

## ORIGINAL ARTICLE

# Effect of high-intensity interval training on cardiovascular disease risk factors and body composition in psoriatic arthritis: a randomised controlled trial

Ruth Stoklund Thomsen,<sup>1,2</sup> Tom Ivar Lund Nilsen,<sup>1,3</sup> Glenn Haugeberg,<sup>4,5</sup>  
Anja Bye,<sup>6,7</sup> Arthur Kavanaugh,<sup>8</sup> Mari Hoff<sup>1,2,4</sup>

**To cite:** Thomsen RS, Nilsen TIL, Haugeberg G, *et al.* Effect of high-intensity interval training on cardiovascular disease risk factors and body composition in psoriatic arthritis: a randomised controlled trial. *RMD Open* 2018;**4**:e000729. doi:10.1136/rmdopen-2018-000729

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/rmdopen-2018-000729>).

Received 18 May 2018

Revised 18 July 2018

Accepted 9 September 2018

## ABSTRACT

**Background** Psoriatic arthritis (PsA) is associated with an accumulation of cardiovascular disease (CVD) risk factors. The aim of this study was to evaluate the effect of high-intensity interval training (HIIT) on CVD risk factors in patients with PsA.

**Methods** We randomly assigned 61 patients with PsA (41 women and 20 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 3 and 9 months with measures on maximal oxygen uptake ( $VO_{2max}$ ), fat percentage and Body Mass Index (BMI). We used linear mixed models to calculate mean difference with 95% CI between the groups according to the intention-to-treat principle.

**Results** At 3 months, the HIIT group had a 3.72 mL/kg/min (95% CI 2.38 to 5.06) higher  $VO_{2max}$  and a 1.28 (95% CI -2.51 to -0.05) lower truncal fat percentage than controls. There was also some evidence that the HIIT group had lower total fat percentage (-0.80; 95% CI -1.71 to 0.10) and slightly lower BMI (-0.31; 95% CI -0.78 to 0.17) than the control group. At 9 months, the HIIT group had still a higher  $VO_{2max}$  (3.08; 95% CI 1.63 to 4.53) than the control group, whereas the difference in other factors were small.

**Conclusion** In patients with PsA, 3 months with HIIT was associated with a substantial increase in  $VO_{2max}$  and a reduction in truncal fat percentage compared with controls. The beneficial effect on  $VO_{2max}$  was also sustained through 9 months.

**Trial registration number** NCT02995460.

## INTRODUCTION

Psoriatic arthritis (PsA) is an inflammatory chronic disease with manifestations such as arthritis, enthesitis, dactylitis and spondylitis. PsA is also associated with obesity, dyslipidemia and insulin resistance, key aspects of the metabolic syndrome, which increases patients' risk of cardiovascular disease (CVD) and mortality.<sup>1-5</sup>

## Key messages

### What is already known about this subject?

- Physical exercise is recommended for patients with psoriatic arthritis (PsA), although there is little evidence for its use and there are no recommendations on the type and intensity of exercise for patients with PsA.
- High-intensity interval training (HIIT) is a kind of cardiorespiratory training that has been proven to increase cardiorespiratory fitness in healthy people. Cardiorespiratory fitness is a predictor of cardiovascular disease.

### What does this study add?

- HIIT for 3 months resulted in a substantial increase in maximal oxygen uptake and reduced the truncal fat mass in patients with PsA.

### How might this impact on clinical practice?

- The findings from this study indicates that HIIT could also be beneficial in patients with PsA in preventing cardiovascular disease by increasing cardiorespiratory fitness and reducing abdominal fat.

Cardiorespiratory fitness is known to be a strong, independent predictor for CVD and all-cause mortality in the general population.<sup>6,7</sup> Measuring the maximal oxygen uptake ( $VO_{2max}$ ) is considered the gold standard of assessing cardiorespiratory fitness, and it is carried out by a cardiopulmonary exercise test to exhaustion.<sup>8</sup>  $VO_{2max}$  commonly increases by an average of ~3%–35% with regular endurance training in a dose-dependent manner,<sup>9-11</sup> and a 3.5 mL/kg/min increase in  $VO_{2max}$  has been associated with 13% decreased risk of death from all causes.<sup>6</sup> Studies have demonstrated that patients with arthritis, including PsA, have a reduced cardiorespiratory fitness, likely due to factors such as a more sedentary lifestyle.<sup>12-14</sup>



© Author(s) (or their employer(s)) 2018. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Ruth Stoklund Thomsen;  
ruth.thomsen@ntnu.no

High-intensity interval training (HIIT) is a method of organising cardiorespiratory training with repeated bouts of short-duration, high-intensity exercise intervals at 80%–95% of maximum heart rate ( $HR_{max}$ ) interrupted by periods of active recovery.<sup>8</sup> Several studies have shown that HIIT increases cardiorespiratory fitness more than moderately intense physical exercise and is less time consuming.<sup>9 15 16</sup>

With the increased CVD morbidity and mortality in PsA, it is important to explore alternative methods to reduce the CVD risk factors since treatment with disease-modifying medication alone is insufficient. There is a paucity of evidence regarding the effects of physical exercise in PsA. Given many patients' unfavourable CVD risk profile, it seems reasonable to recommend physical exercise.

The aim of this study was to evaluate the effect of HIIT on CVD risk factors such as cardiorespiratory fitness and body composition in patients with PsA. Furthermore, we aimed to see if any benefit was enduring beyond the study time.

## METHODS

### Design

We conducted a randomised controlled trial (RCT) with two parallel groups, comparing an intervention group performing HIIT three times per week for 11 weeks with 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. Results are presented according to the Consolidated Standards of Reporting Trials statement.<sup>17</sup>

### Participants

To be eligible, patients with PsA needed to be between ages 18 and 65 years and fulfil the CASPAR (Classification for Psoriatic ARthritis) criteria. Exclusion criteria included patients with inability to exercise; patients with unstable ischaemic CVD or severe pulmonary disease; pregnancy; breast feeding; drug or alcohol addictions; and an anticipated need for a change in synthetic or biologic disease-modifying antirheumatic drugs (DMARDs) during the intervention period. However, a change of DMARDs was possible during the follow-up period from 3 to 9 months. A change in corticosteroid doses and intra-articular corticosteroid injections were allowed until 4 weeks before any follow-up. In addition, the investigator interviewed the participants about physical exercise habits. Those who reported vigorous endurance training like running, bicycling and so on once or more a week for the last 3 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.

### Cardiorespiratory fitness testing

Maximal oxygen uptake ( $VO_{2max}$ ) was assessed with a maximal bicycling test on an ergometer bike (Monark 839 Medical) using a portable metabolic measurement system for measurements of gas exchange and ventilation (MetaMax II).<sup>18</sup> The test was initiated by a warm-up and proceeded by an increase in resistance and speed until subjects reached  $VO_{2max}$ . Levelling-off of oxygen uptake despite an increase in workload and respiratory exchange ratio  $>1.10$  were used as a criteria for reaching  $VO_{2max}$ . The highest HR was recorded during the  $VO_{2max}$  test and  $HR_{max}$  was then calculated by adding five beats to that value.<sup>19</sup>  $HR_{max}$  was used to calculate the required individual heart rate during the exercise intervention. All tests were performed at the Cardiac Exercise Research Group (CERG) by professionals with educational backgrounds in physiology and bioengineering, who were certified to do cardiorespiratory fitness testing by the CERG or NeXtMove facilities, NTNU.

### Intervention

The exercise intervention was performed as a supervised HIIT programme starting with a 10 min warm-up, followed by four times 4 min exercise at 85%–95% of  $HR_{max}$  interspersed by 3 min exercise at 70% of the  $HR_{max}$ .<sup>20</sup> The supervised HIIT was performed on a stationary bicycle at CERG twice a week with an intermitting day of rest. The supervisors were experienced in guiding a HIIT, and 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 for example, running, bicycling or walking uphill. All exercises were supported by a heart rate monitor. During the period of follow-up from 3 to 9 months, the participants in the HIIT group were encouraged to keep on exercising, but without guidance. To reinforce adherence to the training programme, diaries were delivered by the HIIT group every week during the intervention period from baseline to 3 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 heart rate and by the 15-point Borg scale (from 6 to 20), the latter being a method of rating perceived exertion.<sup>21 22</sup> During follow-up from 3 to 9 months, the HIIT group did not fill in diaries or collect data such as heart rates. Participants in the control group were instructed to not change their pre-study physical exercise habits. However, in the follow-up period from 3 to 9 months, they were encouraged to start exercising. Nevertheless, they were not given diaries or instruction regarding the Borg scale. Neither were they given any specific instructions in how to perform HIIT. At the 9-month follow-up, the investigator interviewed all participants. If they were reporting vigorous endurance training once or more a week, they were classified as 'doing endurance exercise'.

### Assessment of outcome measures and baseline data

Outcome measures were assessed at baseline, and at 3 and 9 months of follow-up. Demographics, comorbidities and medications used were obtained from the medical journal system and the GoTreatIT Rheuma computer tool<sup>23</sup> (www.diagraphit.com).

### Main outcome measure

$VO_{2max}$  (mL/kg/min) was the main outcome and assessment was performed as described above.

### Secondary outcome measures

Body Mass Index (BMI, kg/m<sup>2</sup>) was calculated based on measurements of height and weight assessed fasting in the morning at the Department of Research and Development, St. Olavs Hospital. Body composition measuring the proportion of fat and lean mass in the whole body was assessed using dual-energy X-ray absorptiometry (DXA) (GE Healthcare Lunar) registering total fat (%), truncal fat (%) and lean muscle mass (g) at the Department of Rheumatology, St. Olavs hospital.<sup>24 25</sup>

Resting heart rate (HR), measured as beats/minute, was assessed repeatedly three times, registering the lowest value at the Department of Research and Development, St. Olavs hospital.

### Sample size

A difference in the main outcome measure ( $VO_{2max}$ ) of 3 mL/kg/min was considered clinically important, and based on a SD of 5<sup>26</sup> and a correlation of 0.4 between repeated measures, we estimated that 30 patients were required in each group to achieve a power of 90 at an alpha level of 0.05.

### Randomisation and blinding

Patients were randomised 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 randomisation did not allow the investigator to reveal the next allocation. The assessors at the laboratory, at CERG, at the Department of Research and Development, and the Department of Rheumatology, St. Olavs Hospital were blinded for allocation.

### 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% CI in outcome variables between the HIIT group and the control group at 3 and 9 months after randomisation. Changes from baseline to 3 and 9 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) to control for possible bias due to baseline imbalances in these factors.

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 SD, or as median and IQR for non-normally distributed variables. All statistical analyses were conducted using STATA V.14.2 (StataCorp, 2015; StataCorp LP, College Station, Texas, USA).

## RESULTS

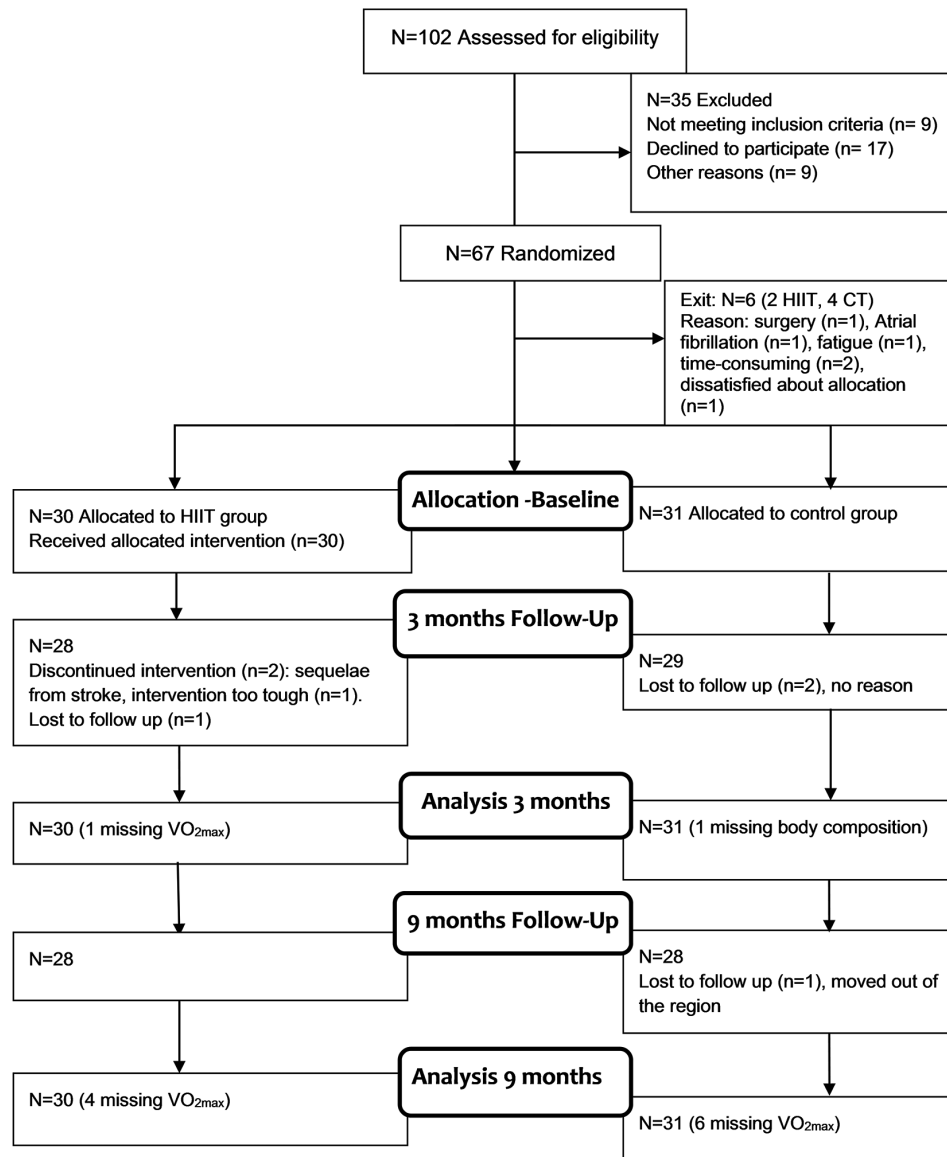
### Participant flow and characteristics

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 randomisation. However, before baseline testing additionally two patients in the HIIT group and four patients in the control group dropped out leaving 30 for allocation to the HIIT and 31 to the control group. More women than men were included in the study (70% and 65% in HIIT and control groups, respectively) and the mean age was 51 (SD 11) in the HIIT group and 45 (SD 12) years among 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 also did more self-guided endurance exercises than requested, that is, 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 9 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 at an interview that they were doing endurance exercise.

### Effect on outcome measures at 3 months

The HIIT group had a 3.72 mL/kg/min (95% CI 2.38 to 5.06) higher  $VO_{2max}$  and 1.28% (95% CI -2.51 to -0.05) lower truncal fat mass than the control group (table 2). Adjusting for baseline BMI, the difference in  $VO_{2max}$  slightly increased to 3.82 mL/kg/min (95% CI 2.49 to 5.15). Adjusting for smoking status did not affect the estimated effect on  $VO_{2max}$ . In addition, there was also some evidence that the HIIT group had slightly lower total fat% (-0.80; 95% CI -1.71 to 0.10), BMI (-0.31; 95% CI -0.78 to 0.17), and resting HR (-3.5; 95% CI -7.6 to 0.6) than the control group. There was no difference in lean muscle mass between the groups (67 g; 95% CI -776 to 911) (table 2).



**Figure 1** Participant flow through the study. CT, control group; HIIT, high-intensity interval training; N, number of subjects;  $VO_{2max}$ , maximum oxygen uptake.

### Outcome at 9 months of follow-up

At 9 months of follow-up, the effect on oxygen uptake was still evident with 3.08 mL/kg/min (95% CI 1.63 to 4.53) higher  $VO_{2max}$  in the HIIT group than the control group. There were no major differences between the two groups for the other outcome measures (table 3), although total and truncal fat percentage declined in the HIIT group.

### Safety

During the period of intervention from baseline to 3 months, two in the HIIT group and none in the control group had intra-articular injections. Injections were given 1 month after start of the intervention. At 3 months of follow-up, four patients in the HIIT group and three in the control group had intra-articular injections. In the 3 to 9 months of 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 4 weeks prior to evaluations. One patient left the HIIT group due to sequelae after stroke previous to the study and found the intervention too hard. No other adverse events were reported during the intervention.

### DISCUSSION

In this RCT, we observed a clear positive effect of HIIT on cardiorespiratory fitness and body composition in patients with PsA. The observed increase in  $VO_{2max}$  corresponds to a 13.5% increase in the HIIT group, that is, 12.6% more than the control group at 3 months. Furthermore, there was an effect with a reduction in truncal fat mass. There was also some evidence that HIIT had favourable effects on other CVD risk factors, such as total fat mass, BMI and resting HR. At 9 months of follow-up, the effect on  $VO_{2max}$  was still evident, and there was still

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

	Intervention (N=30)	Control (N=31)
<b>Demographics/medication</b>		
Age, years, mean (SD)	50.5 (11.1)	44.9 (12.1)
Female, n (%)	21 (70)	20 (65)
Disease duration, years, median (p25, p75)	6 (2–12)	4 (2–11)
Synthetic DMARDs, n (%)	28 (93)	25 (81)
Biologic DMARDs, n (%)	11 (37)	9 (29)
Antihypertensive, n (%)	4 (13)	4 (13)
Statins, n (%)	3 (10)	0 (0)
<b>Cardiovascular assessment</b>		
Current smoker, n (%)	6 (20)	4 (13)
VO <sub>2max</sub> (mL/kg/min), mean (SD)	28.73 (6.41)	30.75 (7.95)
Resting HR (beats/min), mean (SD)	65.3 (11.5)	66.4 (9.5)
Systolic BP (mm Hg), mean (SD)	124 (12)	125 (16)
Diastolic BP (mm Hg), mean (SD)	77 (8)	78 (11)
Cholesterol (mmol/L), mean (SD)	5.2 (0.8)	5.1 (1.0)
Triglyceride (mmol/L), median (p25, p75)	1.1 (0.8–1.9)	1.0 (0.7–1.4)
LDL (mmol/L), mean (SD)	3.2 (0.8)	3.3 (0.7)
<b>Body composition</b>		
BMI (kg/m <sup>2</sup> ), mean (SD)	28.6 (4.2)	27.6 (4.4)
Total fat%, mean (SD)	40.3 (7.1)	38.7 (7.7)
Truncus fat%, mean (SD)	43.7 (8.2)	41.3 (8.7)
Lean muscle mass (g), mean (SD)	48 423 (10163)	48 436 (12066)
Waist circumference (cm), mean (SD)	100.1 (10.5)	96.0 (13.8)
<b>Disease activity</b>		
HS-CRP (g/L), median (p25, p75)	1.56 (0.9–4.5)	1.87 (0.86–4.74)
DAS44, mean (SD)	2.00 (0.79)	1.94 (0.76)
Swollen joints, median (p25, p75)	0 (0–1)	0 (0–2)
Tender joints 66, median (p25, p75)	5 (1–10)	6 (1–10)
PGA (VAS 0–100), mean (SD)	38.4 (23.7)	41.6 (20.8)
MHAQ, median (p25, p75)	0.32 (0–0.75)	0.25 (0.13–0.63)

BMI, Body Mass Index; BP, blood pressure; DAS44, disease activity score of 44 joints; DMARD, disease-modifying antirheumatic drug; HR, heart rate; HS-CRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein; MHAQ, Modified Health Assessment Questionnaire; PGA, patient global assessment; VAS, Visual Analogue Scale; VO<sub>2max</sub>, maximal oxygen uptake.

a reduced total and truncal fat mass in the HIIT group whereas the difference between the two groups was not as pronounced. Patients with PsA are considered to have an increased risk of CVD. However, it is still unclear to what extent this is caused by inflammation, traditional CVD risk factors or both.<sup>2</sup> Further, patients with PsA are found to have an increased prevalence of several traditional CVD risk factors such as obesity, smoking, high triglyceride level, low HDL-c level and hypertension, indicating that reducing these risk factors will be of great importance as a supplement to disease-modifying treatment.<sup>4</sup> Thus, improving cardiorespiratory fitness could be a means for prevention of CVD among these patients. Moreover, as patients with PsA are at risk of developing enthesitis from mechanical stress,<sup>27 28</sup> exposing them to

vigorous exercise could result in an anticipated increase in disease activity. However, it is of importance to notice that the disease activity was stable as demonstrated in a recently published study from the same sample.<sup>29</sup>

The observed effect on VO<sub>2max</sub> is in line with previous studies of HIIT in otherwise healthy people,<sup>20 30</sup> as well as in patients with heart disease<sup>10</sup> and arthritis.<sup>26 31</sup> In addition, the magnitude of the increase in VO<sub>2max</sub> in our patients exceeds the value that corresponds to a 13% decrease in all-cause mortality.<sup>6</sup> Baseline VO<sub>2max</sub> in our patients was similar to that of healthy inactive people in Norway, indicating recruitment of patients with a sedentary lifestyle.<sup>32</sup> Partially, the low VO<sub>2max</sub> could also be explained by a high BMI and a preponderance of women in the study, as individual VO<sub>2max</sub> is associated with age, gender and weight.<sup>33</sup> Improving VO<sub>2max</sub> is important if the aim of physical exercise is to reduce the risk of CVD, as higher levels of cardiorespiratory fitness protect against CVD and all-cause mortality.<sup>34 35</sup> In fact, low cardiorespiratory fitness is found to be a more powerful predictor of mortality than traditional risk factors, such as hypertension, smoking, obesity, hyperlipidemia and type 2 diabetes.<sup>36 37</sup> In our study, there was a long-term effect on VO<sub>2max</sub> measured at 9 months' follow-up, indicating that the effect on cardiorespiratory fitness could be maintained even with less training effort over time.

The observed reduction in fat percentage after HIIT is also in line with previous studies in which a marked effect on body composition with decreased total body fat and increased fatty acid oxidation has been demonstrated after 12 weeks of sprint interval training in untrained men and women, with a more pronounced effect in men.<sup>38</sup> In patients with spondyloarthritis, the effect of HIIT and strength exercise for 3 months on body composition was evident in both genders.<sup>26</sup> The more pronounced effect of sprint interval training on reduction in truncal fat percentage in men might be a result of the androgenic fat distribution.<sup>38</sup> However, we observed a clear effect on truncal fat reduction even with a preponderance of women in the study. Central obesity is more pronounced in perimenopausal and postmenopausal women, which could partially explain the observed effect,<sup>39</sup> and the baseline BMI and truncal fat percentage was high in our patients. In our trial, we measured the truncal fat percentage with DXA, which provide results highly correlated to abdominal fat percentage.<sup>25</sup> Abdominal fat and especially visceral fat is playing a central role in the metabolic syndrome<sup>40 41</sup> and is associated with CVD risk.<sup>42</sup> The adipose tissue is an endocrine organ producing inflammatory mediators like several different adipokines, which influence the pathophysiology of both CVD and inflammatory diseases as in psoriatic diseases.<sup>43 44</sup> In addition, higher BMI, higher waist circumference and higher waist:hip ratio are associated with increased risk of premature death.<sup>45</sup>

Motivating the patients to do physical exercise is a challenge.<sup>46 47</sup> However, our study demonstrates that 40 min of HIIT performed two to three times weekly are

**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 3 months of follow-up

N=61	Baseline mean both groups	3 months change from baseline		Mean difference between groups 3 months
		Control	Intervention	
<b>Cardiorespiratory fitness</b>				
VO <sub>2max</sub> (mL/kg/min)	29.51	0.25	3.97	3.72
95% CI	27.97 to 31.05	-0.71 to 1.20	3.01 to 4.93	2.38 to 5.06
P values		0.61	<0.001	<0.001
HR (beats/min)	65.8	-1.0	-4.5	-3.5
95% CI	63.3 to 68.3	-4.0 to 2.0	-7.6 to -1.4	-7.6 to 0.6
P values		0.50	0.004	0.09
<b>Body composition</b>				
Truncal fat%	42.53	-0.11	-1.39	-1.28
95% CI	40.43 to 44.63	-0.98 to 0.76	-2.27 to -0.52	-2.51 to -0.05
P values		0.80	0.002	0.04
Total fat%	39.48	-0.26	-1.06	-0.80
95% CI	37.91 to 41.05	-0.90 to 0.39	-1.70 to -0.42	-1.71 to 0.10
P values		0.44	0.001	0.08
BMI (kg/m <sup>2</sup> )	28.10	-0.04	-0.35	-0.31
95% CI	27.07 to 29.14	-0.38 to 0.29	-0.69 to -0.01	-0.78 to 0.17
P values		0.78	0.05	0.21
Lean muscle mass (g)	48 460	46	114	67
95% CI	47 074 to 49 847	-552 to 644	-487 to 714	-776 to 911
P values		0.88	0.71	0.88

Adjusted for age and sex.

BMI, Body Mass Index; HR, resting heart rate; VO<sub>2max</sub>, maximal oxygen uptake.

efficacious, and other studies indicate that only 2–4 min of high-intensity training performed three times a week might be adequate to improve VO<sub>2max</sub> by 10% and reduce total body fat after 10–12 weeks.<sup>38 48</sup>

Informing the patients that HIIT is a method of physical exercise that is less time consuming but more beneficial in improving cardiorespiratory fitness with an additive effect on fat metabolism could be a possible approach.

A strength of this study was the randomised design, the use of objective outcome measures and that the assessors of the outcome measures were blinded to allocation. In addition, both groups had the same type and amount of follow-up and the diagnosis was confirmed before enrolment by an experienced rheumatologist. Furthermore, the training intervention was individualised with the same relative intensity according to the HIIT principle. In the HIIT group, the adherence to the guided exercise sessions was good and the exercises were performed with a high intensity according to the diaries. However, the controls were not delivering diaries and we have no information about their physical activity habits during the intervention period from baseline to 3 months. A potential increase in physical activity could imply a reduced difference in effect between the groups. The drop-out rate was only 6%–7% in both groups, which makes the estimates of effect from the intention-to-treat analyses more valid. Moreover, disease duration and disease activity measured by

patient global assessment as well as medical treatment are comparable with that of other patients with PsA indicating a high external validity of our results.<sup>49 50</sup> Nevertheless, patients who volunteer to participate in a trial involving physical exercise might be more experienced with and more motivated for physical activity and exercise than non-participants, hence reducing the generalisability of our results. In addition, performing physical exercise in groups might reinforce both the individual adherence and effort. Some other limitations of the study are worth mentioning, such as the relatively small sample size that reduces the precision of the estimated effects. The small sample size might also explain the baseline imbalance in age and sex with lower age and more men in the control group, which may have contributed to a slightly higher baseline VO<sub>2max</sub> among controls. However, all analyses were adjusted for baseline age and sex. Nevertheless, the joint baseline category between the intervention and control group could have attenuated the observed effect. 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 practise endurance exercises from 3 to 9 months to enhance their willingness to

**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 9 months of follow-up

N=61	Baseline mean both groups	9 months change from baseline		Mean difference between groups 9 months
		Control	Intervention	
<b>Cardiorespiratory fitness</b>				
VO <sub>2max</sub> (mL/kg/min)	29.51	0.21	3.29	3.08
95% CI	27.97 to 31.05	-0.81 to 1.22	2.23 to 4.34	1.63 to 4.53
P values		0.69	<0.001	<0.001
HR (beats/min)	65.8	-0.4	1.9	2.2
95% CI	63.3 to 68.3	-3.4 to 2.7	-1.2 to 4.9	-1.9 to 6.3
P values		0.82	0.24	0.29
<b>Body composition</b>				
Truncal fat%	42.53	-0.17	-1.08	-0.92
95% CI	40.43 to 44.63	-1.03 to 0.70	-1.96 to -0.21	-2.14 to 0.31
P values		0.71	0.02	0.14
Total fat%	39.48	-0.29	-0.80	-0.50
95% CI	37.91 to 41.05	-0.93 to 0.35	-1.44 to -0.16	-1.41 to 0.40
P values		0.37	0.02	0.27
BMI (kg/m <sup>2</sup> )	28.10	0.07	-0.32	-0.39
95% CI	27.07 to 29.14	-0.27 to 0.41	-0.66 to 0.02	-0.87 to 0.09
P values		0.67	0.07	0.11
Lean muscle mass (g)	48 460	-71	-524	-453
95% CI	47 074 to 49 847	-669 to 527	-1125 to 76	-1297 to 390
P values		0.82	0.09	0.29

Adjusted for age and sex.

BMI, Body Mass Index; HR, resting heart rate; VO<sub>2max</sub>, maximal oxygen uptake.

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.

The differences in the estimates of effect regarding secondary outcomes might not be of clinical relevance. However, the study duration of 11 weeks was relatively short and with an extended duration of the intervention, one might expect an effect of clinical relevance especially regarding the reduction in truncal fat.

Finally, we cannot rule out that the reduction in fat percentage could partly be explained by a change towards a healthier lifestyle when it comes to diet, nutrition and overall physical activity. However, the lean muscle mass was unchanged, assuming that the reduction of fat mass was not mainly a result of dietary change since that might have caused a reduction in muscle mass as well.

## CONCLUSION

In patients with PsA, 3 months with HIIT was associated with a substantial increase in VO<sub>2max</sub> and a reduction in truncal fat percentage compared with controls. In addition, there was a long-term effect on the increase of VO<sub>2max</sub>. This indicates that HIIT is also beneficial in patients with PsA in preventing CVD by increasing cardiorespiratory fitness and reducing abdominal fat.

## Author affiliations

<sup>1</sup>Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

<sup>2</sup>Department of Rheumatology, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway

<sup>3</sup>Department of Anaesthesia and Intensive Care, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway

<sup>4</sup>Department of Neuromedicine and Movement Science, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

<sup>5</sup>Division of Rheumatology, Department of Medicine, Hospital of Southern Norway Trust, Kristiansand, Norway

<sup>6</sup>Department of Circulation and Medical Imaging, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

<sup>7</sup>St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway

<sup>8</sup>Division of Rheumatology, Allergy, and Immunology, School of Medicine, University of California, San Diego, California, USA

**Acknowledgements** NeXt Move, Norwegian University of Science and Technology (NTNU), provided the testing of maximal oxygen uptake and maximum heart rate. NeXt Move is funded by the Faculty of Medicine and Health at NTNU and Central Norway Regional Health Authority. The authors would also like to thank the participating patients.

**Contributors** RST: conception and design of the trial, performing the trial, statistical analyses and interpretation of the data, writing. TILN: 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.

**Funding** RST has received a grant from The Norwegian ExtraFoundation for Health and Rehabilitation.

**Disclaimer** The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

**Competing interests** None declared.

**Patient consent** Obtained.

**Ethics approval** The study was approved by the Regional Committee for Medical Research Ethics in South-Eastern Norway.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** There are no additional unpublished data from the study.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

## REFERENCES

- Gladman DD, Ang M, Su L, *et al.* Cardiovascular morbidity in psoriatic arthritis. *Ann Rheum Dis* 2009;68:1131–5.
- Jamnicki A, Symmons D, Peters MJ, *et al.* Cardiovascular comorbidities in patients with psoriatic arthritis: a systematic review. *Ann Rheum Dis* 2013;72:211–6.
- Eder L, Wu Y, Chandran V, *et al.* Incidence and predictors for cardiovascular events in patients with psoriatic arthritis. *Ann Rheum Dis* 2016;75:1680–6.
- Gulati AM, Semb AG, Rollefstad S, *et al.* On the HUNT for cardiovascular risk factors and disease in patients with psoriatic arthritis: population-based data from the Nord-Trøndelag Health Study. *Ann Rheum Dis* 2016;75:819–24.
- Polachek A, Touma Z, Anderson M, *et al.* Risk of cardiovascular morbidity in patients with psoriatic arthritis: a meta-analysis of observational studies. *Arthritis Care Res* 2017;69:67–74.
- Kodama S, Saito K, Tanaka S, *et al.* Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA* 2009;301:2024–35.
- Davidson T, Vainshelboim B, Kokkinos P, *et al.* Cardiorespiratory fitness versus physical activity as predictors of all-cause mortality in men. *Am Heart J* 2018;196:156–62.
- Karlsen T, Aamot IL, Haykowsky M, *et al.* High intensity interval training for maximizing health outcomes. *Prog Cardiovasc Dis* 2017;60:67–77.
- Nes BM, Janszky I, Aspenes ST, *et al.* Exercise patterns and peak oxygen uptake in a healthy population: the HUNT study. *Med Sci Sports Exerc* 2012;44:1881–9.
- Wisløff U, Støylen A, Loennechen JP, *et al.* Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation* 2007;115:3086–94.
- Bacon AP, Carter RE, Ogle EA, *et al.* VO<sub>2</sub>max trainability and high intensity interval training in humans: a meta-analysis. *PLoS One* 2013;8:e73182.
- Hagel S, Lindqvist E, Bremander A, *et al.* Team-based rehabilitation improves long-term aerobic capacity and health-related quality of life in patients with chronic inflammatory arthritis. *Disabil Rehabil* 2010;32:1686–96.
- Iversen MD, Frits M, von Heideken J, *et al.* Physical activity and correlates of physical activity participation over three years in adults with rheumatoid arthritis. *Arthritis Care Res* 2017;69:1535–45.
- Tureson C, Matteson EL. Cardiovascular risk factors, fitness and physical activity in rheumatic diseases. *Curr Opin Rheumatol* 2007;19:190–6.
- Weston KS, Wisløff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med* 2014;48:1227–34.
- Milanović Z, Sporiš G, Weston M. Effectiveness of high-intensity interval training (hit) and continuous endurance training for vo<sub>2</sub>max improvements: a systematic review and meta-analysis of controlled trials. *Sports Med* 2015;45:1469–81.
- Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2011;9:672–7.
- Larsson PU, Wadell KM, Jakobsson EJ, *et al.* Validation of the MetaMax II portable metabolic measurement system. *Int J Sports Med* 2004;25:115–23.
- Zisko N, Stensvold D, Hordnes-Slagsvold K, *et al.* Effect of change in vo<sub>2</sub>max on daily total energy expenditure in a cohort of Norwegian men: a randomized pilot study. *Open Cardiovasc Med J* 2015;9:50–7.
- Helgerud J, Høydal K, Wang E, *et al.* Aerobic high-intensity intervals improve VO<sub>2</sub>max more than moderate training. *Med Sci Sports Exerc* 2007;39:665–71.
- Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–81.
- Borg-scale, 1982. <https://www.hsph.harvard.edu/nutritionsource/borg-scale/1982>
- DiaGraphIT, 2015. GoTreatIT Rheuma software program. <http://www.diagrapht.com/>
- Andreoli A, Scalzo G, Masala S, *et al.* Body composition assessment by dual-energy X-ray absorptiometry (DXA). *Radiol Med* 2009;114:286–300.
- Bea JW, Blew RM, Going SB, *et al.* Dual energy X-ray absorptiometry spine scans to determine abdominal fat in postmenopausal women. *Am J Hum Biol* 2016;28:918–26.
- Sveaas SH, Berg IJ, Provan SA, *et al.* Efficacy of high intensity exercise on disease activity and cardiovascular risk in active axial spondyloarthritis: a randomized controlled pilot study. *PLoS One* 2014;9:e108688.
- Watad A, Cuthbert RJ, Amital H, *et al.* Enthesitis: much more than focal insertion point inflammation. *Curr Rheumatol Rep* 2018;20:41.
- Jacques P, Lambrecht S, Verheugen E, Res L C (Hoboken) S, *et al.* Proof of concept: enthesitis and new bone formation in spondyloarthritis are driven by mechanical strain and stromal cells. *Ann Rheum Dis* 2014;73:437–45.
- Thomsen RS, Nilsen TIL, Haugeberg G, *et al.* The impact of high intensity interval training on disease activity and patient disease perception in patients with psoriatic arthritis: a randomized controlled trial. *Arthritis Care Res* 2018.
- Rognmo Ø, Hetland E, Helgerud J, *et al.* High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2004;11:216–22.
- Sandstad J, Stensvold D, Hoff M, *et al.* The effects of high intensity interval training in women with rheumatic disease: a pilot study. *Eur J Appl Physiol* 2015;115:2081–9.
- Aspenes ST, Nilsen TI, Skaug EA, *et al.* Peak oxygen uptake and cardiovascular risk factors in 4631 healthy women and men. *Med Sci Sports Exerc* 2011;43:1465–73.
- Myers J, Kaminsky LA, Lima R, *et al.* A reference equation for normal standards for VO<sub>2</sub> max: analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). *Prog Cardiovasc Dis* 2017;60:21–9.
- Myers J, McAuley P, Lavie CJ, *et al.* Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: their independent and interwoven importance to health status. *Prog Cardiovasc Dis* 2015;57:306–14.
- Gulati M, Pandey DK, Arnsdorf MF, *et al.* Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation* 2003;108:1554–9.
- Williams PT. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Med Sci Sports Exerc* 2001;33:754–61.
- Myers J, Kaykha A, George S, *et al.* Fitness versus physical activity patterns in predicting mortality in men. *Am J Med* 2004;117:912–8.
- Bagley L, Slevin M, Bradburn S, *et al.* Sex differences in the effects of 1<sub>2</sub> weeks sprint interval training on body fat mass and the rates of fatty acid oxidation and VO<sub>2</sub>max during exercise. *BMJ Open Sport Exerc Med* 2016;2:e000056.
- Cao Y, Zhang S, Zou S, *et al.* The relationship between endogenous androgens and body fat distribution in early and late postmenopausal women. *PLoS One* 2013;8:e58448.
- Xiao T, Fu YF. Resistance training vs. aerobic training and role of other factors on the exercise effects on visceral fat. *Eur Rev Med Pharmacol Sci* 2015;19:1779–84.
- Feld J, Nissan S, Eder L, *et al.* Increased prevalence of metabolic syndrome and adipocytokine levels in a psoriatic arthritis cohort. *J Clin Rheumatol* 2018;24:302–7.
- Lee JJ, Pedley A, Hoffmann U, *et al.* Association of changes in abdominal fat quantity and quality with incident cardiovascular disease risk factors. *J Am Coll Cardiol* 2016;68:1509–21.
- Gerdes S, Rostami-Yazdi M, Mrowietz U. Adipokines and psoriasis. *Exp Dermatol* 2011;20:81–7.
- Scotece M, Conde J, Gómez R, *et al.* Role of adipokines in atherosclerosis: interferences with cardiovascular complications in rheumatic diseases. *Mediators Inflamm* 2012;2012:125458–.
- Pischon T, Boeing H, Hoffmann K, *et al.* General and abdominal adiposity and risk of death in Europe. *N Engl J Med* 2008;359:2105–20.
- Jacquemin C, Servy H, Molto A, *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.



47. Katz P, Margaretten M, Gregorich S, *et al.* Physical activity to reduce fatigue in rheumatoid arthritis: a randomized controlled trial. *Arthritis Care Res* 2018;70:1–10.
48. Tjønnå AE, Leinan IM, Bartnes AT, *et al.* Low- and high-volume of intensive endurance training significantly improves maximal oxygen uptake after 10-weeks of training in healthy men. *PLoS One* 2013;8:e65382.
49. Michelsen B, Fiene R, Diamantopoulos AP, *et al.* A comparison of disease burden in rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis. *PLoS One* 2015;10:e0123582.
50. Desthieux C, Granger B, Balanescu AR, *et al.* Determinants of patient–physician discordance in global assessment in psoriatic arthritis: a multicenter European study. *Arthritis Care Res* 2017;69:1606–11.