

## Running head: HIIT in PsA

# The impact of high intensity interval training on disease activity and patient disease perception in patients with psoriatic arthritis: a randomized controlled trial.

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## **ABSTRACT**

### **Objective**

The aim of this study was to evaluate the impact of high intensity interval training (HIIT) on disease activity and patient disease perception in patients with psoriatic arthritis (PsA), and evaluating if a potential effect could be sustained for a longer period.

**Methods** We randomly assigned 67 PsA patients (43 women and 24 men) to an intervention group performing HIIT for 11 weeks or a control group who were instructed to not change their physical exercise habits. Outcomes were assessed at three and nine months with the patient global assessment (PGA), fatigue, and pain measured on a 100 mm visual analog scale and the composite disease activity score of 44 joints (DAS44) was calculated. We used linear mixed models to calculate mean difference with 95% confidence interval (CI) between the groups according to the intention-to-treat principle.

**Results** At three months there was no clear difference in PGA (-0.49; 95% CI -10.91 to 9.94), DAS44 (-0.08; 95% CI -0.36 to 0.20) or pain intensity (5.45; 95% CI -4.36 to 15.26) between the groups. However, the HIIT group reported less fatigue (-12.83; 95% CI -25.88 to 0.23) than the control group. There was no evidence of long-term effects of HIIT on outcomes measured at nine months.

**Conclusion** HIIT showed no clear effects on disease activity markers in patients with PsA, but the exercise group reported meaningfully less fatigue after the intervention period. This study suggests that PsA patients tolerate HIIT without deterioration of disease activity and with improvement in fatigue.

**Keywords** Psoriatic Arthritis, Disease Activity, Fatigue, Physical Activity, Clinical Trial

**Trial Registration** ClinicalTrials.gov NCT02995460

### **Significance and Innovations**

- Physical exercise is recommended for all patients with arthritis, although there is little evidence for its utility in psoriatic arthritis (PsA). Further, there are no recommendations on the type and intensity of exercise for PsA patients.
- High intensity interval training did not result in deterioration of disease activity or patient disease perception in patients with PsA.
- Fatigue improved after high intensity interval training.
- High intensity interval training may be a relevant mode of physical exercise among PsA patients.

Psoriatic arthritis (PsA) is a chronic heterogeneous inflammatory disease. Inflammation in the musculoskeletal system may present as enthesitis, dactylitis, arthritis and spondylitis. The consequence for the PsA patient may include fatigue, pain, impaired physical function and reduced quality of life (QoL).(1-3) With standard treatment, using synthetic and biologic disease modifying anti-rheumatic drugs (DMARDs), the aim is to reduce inflammatory activity.(4) However, medical treatments do not always appear to eliminate symptoms like fatigue and pain, which are significantly related to QoL.(4)

Physical exercise is recommended as a supplement to medical therapy for all patients with arthritis, although there is little evidence for its utility in PsA.(5) High intensity interval training (HIIT) is a system of organizing cardiorespiratory training with repeated bouts of short duration, high-intensity exercise intervals at 80-95% of maximum heartrate ( $HR_{max}$ ) interrupted by periods of lower intensity intervals of active recovery.(6) The impact and tolerability of HIIT in PsA is unknown. Further, there are no recommendations on type and intensity of exercise for PsA patients. There is also a concern that vigorous physical exercise may cause increased disease activity in PsA patients by generating more enthesitis. This relates to the notion that mechanical strain can drive entheseal inflammation.(7, 8)

The aim of this randomized controlled trial in PsA patients was to evaluate the impact of HIIT on disease activity and patient disease perception, and to evaluate if a potential effect could be sustained for a longer period.

## **PATIENTS AND METHODS**

### **Design**

We conducted a randomized controlled trial (RCT) with two parallel groups, comparing an intervention group performing HIIT three times per week for 11 weeks to a control group with no change in pre-study physical exercise habits. The study was conducted according to

Good Clinical Practice and Declaration of Helsinki principles. The trial was approved by the regional ethical committee (RECNr 2012/1646) and registered in ClinicalTrials.gov (NCT02995460). Results are presented according to the CONSORT statement.(9)

### **Participants**

All eligible PsA participants, age 18-65 years fulfilled the CLASSification for Psoriatic ARthritis (CASPAR) criteria. Exclusion criteria included: patients with inability to exercise; patients with unstable ischemic cardio vascular disease or severe pulmonary disease; an anticipated need for a change in synthetic or biologic DMARDs during the intervention period (However, a change of DMARDs was possible during the follow-up period from three to nine months. A change in corticosteroid doses and intra-articular corticosteroid injections were allowed until four weeks before any follow-up); pregnancy; breastfeeding; and drug or alcohol addictions. In addition, the investigator interviewed the participants about physical exercise habits. Those who reported vigorous endurance training like running, bicycling etc once or more a week for the last three months were excluded. Participants were recruited through local advertisement at the Department of Rheumatology, St. Olavs hospital; The Psoriasis and Eczema Association of Norway; and The Norwegian Rheumatism Association. The study was conducted at St. Olavs hospital and NTNU - Norwegian University of Science and Technology, Trondheim, Norway from 2013 to 2015.

### **Intervention**

At baseline the participants performed a max-test measuring their  $HR_{max}$  and maximal oxygen uptake ( $VO_{2max}$ ) on a stationary bicycle.(10) All tests were carried out at the Cardiac Exercise Research Group (CERG), NTNU. The exercise intervention was performed as a supervised HIIT program starting with a 10 minutes of warm up, followed by four times four minutes exercise at 85-95 % of  $HR_{max}$  interrupted by three minutes exercise at 70 % of the

HR<sub>max</sub>.<sup>(11)</sup> The supervised HIIT was performed on a stationary bicycle at CERG twice a week with an intermitting day of rest. The supervisors were students from physiotherapy and physiology and they were experienced in guiding a HIIT. One supervisor guided a maximum of six participants at a time. Additionally, the participants did one self-guided HIIT a week. They were instructed in using the HIIT concept by e.g. running, bicycling or walking uphill. All exercises were supported by a heart rate monitor. During the period of follow-up from three to nine months, the participants in the HIIT group were encouraged to keep on exercising, but without guidance. To reinforce adherence to the training program diaries were delivered by the HIIT group every week during the intervention period from baseline to three months, and included information on the type of exercise, time, location, and with whom it was performed. Moreover, the intensity was rated by the registered pulse and by the 15 point Borg scale (from 6-20), the latter being a method of rating perceived exertion.<sup>(12, 13)</sup> Participants in the control group were instructed to not change their pre-study physical exercise habits. However, in the follow-up period from three to nine months they were allowed to start exercising.

### **Assessment of outcome measures**

Outcome measures were assessed at baseline, and at three and nine months of follow-up. These included questionnaires, clinical examinations and laboratory measurements. An experienced rheumatologist (RST) performed the clinical examinations including joint and entheses assessment. Blood samples and baseline body mass index were assessed at the Department of Research and Development, St. Olavs hospital. Demographics, disease measures, comorbidities and medication were obtained from the medical journal system and the GoTreatIT<sup>®</sup> Rheuma computer tool,<sup>(14)</sup> the latter developed for use in daily clinical care and for research purposes ([www.diagraphit.com](http://www.diagraphit.com)).

### *Main outcome measure*

The main outcome was patient global assessment (PGA) based on the question “In all the ways in which your PSORIASIS and ARTHRITIS, as a whole, affects you, how would you rate the way you felt over the past week?” and reported on a 100 mm visual analogue scale (VAS). PGA has been found to be a reliable tool in the assessment of both joint and skin disease(15) and a PGA  $\leq 20$  is defined as low disease activity.(16)

### *Secondary outcome measures*

Patients reported fatigue and intensity of pain on a 100 mm VAS. Fatigue was based on the question “To what degree has unusual tiredness or exhaustion been a problem for you the last week?” and pain on the question “How much pain did you experience during the last week?” A change in VAS of  $\geq 10$  mm is considered as the minimal clinically important difference.(17)

Peripheral joint inflammation was assessed by the disease activity score using 44 joints count of tender and swollen joints (DAS44).(18) This is a composite score combining information on the number of tender and swollen joints, PGA, and high sensitivity C-reactive protein (HS-CRP), mg/L.(19) DAS44 was chosen instead of DAS28 since joints in the ankle and feet are included.

Axial inflammation was evaluated by the Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) which is a continuous score based on four questions and level of HS-CRP.(20)

The burden of enthesitis was defined by the Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC-EI) where 18 enthesial sites are examined for the presence or absence of tenderness that provides a score ranging from 0-16.(21, 22)

### *Sample size*

A difference in the main outcome measure (PGA) of 10 mm in VAS (0-100 mm) was considered clinically important,(17) and based on a standard deviation of 15 and a correlation of 0.4 between repeated measures(23) we estimated that 30 patients were required in each group to achieve a power of 90 % at an alpha level of 0.05.

### **Randomization and blinding**

Patients were randomized to either a HIIT group or control group according to a 1:1 allocation in permuted blocks after the signed consent and clinical investigation using a computer random-number-generator (Unit for Applied Clinical Research, St. Olavs hospital). Participants were stratified according to sex. The block randomization did not allow the researchers to reveal the next allocations. The rheumatologist (i.e., one of the researchers) was blinded to the group allocation at baseline evaluations, but not at three and nine months follow-up. The assessors at the laboratory (blood samples) were blinded through all follow-ups.

### **Statistical analyses**

The main analyses of both primary and secondary outcomes were conducted according to an intention to treat strategy using all available data from all time points. We used a linear mixed model for repeated measures to estimate mean difference with 95% confidence interval (CI) in outcome variables between the HIIT group and the control group at three and nine months after randomization. Changes from baseline to three and nine months were calculated using a joint baseline level of the outcome measure, assuming that any baseline differences between groups are due to chance. From these models, we also estimated mean change in outcome variables within each group.

All measures of effect were adjusted for sex (men, women) and age (continuous). Due to non-normal distribution of HS-CRP we used a logarithmic transformation of the variable in



the regression model before transforming back the estimates. The results for HS-CRP are thus expressed as geometric means.

Logistic regression analysis were performed to calculate the odds ratio (OR) with 95 % CI for worsening in SPARCC-EI between the HIIT group and the control group. The difference in SPARCC-EI between baseline and three months was used to classify patients as having worse or same/improved enthesitis burden.

The diaries were reviewed to find the number of accomplished supervised and self-guided exercises. The mean intensity referring to the BORG scale was calculated according to the values recorded in the diaries.

Descriptive statistics are presented as means and standard deviation (SD), or as median and interquartile range for non-normally distributed variables. All statistical analyses were conducted using STATA version 14.2 (StataCorp. 2015. College Station, TX: StataCorp LP).

## **RESULTS**

### **Participant flow and characteristics**

A total of 102 patients were assessed for eligibility of whom 35 were excluded due to exclusion criteria or withdrawal (Figure 1). This left 67 eligible patients for randomization and allocation to either the HIIT (n=32) or control group (n=35). More women than men were included in the study (66 % and 63 % in HIIT and control groups, respectively) and the mean age was 51 (SD 11) in the HIIT group and 46 (SD 12) years in controls. Baseline characteristics are presented in Table 1.

The participants in the HIIT group delivered completed diaries for 95 % of all the weeks. The completion of the guided exercises was 78 % of sessions. However, they did more self-guided endurance exercises than requested, i.e. 1.2 times a week. According to diaries, the mean intensity during guided exercise was 16.4 (SD 3.3) referring to the Borg scale which is

considered 'very hard' effort. The intensity during self-guided exercise was 12.8 (SD 3.4) referring to the Borg scale which is considered 'moderate' effort. At nine months of follow-up 28 participants remained in each arm. Of these, 12 (43 %) in the HIIT and 5 (18 %) in the control group reported that they were doing endurance exercise.

### **Effect on outcome measures at three months**

Overall, there was no clear difference in PGA (-0.49 mm; 95% CI -10.91 to 9.94), DAS44 (-0.08 mm; 95% CI -0.36 to 0.20), pain intensity (5.45 mm; 95% CI -4.36 to 15.26), ASDAS-CRP (-0.14; 95% CI -0.53 to 0.25), or HS-CRP (-0.11 mg/L; 95% CI -0.97 to 0.75) between the groups at three months (Table 2). Although there were no differences in disease activity and pain measures, the HIIT group reported lower fatigue than controls (-12.83 mm; 95 % CI -25.88 to 0.23). Moreover, within-group analyses showed that both groups experienced reductions in PGA, pain intensity, DAS44 and fatigue levels from baseline to three months. There was no difference in change of SPARCC-EI between the two groups with an OR of 0.80 (95 % CI 0.19 to 3.35) for worsening comparing the HIIT with the control group.

### **Outcome at nine months of follow-up**

At nine months of follow-up, there were no clinically important differences between the two groups for all outcome measures (Table 3). Similar to three months data, there was some decline in most of the outcome variables from baseline to nine months, although the magnitude of change was small.

### **Safety**

During the period of intervention from baseline to three months, two in the HIIT group and none in the control group had intra-articular injections. Injections were given one month after start of the intervention. At the three months follow-up, four patients in the HIIT group and three in the control group had intra-articular injections. In the three to nine months

follow-up, four in the HIIT group and seven in the control group had intra-articular injections. None of the injections were given closer than four weeks prior to DAS44 evaluations. One patient left the HIIT group due to sequelae after stroke previous to the study and found the intervention too tough. No other adverse events were reported during the intervention.

## **DISCUSSION**

In this RCT, we found that although HIIT in patients with PsA had no effect on markers of disease activity, patients performing HIIT had a clinically relevant improvement in fatigue at three months, compared to controls. Unfortunately, there were no longer clinically relevant effects of HIIT at nine months. To our knowledge, this is the first study investigating the impact of HIIT on disease activity and patient disease perception in PsA. Previous studies in rheumatoid arthritis (RA) and spondyloarthritis (SpA) suggest reduced inflammatory activity after HIIT.(24-26) Otherwise, the concept of HIIT, performed at 85-95 % of HR<sub>max</sub>, has mainly been associated with an increased cardiorespiratory fitness.(11, 27)

Disease activity, assessed by both by the primary outcome measure PGA and the secondary outcome measures DAS44, ASDAS-CRP and HS-CRP were either reduced or stable within each study group. One could have hypothesized before the study that an increase in disease activity might result from performing vigorous exercise in PsA, especially for enthesitis.(7) Encouragingly, this was not observed.

At inclusion, the PGA indicated a higher disease activity than judged by the DAS44 and HS-CRP. Discrepancy between physicians and patients` perception of disease activity is a well-known phenomenon.(28-30) Both physicians and patients` perception as well as the HS-CRP level influence the DAS score. Further, PGA could also be influenced by other factors than disease activity,(31, 32) for instance experience of pain for other reasons than inflammatory disease activity. A recent study suggests an association between physical exercise and

skeletal damage related to the Achilles tendon insertion in PsA.(33) However, the type of exercise was not defined. In our patients, SPARCC-EI did not increase more in the HIIT group compared to controls and ASDAS-CRP showed a reduction after 3 months. A partial explanation may be that the supervised exercise was performed on a stationary bicycle versus a treadmill, minimizing the mechanical stress to lower limbs and back.

Interestingly, we observed that patients in the HIIT group had a clinically relevant improvement in fatigue at three months compared to controls. However, this difference in fatigue score was not evident at nine months when physical activity was not maintained.

Although fatigue is a major problem in PsA,(1) its etiology is not well understood. Partially, it could be explained by inflammation,(34) and a higher degree of fatigue has been associated with a higher disease activity measured by enthesitis, joint count and skin disease.(1, 35) In a multicenter cross-sectional study it was found that fatigue among patients with PsA was associated with female gender; level of education; skin psoriasis; enthesitis; as well as tender and swollen joints.(1) Among our participants, the association to female gender was possible since two thirds were women but an association with disease activity was not apparent. In RA patients, increased fatigue seems to be associated with increased pain.(32) We observed no strong effect on pain intensity in parallel to the reduction of fatigue in our data.

However, the baseline pain score among our patients was mild to moderately high,(36) and thus the potential for a reduction in pain could be lower than among people with higher pain intensity levels. Another explanation for the reduction in fatigue score could be an exercise induced endorphin response(37) or improvement in aerobic capacity.(38) Nevertheless, the effect on fatigue in our study is in line with results from previous studies investigating physical exercise in patients with SpA and RA.(39-41) Furthermore, graded aerobic exercise

at 40 -70% of  $HR_{max}$  has been reported to reduce fatigue in people with chronic fatigue syndrome.(42)

After the three months intervention period, the participants were responsible for the exercise themselves and less than half of the HIIT group managed to continue exercising. Moreover, for those who did exercise, the intensity level was usually reduced. Patients in the control group were encouraged to exercise, but only 18 % managed to start with endurance exercises. The lack of persistence could explain why the effect on fatigue in the HIIT group was not sustained. This may emphasize that PSA patients need continuous motivation to perform physical exercise, and this has also been suggested by others.(41, 43)

The observed minor reduction in all of the outcome measures in both groups may be explained by the “Hawthorne effect”, that people change their behaviors when they know they are being observed.(44)

A strength of this study was the randomized design; both groups had the same type and amount of follow-up; and the diagnosis was confirmed before enrollment by an experienced rheumatologist. In the HIIT group, the adherence to the guided exercises was good and the exercises were performed with a high intensity according to the diaries. The drop-out rate was only 12.5% in the HIIT group, but a little higher among controls (17.1%). Moreover, disease duration and disease activity measured by PGA are comparable to that of other PsA patients in Norway,(45) indicating that the external validity of our results is high. The baseline median number of swollen joint count was low, but a risk of a flare caused by mechanical stress would be likely even with low disease activity. On the other hand, an improvement in disease activity would be less likely with a low baseline value.

The need for intra-articular injections during the study could be considered as adverse events. However, a total of ten intra-articular corticosteroid injections in each group during

the total study period could be due to flares caused by a natural disease course. The injections were given at least four weeks prior to any follow-up and therefore should not affect the result of the DAS44. Other limitations included the relatively small sample size that reduces the precision of the estimated effects. Further, ideally all of the HIIT sessions ought to be guided, but for practical reasons and time constraints for the participants, only two of three exercises were supervised. This could have resulted in lower exercise intensities for the unsupervised sessions, and consequently a smaller observed effect of HIIT between the groups. In addition, the controls were allowed to practice endurance exercises from three to nine months to enhance their willingness to participate in the study. This could mask potential long-term effects. However, only 5 of the 28 participants in the control group reported vigorous exercise during this period.

Furthermore, patients who volunteer to participate in a trial involving physical exercise might be more experienced with physical activity and exercise than non-participants, thereby reducing the generalizability of our results. In addition, the lack of blinded intervention and assessment could potentially have influenced the results. Moreover, patient reported outcome measures might be difficult to interpret since other issues than actual disease activity, such as permanent damage, psychological distress and comorbidities, could influence the reporting.(46) In addition, we cannot rule out that controls might have performed endurance exercise during the intervention period. Finally, HIIT is a method of exercise that may be hard to perform without guidance over time.

## **CONCLUSIONS**

No clear effects on disease activity markers and pain were observed after HIIT in PsA patients. However, fatigue improved during the HIIT period. Thus, we conclude that HIIT was well tolerated in PsA patients evaluated both by measures of disease activity and patient

disease perception. However, the benefit does not last if HIIT is not maintained. A challenge and a goal for health care providers is to motivate and encourage the patients to remain physical active.

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**Author contributions** RST: conception and design of the trial, performing the trial, statistical analyses and interpretation of the data, writing. TIL: statistical analyses and interpretation of the data, writing. GH: interpretation of the data, writing. AB: design of the trial, writing. AK: interpretation of the data, writing. MH: conception and design of the trial, interpretation of the data, writing.

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**Competing interests** None.

**Patient consent** Obtained.

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**Supporting Information** CONSORT Checklist

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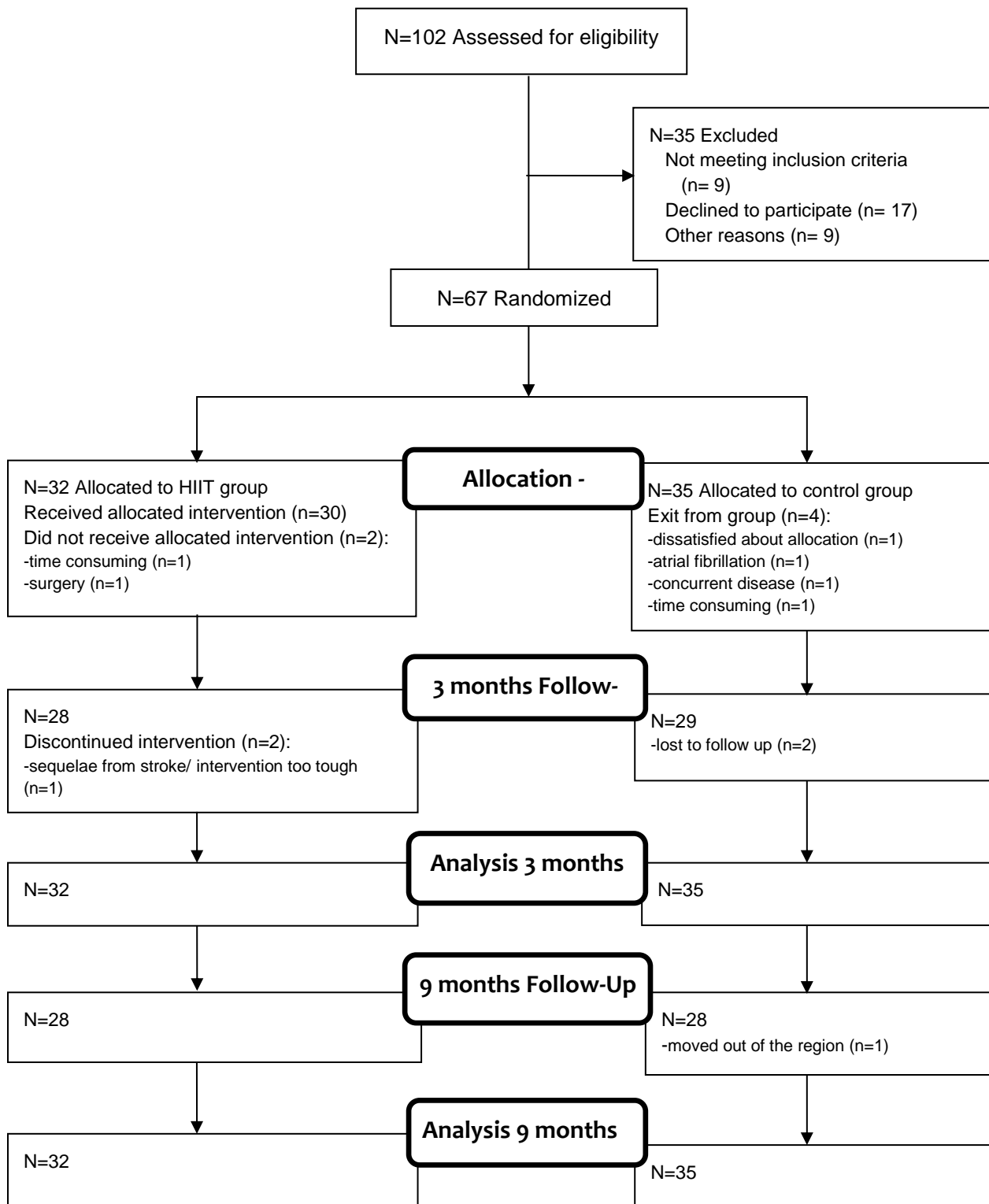


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## FIGURE LEGENDS

**Figure 1** Participant flow through the study. *N* numbers of subjects, *HIIT* high intensity interval training.



**Table 1** Baseline characteristics of psoriatic arthritis patients in the intervention and control groups

	<b>Intervention (N=32)</b>	<b>Control (N=35)</b>
<b>Age, years, Mean(SD)</b>	50.7 (11.0)	45.6 (11.5)
<b>Female, n(%)</b>	21 (66)	22 (63)
<b>Disease duration, years, Median (p25, p75)</b>	5.5 (2-12)	3 (2-11)
<b>Synthetic DMARDS, n (%)</b>	29 (91)	28 (80)
<b>Biologic DMARDS, n (%)</b>	11 (34)	10 (29)
<b>VO2 max (ml/kg/min), Mean(SD)*</b>	28.73 (6.41)	30.75 (7.95)
<b>Current smoker, n (%)</b>	6 (19)	5 (14)
<b>BMI (kg/m<sup>2</sup>), Mean (SD)</b>	28.6 (4.1)	28.0 (4.5)
<b>HS-CRP (mg/L), Median (p25, p75)**</b>	1.67 (0.9-4.5)	1.87 (0.86-4.74)
<b>Patient global assessment (PGA) VAS 0 – 100, Mean(SD)</b>	37.4 (23.4)	42.9 (20.8)
<b>DAS44, Mean(SD)****</b>	1.98 (0.77)	2.00 (0.74)
<b>Tender joints 66, Median (p25, p75)</b>	4.5 (1-9)	6 (1-9)
<b>Swollen joints 68, Median (p25, p75)</b>	0 (0-1)	0 (0-2)
<b>Fatigue VAS 0 – 100, Mean(SD)***</b>	43.5 (30.7)	52.9 (28.2)
<b>Pain VAS 0 – 100, Mean(SD)</b>	35.3 (21.0)	39.2 (22.8)
<b>ASDAS-CRP, Mean(SD)****</b>	2.08 (0.96)	2.18 (0.89)

<b>SPARCC-EI, Median (p25, p75)</b>	<b>3 (1-6)</b>	<b>3 (0-5)</b>
<b>MHAQ, Median (p25, p75)</b>	<b>0.32 (0- 0.69)</b>	<b>0.38 (0.25- 0.63)</b>
<b>PASI, Median (p25, p75)</b>	<b>0 (0-1)</b>	<b>0.5 (0-2.7)</b>

Disease modifying anti-rheumatic drugs (DMARDS). Maximal oxygen uptake (VO2 max). High sensitivity-CRP (HS-CRP). Disease activity score of 44 joints (DAS44). Ankylosing Spondylitis Disease Activity Score - CRP (ASDAS-CRP). Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC-EI). Modified Health Assessment Questionnaire (MHAQ) Psoriasis Area Severity Index (PASI)

\*missing baseline for 4 participants in the control group and 2 in the intervention group

\*\*missing baseline for 4 participants in the control group and 1 in the intervention group

\*\*\*missing baseline for 1 in the control group

\*\*\*\*calculated based on regular CRP for those missing HSCR at baseline

**Table 2** Changes in outcome between the intervention group doing high intensity interval training and the control group and changes within the groups from baseline to three months of follow-up

<b>N=67</b>	<b>Baseline Mean Both groups</b>	<b>3 months Change from baseline</b>		<b>Mean Difference Between Groups 3 months</b>
		<b>Control</b>	<b>Intervention</b>	
<b>PGA</b> (VAS 0-100)	40.41	-5.37	-5.86	-0.49
95% CI	34.79 to 46.02	-13.12 to 2.37	-13.74 to 2.02	-10.91 to 9.94
p-value		0.17	0.15	0.93
<b>Fatigue</b> (VAS 0-100)	48.74	-3.03	-15.86	-12.83
95% CI	41.74 to 55.73	-12.82 to 6.75	-25.66 to -6.75	-25.88 to 0.23
p-value		0.54	0.002	0.05
<b>DAS44</b>	2.00	-0.30	-0.38	-0.08
95% CI	1.84 to 2.16	-0.50 to -0.09	-0.59 to -0.17	-0.36 to 0.20
p-value		0.004	<0.001	0.56
<b>Pain</b> (VAS 0-100)	37.57	-11.03	-5.58	5.45
95% CI	32.49 to 42.65	-18.38 to -3.68	-13.06 to 1.90	-4.36 to 15.26
p-value		0.003	0.14	0.28
<b>ASDAS-CRP</b>	2.14	-0.17	-0.31	-0.14
95% CI	1.91 to 2.36	-0.46 to 0.12	-0.60 to -0.02	-0.53 to 0.25
p-value		0.24	0.04	0.49
<b>HS-CRP*</b> (mg/L)	1.87	-0.00	-0.11	-0.11
95% CI	1.33 to 2.42	-0.65 to 0.64	-0.74 to 0.52	-0.97 to 0.75
p-value		0.99	0.73	0.81

PGA, Patient Global Assessment; DAS44, Disease activity score of 44 joints; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score - CRP; HS-CRP, High sensitivity-CRP.

Baseline-data on PGA, DAS44, pain, ASDAS from 67 patients; on fatigue from 66; on HS-CRP from 62.

Adjusted for age and sex.

\*geometric mean

**Table 3** Changes in outcome between the intervention group doing high intensity interval training and the control group and changes within the groups from baseline to nine months of follow-up

<b>N=67</b>	<b>Baseline Mean Both groups</b>	<b>9 months Change from baseline</b>		<b>Mean Difference Between Groups 9 months</b>
		<b>Control</b>	<b>Intervention</b>	
<b>PGA</b> (VAS 0-100)	40.41	-6.35	-5.36	0.99
95% CI	34.79 to	-14.20 to	-13.24 to	-9.51 to 11.49
p-value	46.02	1.50	2.52	0.85
		0.11	0.18	
<b>Fatigue</b> (VAS 0-100)	48.74	-7.92	-2.72	5.20
95% CI	41.74 to	-17.92 to	-12.52 to	-8.00 to 18.41
p-value	55.73	2.08	7.08	0.44
		0.12	0.59	
<b>DAS44</b>	2.00	-0.34	-0.16	0.18
95% CI	1.84 to 2.16	-0.54 to -0.13	-0.37 to 0.05	-0.10 to 0.46
p-value		0.001	0.13	0.22
<b>Pain</b> (VAS 0-100)	37.57	-7.94	-4.29	3.64
95% CI	32.49 to	-15.39 to -	-11.77 to	-6.23 to 13.51
p-value	42.65	0.49	3.18	0.47
		0.04	0.26	
<b>ASDAS-CRP</b>	2.14	-0.17	-0.01	0.16
95% CI	1.91 to 2.36	-0.46 to 0.12	-0.30 to 0.29	-0.23 to 0.56
p-value		0.26	0.96	0.42
<b>HS-CRP*</b> (mg/L)	1.87	-0.04	0.63	0.67
95% CI	1.33 to 2.42	-0.69 to 0.61	-0.22 to 1.48	-0.39 to 1.72
p-value		0.92	0.11	0.20

PGA, Patient Global Assessment; DAS44, Disease activity score of 44 joints; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score - CRP; HS-CRP, High sensitivity-CRP.

Baseline-data on PGA, DAS44, pain, ASDAS from 67 patients; on fatigue from 66; on HS-CRP from 62.

Adjusted for age and sex.

\*geometric mean