 [34%], p=0.02), and fewer exercised at light intensity (3 [8%] vs. 14 [44%], p=0.002). "Participation in the EG" (Odds ratio [OR] 6.7 [95%CI: 2.4, 18.6], <0.001) and "being physically active at baseline" (OR 4.7 [95%CI: 1.4, 15.8], p=0.01) were the factors most associated with being physically active. There were no differences between the groups in ASDAS (p=0.79). **Conclusion.** A 3-month exercise programme had a beneficial long-term effect on leisure time physical activity in individuals with axSpA, thus indicating a more beneficial health profile. Still, few individuals continued the intensive programme, and there was no difference between the groups in disease activity after 12 months.

#### INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that mainly affects the axial skeleton(1). The disease is characterized by inflammatory back pain, and may also lead to reduced spinal mobility, arthritis, enthesitis, stiffness, fatigue(1) as well as an increased risk of cardiovascular (CV) diseases(2).

Physical activity is recommended as an important part of the management of axSpA(3), but it has been a worry that exercise at a vigorous intensity might exacerbate disease activity in individuals with axSpA, and they have generally been advised to engage in light intensity exercises(4, 5). However, in recently published recommendations, individuals with inflammatory arthritis are advised to adhere to the general physical activity recommendations(6). These recommendations state that adults should perform moderate intensity aerobic activity for a minimum of 30 minutes on five days per week or vigorous intensity aerobic activity for a minimum of 20 minutes on three days per week (or a combination), and engage in strength exercises two to three days per week. Hence, these recommendations represent a shift towards a more active approach with cardiorespiratory and strength exercises.

Exercise reduces the disease burden in individuals with axSpA as it has beneficial effects on disease activity, physical function, stiffness(7-9) and CV health(10). Despite this, individuals with axSpA tend to be less physically active than recommended(11-13), and they report to engage less in activities of moderate and vigorous intensity(14, 15). The most frequent exercise modes are pool exercises, stretching and walking(13, 16, 17), and a recent cross-sectional study reported that less than a third of individuals with axSpA engage in regular aerobic activities(13). Hence, it is important to investigate how physical activity can be implemented into daily life for this group. Staying physically active over time is important to secure health benefits(18), but few studies have investigated the long-term effect of exercise programs on physical activity level in axSpA. The aim of this study was therefore to explore long-term physical activity level after a 3-month exercise programme in individuals with axSpA.

## MATERIAL AND METHODS

#### Design

This is a secondary analysis of a multicenter randomized controlled trial (RCT) comparing the effects of 12 weeks of supervised exercise with usual care. The trial was conducted at outclinic rheumatology departments in Norway (Diakonhjemmet Hospital [DH], Martina Hansen Hospital [MHH] and the University Hospital of North Norway) [UNN] and in Sweden (Sahlgrenska University Hospital [SUH]). The study was approved by the Regional Committee for Medical and Health Research Ethics (REK South East 2015/86) in Norway and the Regional Ethical Review Board Gothenburg in Sweden (032-16). All procedures followed the Declaration of Helsinki, and all participants gave written and oral informed consent before entering. The study protocol is registered at ClinicalTrials.gov (NCT02356874).

#### Participants

Participants were recruited from outpatient rheumatology departments as well as through various social media-channels. The inclusion criteria were fulfilment of the Assessment of SpondyloArthritis international Society (ASAS) criteria for axSpA (19), age 18-70 years, no change in TNF-inhibitor use during the last three-months and moderate to high disease activity (Bath AS Disease Activity Index [BASDAI] ≥3.5). In addition, participants should not have participated in regular exercises (>1 hour per week) during the last six months with the aim of increasing cardiorespiratory fitness or muscular strength(20). Even though they could have been physical active in activities like pool exercises, walking and stretching, the program should have the potential to further increase their cardiorespiratory fitness and muscular strength. Exclusion criteria were established or symptoms of coronary heart disease, other comorbidity involving reduced exercise capacity, inability to participate in weekly exercise sessions and pregnancy.

#### Exercise group

#### Exercise program

The exercise group had access to supervised sessions during a 3-month period. A physiotherapist with experience in the field of rheumatology and trained in the exercise

protocol supervised the sessions twice a week. The program followed the American College of Sports Medicine (ACSM) recommendations for cardiorespiratory- and strength exercises (Sveaas et al. 2019 for details(21)). Some pain was tolerated during the exercises (≤5 on a scale from 0-10), but the exercises were adapted if the pain got worse the day after.

The cardiorespiratory exercise was performed three times per week for  $\geq$ 40 minutes. Two times per week the exercise group performed intervals on a treadmill or a cycle ergometer at vigorous intensity level (10 minutes warm up, thereafter four minutes at 90-95% of maximal heart rate (HR) followed by three minutes of active resting at 70% of maximal HR repeated four times)(22). Maximal HR was determined at baseline and monitored by a pulse-watch. Once a week participants in the exercise group performed  $\geq$ 40 minutes on a moderate intensity level (>70% of maximal HR) on their own.

The strength exercises were performed twice a week with eight to 10 repetitions maximum in two to three sets. The exercises were individually adapted and focused on major muscle groups (squat, leg press, deadlifts, rows to chest, bench press, shoulder press, pulldowns and sit-ups).

### Behavior change techniques

Several behavior change techniques(23) were used in the delivery of the intervention. The most important was the use of supervision that gave the participants a detailed plan, individual feedback and information. Two of the hospitals organized the exercise program as group sessions (UNN and SUH), while the physiotherapist were available for the participants during a fixed time point at the two others (DS and MHH). Equal for all the participants in the exercise group was that they had committed to exercise, the intensity was monitored during the sessions, and adherence was recorded by the physiotherapist as well as self-reported in an exercise diary. Participants in both the exercise- and the control group tested their physical fitness before and after the intervention period.

After the three-month period the exercise intervention ended, and participants were not given any instructions or reminders regarding physical activity.

### Control group

Participants in the control group received no intervention and were asked to continue their usual physical activity habits during the intervention period. All included participants received standard outpatient care from their respective hospitals, but before inclusion in the study it was specified that no change in medication before the three-month assessment was desirable. After the three-month assessment, participants in the control group were not given any instruction in physical activity.

### Assessments

All participants underwent a clinical examination and filled out questionnaires at baseline and three-months after inclusion. After 12 months, a questionnaire was sent by postal mail to all participants together with a prepaid envelope. Accompanied by the questionnaire was a request to visit the local study center for taking blood samples analyzed for C-reactive protein (CRP) and erythrocyte sedimentation rate. Up to two reminders were given by phone calls or text messages.

Variables such as age, educational level, working status, disease characteristics and medication were obtained from the questionnaires. Cardiorespiratory fitness was tested using a maximal walking test on treadmill for estimation of peak oxygen uptake (VO<sub>2</sub>peak) at baseline. Spinal mobility was assessed by the Bath AS Metrology Index (BASMI, 0-10 [10=worst]) (24).

### Outcome measures

#### Physical activity level

To assess physical activity we used the questions from the Nord-Trøndelag Health Study (HUNT1)(25) and the International Physical Activity Questionnaire short form (IPAQ-sf)(26). The HUNT1 questions are reported to be valid to assess leisure time physical activity as higher values of the summary index correlates positively with higher values of VO<sub>2</sub>max and also with accelerometer data. Further, HUNT1 questions is reported to have high test-retest reliability with correlation coefficient's from 0.76 to 0.87. Participants were asked "how often do you exercise? (never, less than once a week, once a week, 2-3 times a week and almost every day) with the text, give an average, exercise means going for walks, skiing, swimming and training/sports". If they exercised ≥1 week they were asked about the intensity (no

sweating/not out of breath [light], sweating/out of breath [moderate] or almost exhausted [vigorous]) and average duration (less than 15 minutes, 16-30 minutes, 30 minutes to one hour or more than one hour). A product of frequency, intensity and duration gave a summary index (scores for the summary index is given in table 2) (25). To categorize individuals into physical activity levels (physically active or inactive), total minutes per week were calculated by multiplying frequency and duration ( frequency; never=0, less than once a week=0, once a week=1, 2-3 times per week=2.5, almost every day=7, duration; less than 15 minutes=0, 16-30 minutes=23 minutes, 30 minutes to one hour=45 minutes, more than one hour=60 minutes)(27). Thereafter, total minutes per week and intensity was used to categorize individuals as either physically inactive (0-420 minutes with light physical activity or 0-59 minutes with moderate/vigorous physical activity per week) and physically active (defined as ≥60 minutes per week with moderate/vigorous physical activity) (27).

IPAQ-sf is reported to have acceptable criterion validity when compared with an activity tracker and to have good test-retest reliability with a correlation coefficient of 0.80 (26). IPAQ-sf consists of six questions about physical activity during the last seven days. Based on the data, metabolic equivalent (MET) scores were calculated, and 1 MET represents the body's resting energy expenditure (www.ipaq.ki.se). All the calculations and data cleaning were performed according to the official scoring protocol, but missing values were coded as none activity on the respective activity level. The MET scores were calculated by multiplying the number of minutes per day by the number of days per week by the activity METs (vigorous intensity = 8 METs, moderate intensity = 4 METs and walking = 3.3 METs). Total physical activity level was calculated by summarizing the MET scores from the three activity levels.

Participants were also asked to list the exercise modes they had been active in during the last year. If they at 12-month follow-up reported to exercise  $\geq 1$ /week, the listed exercise modes were categorized into relevant categories for analytical purposes.

## Disease activity and physical function

Disease activity was measured with the Ankylosing Spondylitis Disease Activity Score (ASDAS) (28) and the BASDAI (29). ASDAS is a composite score of CRP and self-reported variables: 1)

neck/back/hip pain, 2) peripheral joint pain, 3) duration of morning stiffness and 4) global assessment. All self-reported variables are reported on a 11 point numeric rating scale (NRS). ASDAS gives a continuous variable (<1.3, low disease activity 1.3 to <2.1, high disease activity 2.1 -3.5, and very high disease activity >3.5). The BASDAI is a self-reported index of five symptoms (fatigue, neck-back-hip pain, peripheral joint pain, tenderness and degree/length of morning stiffness)(29). Physical function was assessed with the Bath AS Functional Index (BASFI), which is a disease specific index (30). Each question in BASDAI and BASFI was answered on an 11 point NRS, and a sum score from 0-10 (10=worst) was calculated.

### Statistical analyses

Data are presented as mean (SD), median (min-max), and number (%) as appropriate. All statistical analyses were performed on an intention-to-treat basis. For comparisons between groups, the chi-square test was used to analyze differences in categorical data and independent sample t-test or Mann Whitney U-test was used to analyze differences in continuous variables as appropriate.

To explore factors associated with being physically active at 12-monthfollow-up, physically active participants were compared with physically inactive participants according to background variables and variables thought to be associated with physical activity level. Thereafter, a multivariate logistic regression analysis was performed to calculate the odds for being physically active at 12-month follow-up. Candidate variables for the multivariable logistic regression analysis were gender, age and variables with p-values <0.1 in simple analyses.

A linear mixed model was used to assess differences between the groups in disease activity and physical function at 12-month follow-up, with adjustments for baseline values and study center and the interaction between treatment and time.

The linear mixed model analyses were performed in Stata, and all other statistical analyses were performed in SPSS. The level of statistical significance was set at p<0.05.

# RESULTS

### Participants

Flow of participants is shown in Figure 1, a total of 97 (97%) and 88 (88%) of 100 participants completed the assessment at three- and 12-month, respectively. Background variables for the exercise- and the control group are shown in Table 1.

## Adherence and adverse events

A total of 38 (76%) participants in the exercise group followed  $\geq$  80% of the prescribed exercise protocol ( $\geq$ 29 of 36 sessions registered by the physiotherapist or in the exercise diary's), while four (8%) participants did not attend more than a few sessions. Two participants reported persistent pain during the exercise period, but completed the prescribed exercise protocol. In addition, one participant experienced chest pain and nausea during the exercises, and completed the intervention at moderate intensity after advice from a cardiologist.

### Long-term effect on physical activity level

The exercise group had a significantly higher exercise summary index at 12-month follow-up (p=0.01) (Table 2). Further, significantly more individuals in the exercise group were physically active (≥1 hour per week with moderate/vigorous physical activity) compared to the control group, p<0.001 (Figure 2). At 12-months follow-up, only 17 of 43 (40%) individuals in the exercise group performed both cardiorespiratory and strength exercises.

A total of 28 of 88 (32%) participants had missing items on the IPAQ. Although not significant, there was a tendency towards more METs at a vigorous intensity level and less walking in the exercise group compared to the control group. Further, more individuals in the control group were physically active on a moderate level than in the exercise group (p=0.02).

### Factors associated with being physically active at 12-months follow-up

The adjusted logistic regression analysis (Table 3) showed that having received the exercise intervention (p<0.001) and being physically active at baseline (p=0.01) were the only factors that were significantly associated with being physically active at 12-months follow-up. The OR for being physically active was 6.0 times higher in the exercise group than in the control group.

In the exercise group, physical activity level at 12-months follow-up was not associated with adherence to the exercise program (number of sessions) or study center.

Long-term effect on disease activity and physical function

The significant beneficial effect of the intervention seen at 3 months follow-up (Sveaas et al. 2019(21)), was no longer present at 12-months follow-up as no statistical differences were seen between the groups in disease activity (ASDAS; p=0.79, BASDAI; p=0.37) or physical function (BASFI; p=0.82) (Figure 3).

## DISCUSSION

The results indicate that participation in an exercise program increases the chance of staying physically active at a health-enhancing level over time in individuals with axSpA. At 12-month follow-up, almost 70% of the individuals in the exercise group were physically active during leisure time ( $\geq$ 1 hour per week with moderate/vigorous intensity activity) compared to 30% in the control group. Hence, individuals in the exercise group were six times more likely to be physically active at 12-month follow-up than those who didn't receive the intervention. Still, few individuals continued with the exercise programme, and the beneficial effect on disease activity and physical function found immediately after the exercise programme, had declined at 12-month follow-up.

Physical activity and exercise is recognized as important in the management of axSpA(3). However, previous research has shown that individuals with axSpA are less physically active than recommended(11-13, 31). The long-term improved physical activity level shown in this study is therefore important, as there are indisputable health effects of even small enhancement in leisure time physical activity(18).

To the best of our knowledge, this is the first study to demonstrate a prolonged beneficial effect on physical activity level after an exercise programme in individuals with axSpA. There are few comparable studies, and previous research is conflicting. Three studies, one in individuals with axSpA(10), one in individuals with osteoarthritis(32) and one in individuals with fibromyalgia(33) concluded with no effect of an exercise programme on long-term activity, while a study of elderly individuals with rheumatoid arthritis(34) found a positive long-term effect on physical activity. The conflicting results might be explained by several reasons. Firstly, the time point for measurement differed between the studies as one of the studies that found no effect on long-

term activity(10) measured physical activity right after completion of the intervention. However, it has been reported that exercise adherence seems to diminish over time(35), hence it is not likely that the physical activity level had been higher at later time point.

Secondly, the difference in results might be explained by differences in exercise modes- and intensities. It is well known that intensity is crucial for achieving effect of exercise(18) and that perceived benefits of exercise is important for adherence(36). The study in rheumatoid arthritis(34) and our study(37), included cardiorespiratory interval exercises (with an intensity of 70-89% and 90-95% of maximal HR, respectively), and both studies demonstrated large effects on general health immediately after the exercise intervention. The experience of immediate benefits may have contributed to the prolonged effect on physical activity level observed in both the rheumatoid arthritis study(34) and the present study.

Motivational and educational interventions have shown beneficial effects on physical activity level in individuals with rheumatic diseases(38-40). Even if these interventions are different from our exercise programme, they are similar in terms of including well-known facilitators for physical activity, such as health professionals providing information(41, 42), focus on motivation for exercise(36, 43, 44) and use of reminders(45). These factors may be of importance for improving physical activity level in individuals with axSpA.

In line with this, a recent systematic review concluded that education and supervision are important factors for adherence to exercise in individuals with axSpA(35). Obviously motivational or educational interventions are more cost-effective than supervised exercise programs. But, it should be noticed that the magnitude of the clinical effect was poor in one of the educational studies(40). Brophy et al.(44) stated that adding motivational strategies to the delivery of exercise programs was most effective in increasing physical activity, hence a combination of motivational and practical programs are probably important to increase physical activity level in patients with axSpA.

We found that physical activity status at baseline and participation in the supervised exercise programme were the factors that were strongest associated with physical activity status at 12-months follow-up. Previous research has shown that lower disease activity(31, 44, 46), better

physical function and quality of life is associated with being physically active in individuals with axSpA(31). However, none of these factors were associated with physical activity level at 12month follow-up in the present study, and the difference in results may be explained by unequal study designs(31, 44, 46) and larger study population in previous studies(31, 44). Our result is in line with the result of a systematic review stating that among several factors; low levels of physical activity at baseline was associated with poor adherence to physiotherapy treatment(47). Exercise experience is known to be essential for achieving exercise selfefficacy(45). In our study, the participants in the exercise group got practical training in exercise, which may perhaps compensate for lack of previous exercise experience.

The diminished effects on disease activity and physical function at 12-months follow-up are in accordance with findings in previous studies(32-34, 48). Despite the beneficial effect on physical activity level, few participants continued with the exercise programme. Our result is in line with earlier research reporting that it is more difficult for people to adhere to exercises at vigorous intensity, and that exercise induced adaptations are reversed over time without adherence to the programme(18). Hence, the clinical implication is that vigorous intensity exercise should be recommended as important in the treatment of individuals with axSpA due to the beneficial effects on disease activity. However, as the effect slowly declines, future studies should investigate if intermittent booster exercise sessions may increase participation in vigorous exercises.

Strengths of the present study are the study design, the relatively large sample size, low dropout rate, and the long-term follow-up period. Further, the exercise programme was based on the ACSM recommendations. The generalization of the study is probably high, as the study was carried out in outpatient's clinics at four different hospitals and several physiotherapists supervised the exercise programme. We have previously shown that the exercise programme was safe and well tolerated in a group of individuals with high disease activity(37). Self-reporting of physical activity level may be considered as a limitation, as participants may have under- or over reported their physical activity(49). Furthermore, participants were not blinded for group assignment, a factor which is reported to exaggerate subjective outcomes(50). Nevertheless, it is a strength that physical activity was measured with standardized, frequently used

questionnaires(27). And, as the numbers of inactive individuals in the control group were unchanged during the study period, we argue that this strengthens the validity of the physical activity questions. Likewise, a limitation is how the exercise mode questions were formulated. Although only answers from individuals exercising  $\geq 1$ /week were included, individuals in the exercise group might have included activities from the intervention period.

In conclusion, a supervised exercise programme seems to increase the chance of staying physically active over time and thereby maintaining a beneficial health profile. Still, few individuals continued the exercise programme, and the beneficial effect on disease activity and physical function at the end of the exercise program had declined at 12-months follow-up.

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# REFERENCES

- 1. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet 2017;390:73-84.
- 2. Mathieu S, Soubrier M. Cardiovascular events in ankylosing spondylitis: A 2018 meta-analysis. Ann Rheum Dis 2018;78:e57.
- 3. van der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the asas-eular management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978-91.
- 4. Iversen MD, Scanlon L, Frits M, Shadick NA, Sharby N. Perceptions of physical activity engagement among adults with rheumatoid arthritis and rheumatologists. Int J Clin Rheumtol 2015;10:67-77.
- 5. Lundberg IE, Nader GA. Molecular effects of exercise in patients with inflammatory rheumatic disease. Nat Clin Pract Rheumatol 2008;4:597-604.
- 6. Rausch Osthoff AK, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 eular recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis 2018;77:1251-60.
- Pecourneau V, Degboe Y, Barnetche T, Cantagrel A, Constantin A, Ruyssen-Witrand A. Effectiveness of exercise programs in ankylosing spondylitis: A meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 2018;99:383-9.e1.
- 8. O'Dwyer T, O'Shea F, Wilson F. Exercise therapy for spondyloarthritis: A systematic review. Rheumatol Int 2014.
- 9. van den Berg R, Baraliakos X, Braun J, van der Heijde D. First update of the current evidence for the management of ankylosing spondylitis with non-pharmacological treatment and non-biologic drugs: A systematic literature review for the asas/eular management recommendations in ankylosing spondylitis. Rheumatology(Oxford) 2012;51:1388-96.
- 10. Niedermann K, Sidelnikov E, Muggli C, Dagfinrud H, Hermann M, Tamborrini G, et al. Effect of cardiovascular training on fitness and perceived disease activity in people with ankylosing spondylitis. Arthritis Care Res(Hoboken) 2013;65:1844-52.
- 11. O'Dwyer T, O'Shea F, Wilson F. Physical activity in spondyloarthritis: A systematic review. Rheumatol Int 2015;35:393-404.
- 12. Jacquemin C, Servy H, Molto A, Sellam J, Foltz V, Gandjbakhch F, et al. Physical activity assessment using an activity tracker in patients with rheumatoid arthritis and axial spondyloarthritis: Prospective observational study. JMIR Mhealth Uhealth 2018;6:e1.
- 13. Fabre S, Molto A, Dadoun S, Rein C, Hudry C, Kreis S, et al. Physical activity in patients with axial spondyloarthritis: A cross-sectional study of 203 patients. Rheumatol Int 2016;36:1711-8.
- 14. Swinnen TW, Scheers T, Lefevre J, Dankaerts W, Westhovens R, de VK. Physical activity assessment in patients with axial spondyloarthritis compared to healthy controls: A technology-based approach. PLoS One 2014;9:e85309.
- 15. O'Dwyer T, O'Shea F, Wilson F. Decreased physical activity and cardiorespiratory fitness in adults with ankylosing spondylitis: A cross-sectional controlled study. Rheumatol Int 2015;35:1863-72.
- 16. Passalent LA, Soever LJ, O'Shea FD, Inman RD. Exercise in ankylosing spondylitis: Discrepancies between recommendations and reality. J Rheumatol 2010;37:835-41.
- Sundstrøm B, Ekergard H, Sundelin G. Exercise habits among patients with ankylosing spondylitis. A questionnaire based survey in the county of vasterbotten, sweden. Scand J Rheumatol 2002;31:163-7.
- 18. Garber CE, Blissmer B, Deschenes MR, Franklin BA, LaMonte MJ, Lee IM, et al. American college of sports medicine position stand. Quantity and quality of exercise for developing and

maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. Med Sci Sports Exerc 2011;43:1334-59.

- 19. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, et al. The development of assessment of spondyloarthritis international society classification criteria for axial spondyloarthritis (part ii): Validation and final selection. Ann Rheum Dis 2009;68:777-83.
- 20. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. Public Health Rep 1985;100:126-31.
- 21. Sveaas SH, Bilberg A, Berg IJ, Provan SA, Rollefstad S, Semb AG, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axspa): A multicentre randomised trial of 100 patients. Br J Sports Med 2019; (in press).
- 22. Helgerud J, Høydal K, Wang E, Karlsen T, Berg P, Bjerkaas M, et al. Aerobic high-intensity intervals improve vo2max more than moderate training. Med Sci Sports Exerc 2007;39:665-71.
- 23. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: Building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013;46:81-95.
- 24. van der Heijde D, Landewe R, Feldtkeller E. Proposal of a linear definition of the bath ankylosing spondylitis metrology index (basmi) and comparison with the 2-step and 10-step definitions. Ann Rheum Dis 2008;67:489-93.
- 25. Kurtze N, Rangul V, Hustvedt BE, Flanders WD. Reliability and validity of self-reported physical activity in the nord-trondelag health study: Hunt 1. Scand J Public Health 2008;36:52-61.
- 26. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. MedSciSports Exerc 2003;35:1381-95.
- 27. Kurtze N, Gundersen KT, Holmen J. Self-reported physical activity in norwegian studies- a methodological problem [article in norwegian]. Norsk Epidemiologi 2003;13:163-70.
- 28. van der Heijde D, Lie E, Kvien TK, Sieper J, Van den Bosch F, Listing J, et al. Asdas, a highly discriminatory asas-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:1811-8.
- 29. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: The bath ankylosing spondylitis disease activity index. J Rheumatol 1994;21:2286-91.
- 30. Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, et al. A new approach to defining functional ability in ankylosing spondylitis: The development of the bath ankylosing spondylitis functional index. J Rheumatol 1994;21:2281-5.
- 31. Haglund E, Bergman S, Petersson IF, Jacobsson LT, Strombeck B, Bremander A. Differences in physical activity patterns in patients with spondylarthritis. Arthritis Care Res(Hoboken) 2012;64:1886-94.
- 32. Svege I, Nordsletten L, Fernandes L, Risberg MA. Exercise therapy may postpone total hip replacement surgery in patients with hip osteoarthritis: A long-term follow-up of a randomised trial. Ann Rheum Dis 2015;74:164-9.
- 33. Larsson A, Palstam A, Lofgren M, Ernberg M, Bjersing J, Bileviciute-Ljungar I, et al. Resistance exercise improves muscle strength, health status and pain intensity in fibromyalgia--a randomized controlled trial. Arthritis Res Ther 2015;17:161.
- 34. Lange E, Kucharski D, Svedlund S, Svensson K, Bertholds G, Gjertsson I, et al. Effects of aerobic and resistance exercise in older adults with rheumatoid arthritis: A randomized controlled trial. Arthritis Care Res (Hoboken) 2018.

- 35. McDonald MT, Siebert S, Coulter EH, McDonald DA, Paul L. Level of adherence to prescribed exercise in spondyloarthritis and factors affecting this adherence: A systematic review. Rheumatol Int 2019.
- 36. Ehrlich-Jones L, Lee J, Semanik P, Cox C, Dunlop D, Chang RW. Relationship between beliefs, motivation, and worries about physical activity and physical activity participation in persons with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2011;63:1700-5.
- 37. Sveaas SH, Bilberg A, Berg IJ, Provan S, Rollefstad S, Semb AG, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axspa): A multicenter randomized trial of 100 patients. Br J Sports Med 2019;In press.
- 38. O'Dwyer T, Monaghan A, Moran J, O'Shea F, Wilson F. Behaviour change intervention increases physical activity, spinal mobility and quality of life in adults with ankylosing spondylitis: A randomised trial. J Physiother 2017;63:30-9.
- 39. Thomsen T, Aadahl M, Beyer N, Hetland ML, Loppenthin K, Midtgaard J, et al. The efficacy of motivational counselling and sms reminders on daily sitting time in patients with rheumatoid arthritis: A randomised controlled trial. Ann Rheum Dis 2017;76:1603-6.
- 40. Rodriguez-Lozano C, Juanola X, Cruz-Martinez J, Pena-Arrebola A, Mulero J, Gratacos J, et al. Outcome of an education and home-based exercise programme for patients with ankylosing spondylitis: A nationwide randomized study. Clin Exp Rheumatol 2013;31:739-48.
- 41. Madsen M, Jensen KV, Esbensen BA. Men's experiences of living with ankylosing spondylitis: A qualitative study. Musculoskeletal Care 2015;13:31-41.
- 42. Manning VL, Hurley MV, Scott DL, Bearne LM. Are patients meeting the updated physical activity guidelines? Physical activity participation, recommendation, and preferences among inner-city adults with rheumatic diseases. J Clin Rheumatol 2012;18:399-404.
- 43. Niedermann K, Nast I, Ciurea A, Vliet Vlieland T, van Bodegom-Vos L. Barriers and facilitators of vigorous cardiorespiratory training in axial spondyloarthritis: Surveys among patients, physiotherapists, rheumatologists. Arthritis Care Res (Hoboken) 2018.
- 44. Brophy S, Cooksey R, Davies H, Dennis MS, Zhou SM, Siebert S. The effect of physical activity and motivation on function in ankylosing spondylitis: A cohort study. Semin Arthritis Rheum 2013;42:619-26.
- 45. Bandura A. Self-efficacy. The exercise of control. . 11 ed. New York: Freeman and company; 1997.
- 46. Plasqui G, Boonen A, Geusens P, Kroot EJ, Starmans M, van der Linden S. Physical activity and body composition in patients with ankylosing spondylitis. Arthritis Care Res(Hoboken) 2012;64:101-7.
- 47. Jack K, McLean SM, Moffett JK, Gardiner E. Barriers to treatment adherence in physiotherapy outpatient clinics: A systematic review. Man Ther 2010;15:220-8.
- 48. van Baar ME, Dekker J, Oostendorp RA, Bijl D, Voorn TB, Bijlsma JW. Effectiveness of exercise in patients with osteoarthritis of hip or knee: Nine months' follow up. Ann Rheum Dis 2001;60:1123-30.
- 49. Prince SA, Adamo KB, Hamel ME, Hardt J, Connor Gorber S, Tremblay M. A comparison of direct versus self-report measures for assessing physical activity in adults: A systematic review. Int J Behav Nutr Phys Act 2008;5:56.
- 50. Wood L, Egger M, Gluud LL, Schulz KF, Juni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: Meta-epidemiological study. BMJ 2008;336:601-5.

*Figure 1.* Flow of participants throughout the randomized controlled trial.

Figure 2. The long-term effect of the supervised exercise program on physical activity level. Bar graphs represents the frequency of physically inactive and physically active participants at baseline, 3-month and 12-month follow-up in the exercise group (n=43) and the control group (n=44). Physically active;  $\geq 60$  min with moderate to vigorous activity.

Physically inactive; 0-420 min per week with light activity or 0-59 min with moderate to vigorous activity

*Figure 3.* The long-term effect of the 3-month supervised exercise programme on disease activity and physical function.

ASDAS-CRP, C-reactive protein based Ankylosing Spondylitis Disease Activity Score (inactive disease <1.3, low disease activity 1.3 to <2.1, high disease activity 2.1 -3.5, and very high disease activity >3.5); BASDAI, Bath Ankylosing Spondylitis Disease Activity Index (0-10, 10=worst); BASFI, Bath Ankylosing Spondylitis Functional Index (0-10, 10=worst).



Figure 1

| Table 2. Comparison of physical activity level at 12-month follow-up between the exercise- and the control group |                       |                      |         |  |
|--|-----------------------|----------------------|---------|--|
|  | Exercise group (n=44) | Control group (n=44) | p-value |  |
| <b>Exercise summary index</b> <sup>*</sup> (0-15, 15=high), median (min-max)                                     | 3.8 (0-15)            | 2.3 (0-15)           | 0.01    |  |
| Exercise frequency   |                       |                      |         |  |
| Never (0)  | 3 (7%)                | 2 (5%)               | 0.63    |  |
| <1 times per week (0.5)  | 2 (5%)                | 10 (23%)             | 0.02    |  |
| 1 per week (1)   | 7 (16%)               | 8 (18%)              | 0.81    |  |
| 2-3 per week (2.5)   | 25(58%)               | 15 (34%)             | 0.02    |  |
| Almost every day (5)   | 6 (14%)               | 9(21%)               | 0.42    |  |
| Exercise intensity <sup>†</sup>  | n=36                  | n=31                 |         |  |
| Not out of breath or sweating (1)  | 2 (6%)                | 13 (42%)             |         |  |
| Out of breath and sweating (2)   | 25 (69%)              | 15 (48%)             | 0.001   |  |
| Almost exhausted (3)   | 9 (25%)               | 3 (10%)              |         |  |
| Exercise duration <sup>+</sup>   | n=38                  | n=31                 |         |  |
| <15 minutes (0.10)   | 0 (0%)                | 0 (0%)               |         |  |
| 16-30 minutes (0.38)   | 1 (3%)                | 6 (19%)              |         |  |
| 30-60 minutes (0.75)   | 27 (71%)              | 19 (61%)             | 0.07    |  |
| >1 hour (1.0)  | 10 (26%)              | 6 (19%)              |         |  |
| Exercise mode  | n=43                  | n=44                 |         |  |
| Cardiorespiratory  | 26 (60%)              | 6 (14%)              | <0.001  |  |
| Muscular strength  | 21 (49%)              | 5 (11%)              | <0.001  |  |
| Cardiorespiratory and muscular strength  | 17 (39%)              | 3 (7%)               | <0.001  |  |
| Walking  | 18 (42%)              | 23 (52%)             | 0.30    |  |
| Pool exercises   | 8 (19%)               | 14 (32%)             | 0.14    |  |
| Physical activity level (METs)   | n=44                  | n=44                 |         |  |
| Total METs, median (min-max)   | 1886 (0-17 892)       | 1386 (0-9600)        | 0.83    |  |
| METs vigorous  | 720 (0-10 080)        | 0 (0-7200)           | 0.15    |  |
| METs moderate  | 120 (0-5040)          | 160 (0, 5040)        | 0.95    |  |
| METs walking   | 363 (0-4158)          | 495 (0-4158)         | 0.21    |  |

\*Calculated based on exercise frequency, duration and intensity with the scores for each response given in the parentheses

<sup>+</sup> Only participants that are exercising  $\geq$ 1 per week are asked about intensity/duration of exercise

MET, Metabolic equivalent

| Table 3. Factors associated with being physically active at 12-month follow-up. |
|---|
| A total of 42 of 87 (48%) participants were physically active.                  |
|   |

|  | Crude estimates     | p-value | Adjusted estimates <sup>3</sup> | p-value |
|--|---------------------|---------|---------------------------------|---------|
|  | Odds ratio (95% CI) |         | Odds ratio (95% CI)             |         |
| Age  |                     |         |                                 |         |
| Continuous   | 1.00 (0.96, 1.04)   | 0.88    | 0.99 (0.95, 1.04)               | 0.79    |
| Gender   |                     |         |                                 |         |
| Male   | Reference           |         | Reference                       |         |
| Women  | 1.38 (0.59, 3.20)   | 0.46    | 1.51 (0.57, 4.02)               | 0.41    |
| Physical activity at baseline <sup>*</sup>   |                     |         |                                 |         |
| Inactive at baseline   | Reference           |         | Reference                       |         |
| Physically active at baseline  | 2.57 (0.95, 6.92)   | 0.062   | 4.73 (1.42, 15.75)              | 0.01    |
| Intervention   |                     |         |                                 |         |
| Control group  | Reference           |         | Reference                       |         |
| Exercise group   | 4.94 (1.99, 12.26)  | 0.001   | 6.72 (2.42, 18.63)              | <0.001  |
| <sup>*</sup> Physically active was defined as ≥1 hour per week with moderate/vigorous physical activity at baseline and physically |                     |         |                                 |         |
| inactive was defined as 0-420 minutes with light activity and <60 minutes with moderate/vigorous activity.                         |                     |         |                                 |         |
|  |                     |         |                                 |         |

| Table 1. Baseline descriptive of all participants, the exercise group and the control group                    |  |                        |                 |  |
|--|--|------------------------|-----------------|--|
|  | All Exercise group Control gro   |                        | Control group   |  |
|  | (n=100)  | (n=50)                 | (n=50)          |  |
| Age, years, mean (min-max)   | 46.2 (23-69)   | 45.1 (23-68)           | 47.2 (24-69)    |  |
| Sex, male, n (%)   | 47 (47%)   | 25 (50%)               | 22 (44%)        |  |
| Radiographic axSpA   | 70 (70%)   | 38 (76%)               | 32 (64%)        |  |
| Married/cohabitant   | 76 (76%)   | 39 (78%)               | 37 (74%)        |  |
| In work, n (%)   | 81 (81%)   | 42 (78%)               | 39 (78%)        |  |
| Current smoking, n (%)   | 12 (12%)   | 5 (10%)                | 7 (14%)         |  |
| Height, cm, mean (SD)  | 172 (11)   | 172 (11)               | 172 (11)        |  |
| Weight, kg, mean (SD)  | 82.9 (17.9)  | 81.5 (19.4)            | 83.1 (19.5)     |  |
| Medication   |  |                        |                 |  |
| NSAIDs, n (%)  | 71 (71%)   | 38 (76%)               | 33 (66%)        |  |
| TNF-inhibitor, n (%)   | 44 (44%)   | 23 (46%)               | 21 (42%)        |  |
| Disease characteristics  |  |                        |                 |  |
| Disease activity (ASDAS-CRP), mean (SD)  | 2.6 (0.7)  | 2.6 (0.8)              | 2.7 (0.6)       |  |
| Disease activity (BASDAI), mean (SD)   | 5.1 (1.6)  | 4.9 (1.6)              | 5.3 (1.5)       |  |
| CRP (mg/L), median (min-max)   | 2 (2-28)   | 2 (2-28)               | 2 (2-13)        |  |
| ESR (mm/h), median (min-max)   | 8 (1-67)   | 8 (2-67)               | 8 (1-28)        |  |
| Physical function (BASFI), median (min-max)  | 3.2 (0.2-9.1)  | 2.6 (0.2-6.7)          | 3.0 (0.4-9.1)   |  |
| Spinal flexibility (BASMI), mean (SD)  | 2.8 (1.3)  | 2.9 (1.3)              | 2.6 (1.3)       |  |
| Cardiorespiratory fitness (VO <sub>2</sub> peak), mean (SD)  | 35.7 (36.3)  | 36.0 (5.9)             | 35.4 (6.9)      |  |
| ASDAS-CRP, C-reactive protein based Ankylosing Spon  | dylitis Disease Activ  | ity Score (inactive di | sease <1.3, low |  |
| disease activity 1.3 to <2.1, high disease activity 2.1 -3   | disease activity 1.3 to <2.1, high disease activity 2.1 -3.5, and very high disease activity >3.5); BASDAI, Bath |                        |                 |  |
| Ankylosing Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing |  |                        |                 |  |
| Spondylitis Metrology Index (All BAS instruments [0-10, 10=worst]); CRP, C-reactive protein; ESR, Erythrocyte  |  |                        |                 |  |
| sedimentation rate; NSAIDS, non-steroidal anti-inflammatory drugs; VO2peak, peak oxygen uptake.                |  |                        |                 |  |

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|  |                     |         |                                 |         |