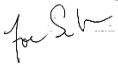
ExeHeart- Improved Cardiovascular Health for Patients with Inflammatory Joint Diseases: Statistical Analysis Plan (SAP) 2.0

NCT04922840

Date: March 8th, 2023

Section 1: Administrative information	**Index**	**Description**
Title and trial registration	1a	ExeHeart- Improved Cardiovascular Health for Patients with Inflammatory Joint Disease: Statistical Analysis Plan
	1b	ClinicalTrials.gov id: NCT04922840 REK south-east id: 201227 Data Protection Officer at Diakonhjemmet Hospital id: 00397
SAP version	2	SAP version 2.0; March 8th, 2023, minor changes to SAP version 1.0 (29th September, 2022)
Protocol version	3	https://doi.org/10.1136/bmjopen-2021-058634
SAP revisions	4a	SAP version 2.0 is the first revision of SAP 1.0
	4b	Amendments in the current version are minor changes from the previous version of SAP: - Items 27a (Analysis methods): VO_{2peak} was erroneously stated as covariate in analyses of secondary outcomes. Correct covariate is baseline data of dependent variable. - Gender was used as stratification factor in the randomization, but omitted as covariate in ANCOVA analyses. This has been remedied in the current version; gender is included as covariate in ANVOCA analyses in addition to age and baseline data of the variable under scrutiny. - Post hoc analysis of proportion of patients per group acquiring an increase ≥3.5 ml/kg/min at follow-up time points (item 27f). This analysis was left out in previous SAP version. - Typo < changed to ≥ in item 8: *Alternative hypotheses*
	4c	Changes in the current version were made at the outset of analyses of longitudinal data from the ExeHeart trial
Roles and responsibility	5	Anne Therese Tveter; project leader (draft of SAP, critical revision and final approval) Kristine Røren Nordén; PhD student (draft of SAP, critical revision and final approval) Joseph Sexton, statistician (SAP critical revision and final approval) Hanne Dagfinrud, co-supervisor (SAP critical revision and final approval) Anne Grete Semb, co-supervisor (SAP critical revision and final approval) Jonny Hisdal, co-supervisor (SAP critical revision and final approval)
Signatures	6a	 *Person writing the SAP (KRN)*
	6b	 *Senior statistician (JS)*
	6c	 *Chief investigator (ATT)*
Section 2: Introduction	**Index**	**Description**
Background and rationale	7	Inflammatory joint diseases (IJD), including rheumatoid arthritis (RA), spondyloarthropathy (SpA) and psoriatic arthritis (PsA) are inflammatory autoimmune diseases with common symptoms of joint inflammation, pain, stiffness and fatigue. Compared to the general population, this large patient-group has an increased risk of cardiovascular disease (CVD) and CVD-related mortality. The elevated CVD risk in IJD is only partly attributed to a higher prevalence and burden of traditional risk factors, and the systemic, chronic inflammation is recognized as an independent CVD risk factor.

		Physical activity is inversely associated with risk of metabolic disease, but cardiorespiratory fitness (CRF) has emerged as an even stronger mediator of health outcomes. National and international data show a strong correlation between high levels of CRF and lower risk of CVD and all-cause mortality. In patients with IJD, disease-related factors and uncertainty regarding the dosage of exercise programs are consistent barriers to physical activity. Less time spent at spent at activities with moderate and vigorous intensity may negatively affect CRF and low levels of CRF are reported in patients with IJD. Collectively, the burden of disease and consequent inactivity may be a catalyst for reduced CRF and thus a component of the elevated CVD risk in IJD. A common notion that intensive exercise can increase disease activity and result in joint destruction and physical discomfort in patients with IJD has previously prevailed, but recent studies demonstrate that vigorous exercise is safe and well-tolerated. High-intensity training (HIIT) is proven superior to exercise at lower intensities in eliciting physiological adaptations. The evidence of HIIT is largely based on supervised clinical trial settings and application of HIIT to real world contexts requires more investigation. Common reservations regarding feasibility, adherence and safety need to be addressed. Although CRF is identified as a robust physiological marker and a prominent/major risk factor for CVD, assessment of CRF is not included in CVD risk models. A routine measure of CRF as a key vital sign is strongly recommended, though seldom performed in health care settings. CRF is often quantified as peak or maximal oxygen uptake (VO_{2peak}) and the gold standard for measurement of VO_{2peak} is a CardioPulmonary Exercise Test (CPET). In absence of CPET, non-exercise algorithms that predict VO_{2peak} are viable options. These models use commonly measured clinical variables to estimate CRF and are thereby feasible for use in both primary and specialized clinical care. Notably, the ability of non-exercise algorithms to detect longitudinal change in VO_{2peak} is unclear and presents an important knowledge need.
Objectives	8	Primary aim of the ExeHeart trial is to determine the effect of a 12-week HIIT program set in physiotherapy primary care on CRF in patients with IJD. *<u>Null hypothesis</u>:* *There is no clinically relevant (<3.5 ml/kg/min) between-group difference in change in VO_{2peak} at 3-month follow-up* *<u>Alternative hypothesis</u>:* *There is a clinically relevant (≥3.5 ml/kg/min) between-group difference in change in VO_{2peak} at 3-month follow-up* Secondary aims are to *a)* Assess the long-term effect of a 12-week HIIT program set in physiotherapy primary care on CRF in patients with IJD. *<u>Null hypothesis</u>:* *There is no clinically relevant (<3.5 ml/kg/min) between-group difference in change in VO_{2peak} at 6-month follow-up* *<u>Alternative hypothesis</u>:* *There is a clinically relevant (≥3.5 ml/kg/min) between-group difference in change in VO_{2peak} at 6-month follow-up*

		b) Assess the effect of HIIT on CVD risk factors (blood pressure, cholesterol levels, arterial stiffness, body composition) and disease activity in patients with IJD *Null hypotheses:* *There is no between-group difference in CVD risk* factors (blood pressure, cholesterol levels, arterial stiffness, body composition) and disease activity at 3- month follow-up. *There is no between-group difference in CVD risk factors (blood pressure, cholesterol levels, arterial stiffness, body composition) and disease activity at 6- month follow-up.* *Alternative hypotheses:* *There is a between-group difference in CVD risk factors (blood pressure, cholesterol levels, arterial stiffness, body composition) and disease activity at 3- month follow-up.* *There is a between-group difference in CVD risk factors (blood pressure, cholesterol levels, arterial stiffness, body composition) and disease activity at 6- month follow-up.* *c)* Assess the association between CRF and disease-specific and CVD-related variables in patients with IJD *Null hypothesis: There is no association between CRF and disease-specific and CVD-related variables in patients with IJD* *Alternative hypothesis: There is one or more associations between CRF and disease-specific and CVD-related variables in patients with IJD* *d)* Explore the feasibility of a HIIT intervention set in physiotherapy primary care in terms of patient's adherence and tolerability to the exercise program *Null hypothesis:* *The HIIT intervention set in physiotherapy primary care is not feasible for patients with IJD in terms of patient's adherence and acceptability* *Alternative hypothesis:* *The HIIT intervention set in physiotherapy primary care is deemed feasible for patients with IJD in terms of patient's adherence and acceptability* *e)* Report on the validity of eCRF algorithms to accurately detect potential changes in CRF *Null hypothesis:* *eCRF algorithms cannot detect longitudinal change in CRF in patients with IJD* *Alternative hypothesis:* *eCRF algorithms can detect longitudinal change in CRF in patients with IJD*
Section 3: Methods	**Index**	**Description**
Trial design	9	Parallel group, randomized controlled trial with repeated measures. Patients are randomly allocated to current clinical practice including CVD risk evaluation, lifestyle advice given at baseline and relevant cardioprotective medication *(control group)* or current clinical practice and a 12-week HIIT intervention *(HIIT group)*
Randomization	10	Study participants are allocated 1:1 by a computer-generated randomization list using permuted blocks of random sizes 4 and 6, stratified by gender.
Sample size	11	A sample size of 25 in each group will have 80% power to detect a 3.5 mL/kg/min difference in means assuming a reported upper

		bound of standard deviation 4.5 ml/kg/min and a 0.05 two-sided significance level. Allowing for a possible 20% attrition rate, we will need 60 patients in total, i.e. 30 in each group.
Framework	12	Superiority trial comparing the effect of HIIT to control
Statistical interim analyses and stopping guidance	13	The trial will be paused in the case of a serious adverse event such as cardiac arrest or death amongst study participants.
Timing of final analyses	14	Baseline data are to be analyzed following completion of study enrollment. All outcomes will be analyzed collectively following completion of study visits for all included patients (anticipated primo 2023).
Timing of outcome assessments	15	Study visits; baseline, 3 months after baseline (±2 weeks) and 6 months after baseline (±2 weeks)
Section 4: Statistical principles	**Index**	**Description**
Confidence intervals and *p*-values	16	All applicable statistical tests will be two-sided and performed with $\alpha = 0.05$
	17	No adjustment for multiple testing will be done. Significance testing with p-values and 95% confidence intervals (CI) will be reported for the intervention effects on the primary outcome variable. 95% CI will be presented for the intervention effects on all secondary outcome variables (1).
	18	Two-sided 95% confidence intervals will be reported
Adherence and protocol deviations	19a	Adherence to the intervention will be recorded by use of the training diary. Adherence is set to 70% of HIIT sessions (17 out of 24 possible sessions)
	19b	Attendance to HIIT sessions is tallied by use of the training diary. HIIT exercise intensity sessions will be calculated as mean %HRpeak and Borg RPE 6-20 across sessions and participants. Duration will be reported as mean session duration and average time spent in high intensity intervals.
	19c	The first two weeks of the HIIT intervention may be performed at reduced intensity and/or duration. The HIIT intervention may be downscaled or ceased should the participant present with symptoms such as dizziness or angina pectoris.
	19d	Protocol deviations will be summarized by non-attendance, early session termination, exercise intensity, exercise duration and adverse events
	20	The primary analysis is an intention-to-treat analysis and will include all randomized patients. The per protocol analysis set will include patients that were randomly assigned to HIIT or control, have baseline and at least one post-baseline measurement of the primary outcome variable and comply to an adherence of ≥70% of HIIT sessions (only applicable to intervention group).
Section 5: Trial population	**Index**	**Description**
Screening data	21	Enrolment: the number of months recruiting, the number of patients screened, the number of patients recruited, the number of screened patients not recruited, and the reason for non-recruitment. This summary will be provided overall and presented in the CONSORT flow chart in the publication of trial results. Reasons for declining to participate *(time constrains, distance to PT clinic, medical issues, satisfied with current exercise regime, other)* and failure to meet eligibility criteria (*see index #22)* will be tallied and reported
Eligibility	22	Inclusion criteria: • Age 18-70 • BMI 18.5-40 • Able to walk unaided ≥15 minutes • IJD verified by physician • Norwegian or English speaking

<table>
<tr><td></td><td></td><td>Exclusion criteria:
• Lower extremity injury and/or surgery <12 months
• Primary neurological disease
• Cognitive impairment
• Participation in high-intensity exercise ≥ 1 session/week in the last 3 months
• American College of Sports Medicine (ACSM) contraindication to maximal exercise test</td></tr>
<tr><td>Recruitment</td><td>23</td><td>A CONSORT flow diagram will be used to summarize the number of patients who were:
• assessed for eligibility at screening
• ineligible at screening or declined to participate
• randomized
• received the randomized allocation
• discontinued the intervention
• did not receive the HIIT intervention
• included in primary analysis at 3 months
• lost to follow-up at 3 months
• included in primary analysis at 6 months
• lost to follow-up at 6 months</td></tr>
<tr><td rowspan="2">Withdrawal/follow-up</td><td>24a</td><td>Withdrawal from the intervention and from follow-up assessments will be reported in the CONSORT diagram</td></tr>
<tr><td>24b+ c</td><td>The number of losses to follow-up (drop-outs and withdrawals) at 3-month and 6-month time point will be summarized by treatment arm</td></tr>
<tr><td rowspan="2">Baseline patient characteristics</td><td>25a</td><td>Please see table 1 and 2 (dummy tables of baseline characteristics).</td></tr>
<tr><td>25b</td><td>Categorical data will be presented as numbers (percentages). Continuous data will be presented as mean (SD) if normally and median (IQR) if skewedly distributed.
The clinical importance of any imbalance between groups will be discussed, but no tests of statistical significance will be performed</td></tr>
<tr><td>Section 6 Analysis</td><td>Index</td><td>Description</td></tr>
<tr><td>Outcome definitions</td><td>26</td><td>Please see protocol article for description of data collection procedures (2)

<table>
<tr><th>Primary outcome (unit)</th><th>Time</th><th>Primary effect estimates</th></tr>
<tr><td>Peak oxygen uptake (VO_{2peak}, $mL \cdot kg^{-1} \cdot min^{-1}$ and $L \cdot min^{-1}$)</td><td>Baseline, 3 mo, 6 mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
<tr><th>Secondary outcomes (unit)</th><th>Time</th><th>Primary effect estimates</th></tr>
<tr><td>Spirometry
Forced Vital Capacity (FVC, L)
Forced Expiratory Volume (FEV1, L)
Peak Expiratory Flow (PEF, $L \cdot min^{-1}$)
Maximal Voluntary Ventilation (MVV, $L \cdot min^{-1}$)</td><td>Baseline, 3mo, 6mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
<tr><td>Peak HR (HR_{peak}, $beat \cdot min^{-1}$)</td><td>Baseline, 3mo, 6mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
<tr><td>Ventilatory threshold 1</td><td>Baseline, 3mo, 6mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
<tr><td>Ventilatory threshold 2</td><td>Baseline, 3mo, 6mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
<tr><td>Maximum minute ventilation at peak exercise (V_{Emax}, $L \cdot min^{-1}$)</td><td>Baseline, 3mo, 6mo</td><td>Change from baseline-3mo (95% CI)</td></tr>
</table>
</td></tr>
</table>

		Breathing reserve at peak exercise (%)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Oxygen pulse at peak exercise (O_2-pulse, ml·beat·min^{-1})	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Ventilatory equivalent for oxygen (V_E/VO_2)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Ventilatory equivalent for carbon dioxide (V_E/VCO_2)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Respiratory Exchange Ratio (RER)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Post-exercise test blood lactate concentration (mmol/L)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Borg RPE (0-10)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Blood samples CRP (mg/L) ESR (mm) Total cholesterol (mmol/L) HDL (mmol/L) LDL (mmol/L) Triglycerides (mmol/L	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Blood pressure and arterial stiffness Systolic (mmHg) Diastolic (mmHg) Mean arterial pressure (mmHg) Resting HR (beat·min^{-1}) Augmentation index (@75) Pulse wave velocity (m/s)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		SCORE2 (%)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Anthropometry Height (cm) Body weight (kg) BMI (kg/m^2) Waist circumference (cm) Fat mass (kg) Fat-free mass (kg) Visceral fat indicator	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Clinical disease activity DAS28 *(for RA)* (0-10) DAPSA *(for PsA)* (0-∞) ASDAS *(for SpA)* (0-∞)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Clinical disease activity (categorized) Remission Low Moderate High	Baseline, 3mo, 6mo	Chi-square (or exact test if overall total <40)
		Self-reported disease activity RAID *(for RA)* (0-10) PsAID *(for PsA)* (0-10) BASDAI *(for SpA)* (0-10) BAS-G *(for SpA)* (0-10)	Baseline, 3mo, 6mo	Change from baseline-3mo (95% CI)
		Health-related variables Smoking and snuff use Use of healthcare services the previous three months (type of profession and number of appointments) CVD history CVD symptoms	Baseline, 3mo, 6mo	Chi-square (or exact test if overall total <40)

		Use of medication; analgesics, IJD and CVD medication BASFI *(for SpA)* (0-10) | | Covid-19 infection and/or quarantine in the past 3 months | Baseline, 3mo, 6mo | Descriptive per treatment arm EuroQol-5D-5L (-0.59 to 1) | Baseline, 3mo, 6mo | Change from baseline-3mo (95% CI) EuroQol-5D-5L VAS (0-100) | Baseline, 3mo, 6mo | Change from baseline-3mo (95% CI) Numerical Rating Scale Pain (0-10) Fatigue (0-10) | Baseline, 3mo, 6mo | Change from baseline-3mo (95% CI) Physical activity index (0-45) | Baseline, 3mo, 6mo | Change from baseline-3mo (95% CI) Exercise beliefs and exercise habits (mean 1-5 for each domain) | Baseline, 3mo, 6mo | Change from baseline-3mo (95% CI)
Analysis methods	27a	**Primary outcome:** ANCOVA. Age, gender and VO_{2peak} @baseline to be included as co-variates. **Secondary outcomes** (please see index #8 for description of objectives: a) ANCOVA. Age, gender and baseline data of dependent variable to be included as covariates. b) ANCOVA. Age, gender and baseline data of dependent variable to be included as covariates. c) Multiple linear regression using CVD and IJD-related variables as independent variables to VO_{2peak} (dependent variable) d) Descriptive statistics, exploratory analysis to be decided in light of final data set e) Evaluated by correlation, illustrated with Bland-Altman plot Table 3 is a dummy table on the effect of the HIIT intervention on cardiorespiratory and cardiovascular variables at 3-month follow-up. Table 4 is a dummy table on the effect of the HIIT intervention on PROMS and disease-related variables at 3-month follow-up.
	27b	Age, VO_{2peak} values at baseline and other relevant factors such as IJD entity
	27c	**Primary outcome:** ANCOVA; dependent variable (change in VO_{2peak} at 3mo) is a continuous variable with normal distribution. Covariates (age and VO_{2peak} at baseline) are continuous variables and independent to categorical variable (group allocation). Gender is used as stratification factor and further included as covariate in analyses. The following assumptions will be checked: Homogeneity of variance (Levene's test), skewness of residuals, and linearity of relationships.
	27d	Regarding ANCOVA; variable transformation will be considered in case of violations. Parametric and non-parametric statistical analyses will be carried out as appropriate based on visual inspection of variable distribution (q-q plots and histograms). If uncertainty arises regarding the normal probability curves, a Shapiro-Wilk test of univariate normality will be applied.
	27e	Sensitivity analyses of primary outcome will be performed to any violations of analysis assumptions, e.g. log-transformation in case of skewed residuals
	27f	Subgroup analysis of per-protocol population in HIIT group

		Post hoc analyses of proportion of patients per group with an increase in VO_{2peak} ≥3.5 ml/kg/min at 3- and 6-month follow-up
Missing data	28	Sensitivity analyses with different methods for handling missing data such as; - Complete case analysis - Single imputation such as last observation carried forward or simple mean imputation - Multiple imputation
Additional analyses	29	Per protocol (as defined by index #20) of primary and secondary outcome variables
Harms/adverse events	30	All adverse event (AE) and serious adverse events (SAE) are recorded in a data file and the following information is described; • AE or SAE • Severity; mild (cold/flu), moderate (requires medical attention), serious (hospitalization, malignant disease, death) • Start and end data of event • Study causality; no/possibly/yes • Patient consequence • Trial consequence SAE will be reported to the project leader, who in turn will decide on further study participation and referral to relevant physician such as GP, rheumatologist, cardiologist. All events will be coded, categorized and summarized. The number and percentage of AE and SAE will be reported per treatment arm. No formal statistical testing.
Statistical software	31	STATA 16.1
References	32a	No plan to include nonstandard statistical methods
	32b	Patient questionnaires: Encrypted data will be sent from nettskjema.no to Sensitive Data Services (TSD) at the University of Oslo, and downloaded to secure research server at Diakonhjemmet Hospital. Patients case report forms: Secured in locked cabinets according to hospital policy and remain stored for 5 years after study completion. All data files will be stored on the secure research server at Diakonhjemmet Hospital with access to files restricted to the following project group members KRN, HD, AGS, JSe, CF, EB and ATT.
	32c	N/Forskning/ExeHeart/Data/DataExeHeart.xls
	32d	Guidelines for the Content of Statistical Analysis Plans in Clinical Trials (3) ExeHeart trial protocol (2)

Table 2: Dummy table of baseline characteristics. Data are presented as mean (SD) unless otherwise indicated.

Baseline characteristics	**Total** **N=**	**HIIT group** **N=**	**Control group** **N=**
Gender, female, n (%)			
Age, years			
Relationship status, solitary, n (%)			
Education, college degree, n (%)			
Employment Full employment, n (%) Sick leave or welfare, n (%) Retired, n (%) Student, n (%)			
Current smoker/snuff user, n (%)			
Diagnosis RA, n (%) SpA, n (%) PsA, n (%)			
Disease duration, years			
Clinical disease activity Remission, n (%) Low, n (%) Moderate, n (%) High, n (%)			
Inflammatory markers CRP, mg/L ESR, mm			
IJD medication Corticosteroids, n (%) NSAIDs, n (%) Conventional DMARDs, n (%) Biologics, n (%) JAKi, n (%)			
Analgesics Non-opioids, n (%) Opioids, n (%)			
CVD medication Statins, n (%) Betablockers, n (%) Anticoagulants, n (%) ACE inhibitor, n (%) Angiotensin II Receptor Blockers, n (%) Calcium blockers, n (%) Diuretics, n (%)			
Comorbidity Diabetes, n (%) Chronic obstructive pulmonary disease, n (%) Inflammatory bowel disease, n (%) Hypertension, n (%)			
Lipids Total cholesterol, mmol/L HDL, mmol/L LDL, mmol/L Triglycerides, mmol/L			
History of CVD, n (%)			

ACE inhibitors: angiotensin-converting enzyme inhibitor, CRP: C-reactive protein, CVD: cardiovascular disease, DMARDs: disease-modifying anti-rheumatic drugs, ESR: erythrocyte sedimentation rate, HDL: high-density lipoprotein, JAKi: Janus Kinase inhibitors, LDL: low-density lipoprotein, NSAIDs: non-steroidal anti-inflammatory drugs, RA: rheumatoid arthritis, PsA: psoriatic arthritis, SCORE2: Systemic COronary Risk Estimation 2, SpA: spondyloarthritis

Table 3: Dummy table of baseline characteristics *(supplementary files)*. Data are presented as mean (SD) unless otherwise indicated.

Baseline characteristics	**Total** **N=**	**HIIT group** **N=**	**Control group** **N=**
CPET variables Forced vital capacity, L Forced expiratory volume, L Peak expiratory flow, L/min Maximal voluntary ventilation, L/min VT1 VO_2 mL/kg/min HR VT2 VO_2 mL/kg/min HR Breathing reserve at peak exercise, % VE/VO_2 at VT1 at VT2 VE/VCO_2 at VT1 atVT2			
Clinical disease activity DAS28 DAPSA ASDAS Remission, n (%) Low, n (%) Moderate, n (%) High, n (%)			
Self-reported disease activity RAID, 0-10, 10= worst PsAID, 0-10, 10= worst BASDAI, 0-10, 10= severe BASFI, 0-10, 10= impossible BAS-G, 0-10, 10= very severe			

ASDAS: Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BAS-G: Bath Ankylosing Spondylitis Patient Global Score, CPET: cardiopulmonary exercise test, DAS28: Disease Activity Score Calculator for RA, DAPSA: Disease Activity Index for PSoriatic Arthritis, HR: heart rate, RAID: Rheumatoid Arthritis Impact of Disease, PsAID: Psoriatic Arthritis Impact of Disease, VCO_2: volume of carbon dioxide, V_E: minute ventilation, VO_2: volume of oxygen, VT1: ventilatory threshold 1, VT2: ventilatory threshold 2

Table 4: Dummy table of effect of HIIT on cardiorespiratory fitness and other cardiovascular disease risk factors at 3-month follow-up. Data are presented as mean (SD) unless otherwise indicated.

	HIIT group		**Control group**		**Mean group difference (95%CI)**
	Baseline	**3 months**	**Baseline**	**3 months**	
Cardiorespiratory fitness					
VO_{2peak}, ml/kg/min					
VO_{2peak}, L/min					
VO_{2peak}, ml/FFM					
Peak HR					
RER					
V_E at peak exercise					
Borg RPE 0-10, 10= max					
Lactate, mmol/L					
Resting HR, beat/min					
Lipids					
Total cholesterol, mmol/L					
HDL, mmol/L					
LDL, mmol/L					
Triglycerides, mmol/L					
Blood pressure					
Systolic, mm Hg					
Diastolic, mm Hg					
Mean arterial pressure, mm Hg					
SCORE2					
Arterial stiffness					
Augmentation index					
Pulse wave velocity, m/s					
Anthropometric measures					
BMI, kg/m^2					
Waist circumference, cm					
Fat mass, kg					
Fat-free mass, kg					
Visceral fat indicator					

Borg RPE: Borg rating of perceived exertion, BMI: body mass index, FFM: fat-free mass, HDL: high-density lipoprotein, HR: heart rate, LDL: low-density lipoprotein, RER: respiratory exchange ratio, SCORE2: Systemic COronary Risk Estimation 2, V_E: minute ventilation, VO_{2peak}: peak oxygen uptake,

Table 5: Dummy table of effect of HIIT on disease activity and patient-reported outcomes at 3-month follow-up. Data are presented as mean (SD) unless otherwise indicated.

	HIIT group		**Control group**		**Mean group difference (95%CI)**
	Baseline	**3 months**	**Baseline**	**3 months**	
Clinical disease activity					
Remission, n (%)					
Low, n (%)					
Moderate, n (%)					
High, n (%)					
Inflammatory markers					
CRP, mg/L					
ESR, mm					
Self-reported measures of disease activity and health					
RAID, 0-10, 10=worst					
PsAID, 0-10, 10=worst					
BASDAI, 0-10, 10=severe					
BASFI, 0-10, 10= impossible					
BAS-G, 0-10, 10= very severe					
NRS Pain last week, 0-10, 0= no pain					
NRS Fatigue last week, 0-10, 0= no fatigue					
EuroQol-5D-5L utility index, 0-1, 1= best health state					
EuroQol-5D-5L, VAS 0-100, 100= best imaginable health					
Exercise beliefs					
Self-efficacy					

Barriers to exercise					
Benefits of exercise					
Impact of exercise on IJD					
Physical activity index					

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BAS-G: Bath Ankylosing Spondylitis Patient Global Score, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, NRS: Numeric rating scale, RAID: Rheumatoid Arthritis Impact of Disease, PsAID: Psoriatic Arthritis Impact of Disease,

References:

1. Harrington D, D'Agostino RB, Sr., Gatsonis C, Hogan JW, Hunter DJ, Normand ST, et al. New Guidelines for Statistical Reporting in the Journal. The New England journal of medicine. 2019;381(3):285-6.
2. Nordén KR, Dagfinrud H, Semb AG, Hisdal J, Viktil KK, Sexton J, et al. Effect of high-intensity exercise on cardiorespiratory fitness, cardiovascular disease risk and disease activity in patients with inflammatory joint disease: protocol for the ExeHeart randomised controlled trial. BMJ open. 2022;12(2):e058634.
3. Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Doré C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. Jama. 2017;318(23):2337-43.