Statistical Analysis Plan

Effect of a Self-Management Intervention for Newly Diagnosed Inflammatory Arthritis: The Multicenter, Randomized Controlled NISMA Trial {1a}

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Introduction

Background and rational {7}

Inflammatory arthritis (IA) (in this trial covering rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA)) constitutes a group of acute and chronic joint diseases characterized by joint pain, swelling, and tenderness caused by underlying inflammation [1–3]. IA affects more than 2% of the population, with considerable variation worldwide [1–3], and can occur at any age and in both sexes. The etiology of IA is incompletely understood, but it involves both genetic and lifestyle factors [1,4,5]. IA mainly presents with joint inflammation, causing leading to pain and stiffness, but can also affect other connective tissues [2,3,6]. If treated insufficiently, these diseases may progress with functional decline, irreversible joint damage, development of various comorbidities, and increased mortality [7,8]. Pharmacological treatment with disease-modifying anti-rheumatic drugs (DMARDs) early after diagnosis improves short- and long-term outcomes [9,10]. Approximately 60% of patients with RA achieve long-term disease remission [11,12], but even in remission, some patients with IA will experience symptoms, and due to the fluctuating nature of the arthritis, symptoms will come and go throughout life with varying intensity [10,13–15]. Thus, after more than two decades of progress in the pharmacological treatment, some aspects of having IA remain less well managed: patients with IA still confront physiological and psychological distress, impacting daily activities, and overall quality of life (QoL) at disease onset, but also later in the disease course, and even when clinical remission is achieved [15,16].

Patients newly diagnosed with IA are particularly challenged and vulnerable. They are about to begin a life with IA that may involve regular blood tests, lifelong pharmacological treatment, side-effects to treatment, symptoms such as pain, fatigue, sleep disturbances, and increased risk of developing co-morbidities such as depression, cardiovascular disease, diabetes, and osteoporosis [7]. Experiencing altered body image, and changes in the family, work, and social life is common [17–23]. Therefore, a crucial but often insufficient aspect of caring for patients with IA is empowering them to gain a thorough understanding of their condition and develop their capacity to effectively manage the practical, physical, and psychological effects of the disease [24]. Several studies have shown that newly diagnosed patients require regular consultations and support from health professionals (HPs) to deal with physical, emotional and social consequences of the arthritis [17–23]. In addition, they have a wide range of educational needs, such as knowledge and management of the arthritis, and lifestyle recommendations. Previous research suggests that increased self-management - defined as the *individual's ability to manage symptoms, treatments, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition* [25], - can improve the QoL life in patients with chronic illness [26–30].

Self-management in rheumatology has been applied across multiple clinical contexts, including symptom pacing for pain and fatigue; adherence to exercise and physical activity; medication adherence and shared decision-making within treat-to-target care; and navigation of multidisciplinary services. Program formats range from brief nurse-led education to structured group programs that integrate problem-solving, goal-setting, and action planning, with demonstrated benefits in patient-reported outcomes and health service use [31,32].

As per recommendations from EULAR (European Alliance of Associations for Rheumatology) (10), self-management should be included in daily rheumatology care to support patients to become active partners in handling the disease [24]. This should include patient education and e.g., key self-management approaches such as problem-solving, goal-setting and action planning. However, when reviewing the numerous systematic reviews of arthritis-specific self-management interventions [33–37], we found it challenging to compare the included studies due to their heterogeneous study designs, program foci, and outcomes. Furthermore, despite the well-documented need for patient guidance following diagnosis [34], we found no IA-specific self-management interventions that have been systematically and specifically developed with a focus on newly diagnosed patients and subsequently tested in a Randomized Controlled Trial (RCT).
NISMA is a systematically developed, theory-informed self-management program for adults newly diagnosed with IA, described in detail elsewhere [38]. Development of NISMA followed the Medical Research Council framework, [39,40] with feasibility and process evaluations subsequently undertaken (manuscripts submitted [41,42]. The present RCT evaluates the program's efficacy compared with usual care.
The hypothesis is that the adapted NISMA intervention will be superior to usual care in increasing self-management skills and techniques and thereby improve symptoms among others. Therefore, the next step will be to test this hypothesis in a randomized NISMA trial. Further, if the intervention proves to be effective, we will conduct a cost-effectiveness analysis subsequently.

Rationale

Compared with usual care NISMA provides structured, individualized coaching with continuity from a dedicated nurse, explicit behavior-change techniques (problem-solving, goal-setting, action planning), and optional peer-supported group sessions. Grounded in Social Cognitive Theory (SCT) and informed by Acceptance and Commitment Therapy (ACT) questioning techniques, NISMA targets self-efficacy, adaptive coping, and healthcare service navigation—mechanisms expected to improve heiQ domains and downstream clinical and psychosocial outcomes.

Objectives {8}

The primary objective of this trial is to compare the short-term efficacy of the NISMA intervention and usual care, relative to usual care alone, on the HeiQ 'self-management skills and techniques' domain in patients newly diagnosed with inflammatory arthritis, from baseline to 12 months from baseline (end of intervention).

Our key secondary objectives are to compare the short-term efficacy of the NISMA intervention and usual care, relative to usual care on self-management skills, anxiety and depression, fatigue, pain self-efficacy, pain intensity, patient global assessment, medication adherence, quality of life, loneliness, and physical function from baseline to 12 months from baseline (end of the intervention).

In the extension study we will explore the longer-term efficacy of the intervention relative to usual care on self-management skills, anxiety and depression, fatigue, pain self-efficacy, pain intensity, patient global assessment, medication adherence, quality of life, loneliness, and physical function at follow-up 24-months from baseline.

Methods

Trial design {9}

The trial is designed as a pragmatic, investigator-initiated, multicenter randomized trial with a two-group parallel design in a superiority framework. Participants will be allocated in a 1:1 ratio; after providing informed consent and completing baseline assessments, they will be randomized to either the NISMA intervention (experimental group) or usual care (control group) with no protocolized added treatment.

Setting

Patients will be included from the following 3 centers: the Center for Rheumatology and Spine Diseases, Rigshospitalet University Hospital, Copenhagen, and the Department of Rheumatology and Spinal Diseases, Holbæk Hospital and Slagelse Hospital; all in Denmark. These three departments cover most of Zealand, which covers an area of 2.5 million residents.

Brief Intervention Description

Comparators

Both groups receive standard care, including scheduled consultations with a rheumatologist and access to nursing, physiotherapy, and occupational therapy services. Patients initiating disease-modifying antirheumatic drugs (DMARDs) receive an additional nurse consultation and a follow-up telephone call. Participants in the control group continue with usual self-management practices, whereas participants in the intervention group receive the NISMA intervention in addition to usual care.

The NISMA Intervention (Experimental Group)

The NISMA intervention is a 12-month, flexible self-management program designed to support patients with inflammatory arthritis. It is grounded in Social Cognitive Theory and incorporates techniques from Acceptance and Commitment Therapy (ACT), with an emphasis on problem-solving, goal-setting, and action planning.

The intervention comprises:

Individual sessions

Three mandatory individual sessions delivered by a specially trained nurse:

1. *Medical management*: understanding inflammatory arthritis and its treatment.
2. *Emotional management*: addressing crisis reactions and supporting acceptance.
3. *Role management*: adapting to changes in personal, social, and professional roles.

The first session is conducted face-to-face, while subsequent sessions may be delivered online or by telephone.

Optional group sessions

Two optional group sessions, each lasting two hours and involving 5–8 participants. Sessions are co-facilitated by a nurse and either a physiotherapist or an occupational therapist. Content focuses on symptom management, lifestyle adaptations, and peer support.

Training and fidelity

Healthcare professionals delivering the intervention receive training in ACT techniques, group facilitation, and use of a detailed intervention manual developed and reviewed by experts in rheumatology and self-management. Intervention fidelity is supported through ongoing supervision led by a project manager and an ACT-trained psychologist.

Randomization and blinding {10}

Randomization in a 1:1 ratio will be performed after the patient has signed informed consent and completed baseline assessments. A computerized random number generator algorithm obtained from the Sealed Envelope website [70] will be used to provide customized randomization tables. Randomization will be stratified by site (3 centers) and type of inflammatory condition (3 diagnoses). To facilitate this, the customized randomization tables will be uploaded for each site to Research Electronic Data Capture (REDCap) [71] allowing for stratification across three individual IA conditions. The REDCap randomization module will be used for allocation generation and to securely maintain the sequence until the intervention is assigned.

The project manager will enroll participants at the individual sites and inform them whether they have been allocated to the intervention group or the control group (see Fig. 1 for participants flow through the trial). For participants randomized to the intervention group, the first individual session will be scheduled as soon as possible after allocation. Due to the nature of the intervention, it is not possible to blind participants or HPs to the allocated intervention. However, data analysis will be performed with blinding to group allocation.

Sample size and power calculation {11}

As no established thresholds exist for clinically relevant changes in heiQ domains, we refer to prior research [68,69]. I prior research in the skills acquisition domain, we found mean differences between groups ranging from 0.22 to 0.38. Therefore, we decided that a minimal important difference probably correspond to a target difference of 0.30 with a standard deviation (SD) of 0.55 for the heiQ 'skill and technique acquisition' domain (primary endpoint) from baseline to 12 months after baseline. To achieve a statistical power of 80% and a significance level set at an alpha of 0.05, our calculations indicated a need for 54 patients per group (i.e., enrolling 108 patients in the Intention to Treat Population (ITT)). Incorporating an anticipated dropout rate of 15% from our feasibility study [41], the sample size would correspond to 127. Consequently, we revised the necessary sample size to approximately 65 patients per group (i.e., 130 patients in the ITT population) to achieve a reasonable statistical power to identify a statistically significant difference between the intervention and control group (i.e., corresponding to a statistical power of 87% in the best-case scenario).

Framework {12}

The trial is based on a two-sided superiority framework. The primary null hypothesis is that there is no immediate difference between the groups (H0: μ[I] = μ[C]) on change in the HeiQ 'self-management skill and techniques acquisition' domain, from baseline to completion of the intervention (12 months from baseline).

Statistical Interim analyses and stopping guidance {13a}

As we do not expect any serious adverse events, no statistical interim analyses are planned on any of the outcomes and no guidelines for stopping the trial early are described. All participants will continue their usual care and will be monitored by the coordinating nurse throughout the intervention period to detect any unintended events. Specific attention will be towards covering any serious adverse events, and mortalities.

Timing of outcome assessments and final analysis {14 and 15}

Analysis of the primary outcome and key secondary outcomes will be conducted with data from baseline to end of intervention (follow-up 12-month after baseline from the included participants and when data have been collected and are cleaned. The analyses of the primary outcome measure, key secondary outcome measures and secondary outcome measures will be conducted on data from 24-month follow-up for the included participants when they have been collected and cleaned. Last patient last visit is anticipated by 31st of March 2028.

Outcomes are collected at three timepoints for each participant; at baseline, 12 and 24 months after baseline (Table 1).

Table 1. Diagram of enrolment, interventions, and assessments – study period 0-12 (and 24 months)

	Measurement	Enrolment	Baseline	End of intervention (Primary endpoint)	Extension study
Time point		**Before Baseline**	**Week -2 to 0**	**12 months after baseline**	**24 months after baseline**
Enrolment					
Eligibility criteria		X			
Informed consent		X			
Allocation			X		
Intervention					
NISMA-intervention			X———	———X	

Usual care			X	X	
Assessments					
Outcomes					
Primary outcome					
Self-management skills and technique measured by HeiQ[1]	HeiQ: Domain 6: Skill and technique acquisition		X	X	X
Key secondary outcomes					
Self-management skills	HeiQ: Domain 1: Health-directed activities		X	X	X
	HeiQ: Domain 2: Positive and active engagement in life		X	X	X
	HeiQ: Domain 3. Emotional distress		X	X	X
	HeiQ: Domain 4: Self-monitoring and insight		X	X	X
	HeiQ: Domain 5: Constructive attitudes and approaches		X	X	X
	HeiQ: Domain 7: Social integration and support		X	X	X
	HeiQ: Domain 8: Health service navigation		X	X	X
Anxiety and depression	HADS Anxiety		X	X	X
	HADS Depression		X	X	X
Fatigue	BRAF-NRS severity		X	X	X
	BRAF-NRS impact		X	X	X
	BRAF-NRS coping		X	X	X
	VAS-fatigue		X	X	X
Pain self-efficacy	ASES-pain		X	X	X
Pain intensity	VAS-pain		X	X	X
Global assessment by	VAS-global		X	X	X
Medication adherence	CQR-5-item scale		X	X	X
Quality of life by	EQ5D-5L		X	X	X
Loneliness by	Three-Item Loneliness Scale		X	X	X
Physical function by	MD-HAQ		X	X	X
Other Secondary outcomes					
Disease activity by condition	DAS28 for RA		X	X	X
	BASDAI for axSpA		X	X	X
	DAPSA for PsA		X	X	X
Acute phase reactant value	C-reactive protein		X	X	X
Additional measures					
Age, sex, educational level, cohabitation, work status	Questionnaire		X		
Diagnosis	Medical record		X		
Pharmacological treatment of arthritis (DMARDS)	Medical record		X		
Use of pain medication	Medical record		X		
Use of glucocorticoids	Medical record		X		
Co-morbidity*	Medical record and Questionnaire		X		
Smoking	Questionnaire		X		
Alcohol	Questionnaire		X		
Hospital (trial site)	Medical record		X		

*Diabetes, hypertension, myocardial infarction, chronic obstructive pulmonary disease, cancer, osteoarthritis, osteoporosis, asthma, depression, or anxiety.

ASES (Arthritis Self-Efficacy Scale); axSpA (axial spondyloarthritis); BASDAI (Bath Ankylosing Spondylitis Disease Activity Index); BRAF-NRS (Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale); CQR-5 (Compliance Questionnaire Rheumatology, 5-item); DAS28 (Disease Activity Score in 28 joints); DAPSA (Disease Activity in Psoriatic Arthritis); DMARDs (disease-modifying antirheumatic drugs); EQ5D-5L (EuroQol 5 Dimensions 5 Levels); HADS (Hospital Anxiety and Depression Scale); heiQ (Health Education Impact Questionnaire); MD-HAQ (Modified Health Assessment Questionnaire); PsA (psoriatic arthritis); RA (rheumatoid arthritis); VAS (visual analogue scale).

Confidence intervals and P values {16,17,18}

All results from statistical analyses on the primary and key secondary endpoints will be accompanied by two-sided 95% Confidence Intervals (95%CIs) and corresponding P values. Superiority is defined as $p<0.05$ for the primary endpoint. The 95%CIs will not be adjusted for multiplicity and should not be used in place of hypothesis testing. To account for multiplicity and preserve the overall type 1 error for the numerous secondary outcomes, a hierarchical (gatekeeping) strategy will be used (see below).

Adherence and Protocol deviations {19}

Adherence to the intervention is defined as participation in the 1) three individual sessions OR 2) two individual sessions and one group session. Number of participants who adhered and did not adhere to the intervention will be summarized and reported.

Analysis of populations {20}

The treatment policy estimand quantifies the average treatment effect among all randomly assigned patients, irrespective of treatment adherence or initiation of rescue interventions, corresponding to the intention-to-treat (ITT) population. The ITT principle states that the effect of a treatment policy can be best assessed by evaluating on the basis of the intention to treat a participant (that is, the planned treatment regimen) rather than the actual treatment given (5, 6). The ITT population will be used to assess the superiority of NISMA versus control for the primary and secondary endpoints in a predefined hierarchical order. For the purpose of sensitivity analysis, the ITT analyses will be followed by per protocol analyses. In the intervention group protocol populations are defined as participants who have attended the three individual sessions or two individual sessions and one group session.

Screening data {21}

Number of patients screened for participation will be reported. This includes number of patients who were approached in the outpatient clinic and the number of patients who were shown the pop-up text in the DANBIO registry after completing the usual questionnaires, number who showed interest to hear more about the study (added their phone number), and were sent the participant information, number contacted,

number of contacted patients who did not meet the eligibility criteria, number of patients who met the eligibility criteria who declined and the number who accepted to participate.

Eligibility criteria {22}

Inclusion Criteria

Patients will be included if they are adults aged 18 years or older with one of the following conditions:

- Rheumatoid Arthritis (RA) with ICD-10 codes: M05.3, M05.9, M05.8, M06.9 diagnosed within the last 6 months
- Psoriatic Arthritis (PsA) with ICD-10 codes: M073.A, M073.B diagnosed within the last 6 months
- Axial Spondyloarthritis (axSpA) with ICD-10 codes: M45.9, M46.1, M46.8, M46.9, diagnosed within the last 12 months, and has initiated biological treatment

Patients with axSpA will have unique inclusion criteria due to NSAIDs being the first-line pharmacological treatment [43]. For those effectively treated with NSAIDs and exercise, treatment is transitioned to their general practitioner. Therefore, we only those who has initiated biological treatment will be included.

Exclusion criteria

Patients will be excluded if they: have insufficient language skills to discuss the topics in the intervention in Danish; are receiving chemo-therapy treatment for malignancies; are pregnant or have severe mental illness.

Recruitment {23}

Eligible patients will be identified either during visits to the outpatient clinic, where the healthcare professionals (HPs) will briefly inform them about the trial and provide written information, or through recruitment via the national Danish Rheumatology Database (DANBIO). If patients express interest, participant materials will be sent to them. The project manager will then contact the interested patients by phone to provide further details about the trial. After obtaining oral consent, written consent forms and a baseline questionnaire will be sent to the participant's electronic mailbox (e-Boks) via REDCap or by postal mail if the patient does not use e-Boks.

The CONSORT trial profile diagram will include the number of individuals screened, deemed eligible, provided consent, randomized, assigned to their respective treatments, and those who withdraw or are lost to follow-up at each time point.

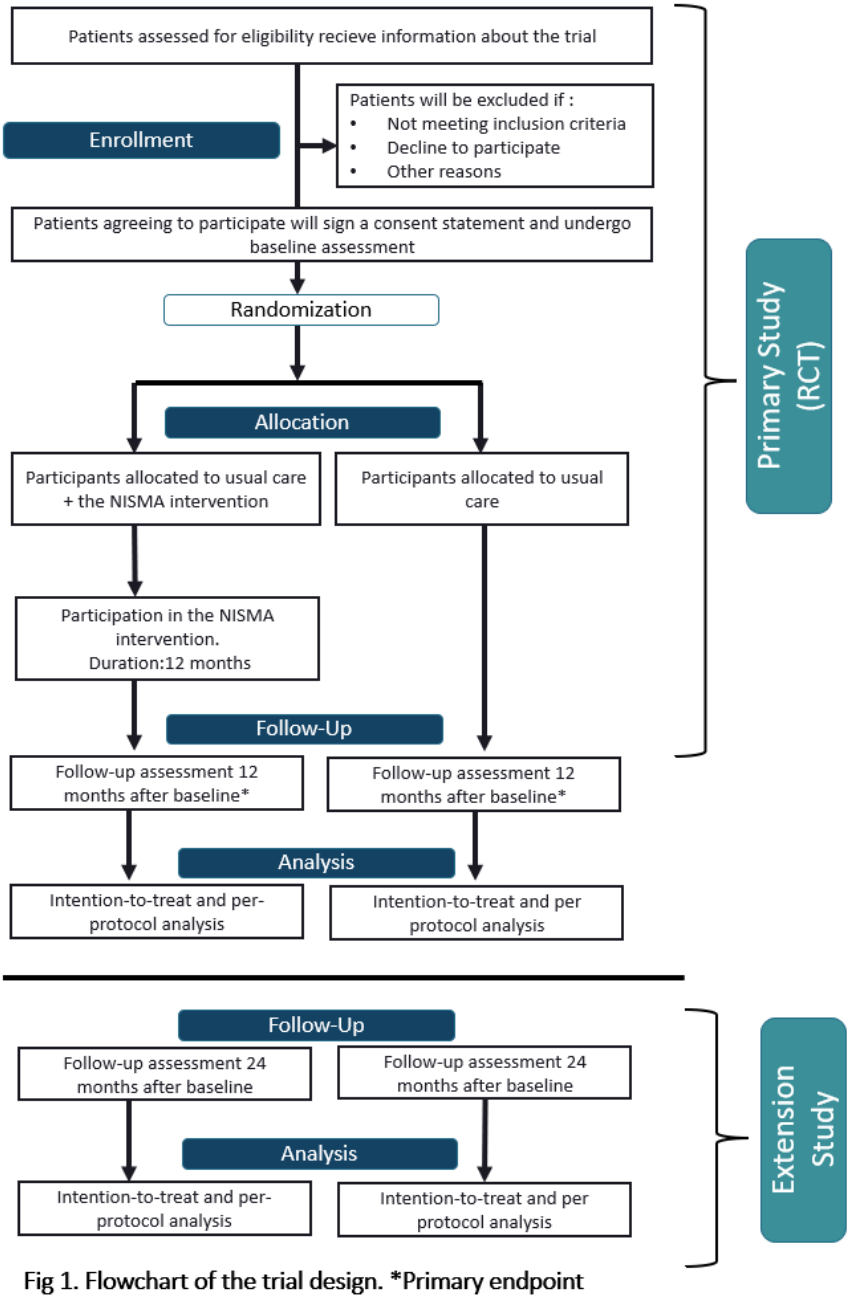

Fig 1. Flowchart of the trial design. *Primary endpoint

Withdrawal and follow-up {24}

Participants may withdraw from the study at any time prior to data analysis. The number of withdrawals after consent, group allocation, baseline sociodemographic and disease characteristics, and the timing of withdrawal or loss to follow-up will be reported. We will attempt to follow up all randomized participants who discontinue the allocated treatment. The level of consent withdrawal will be documented and tabulated as one of the following categories: consent to continue both follow-up and data collection; consent to continue data collection only; or complete withdrawal, with no further follow-up or data collection.

Baseline patient characteristics {25}

Baseline characteristics (age, sex, educational level, cohabitation, work status, diagnosis, pharmacological treatment of arthritis, use of pain medication, use of glucocorticoids, co-morbidity, smoking, alcohol, hospital (trial site)) will be descriptively summarized.

Analysis

Outcomes {26}

Self-management is a complex concept that primarily has been utilized in the research of patients with chronic diseases. There is no consensus on how to measure self-management in IA (or any other chronic disease) [47]. Early IA presents multidimensional challenges (symptoms, function, mental health, self-efficacy, service navigation). The outcome set captures these domains while prioritizing a single primary endpoint (heiQ ‘skill and technique acquisition’). Key secondary endpoints follow a pre-specified hierarchy based on feasibility results; interpretation will consider heterogeneity of scales.

Primary outcome and endpoint

The primary outcome is self-management skills assessed with the heiQ "skill and technique acquisition" domain [48]. We consider the" self-management skill and technique acquisition" domain to best reflect the changes we aim to achieve through our intervention, and therefore it is considered our primary outcome. This domain captures knowledge-based skills and techniques used to manage disease-related symptoms and health problems. The heiQ comprises eight independent domains (health-directed activity; positive and active engagement in life; emotional wellbeing; self-monitoring and insight; constructive attitudes and approaches; skill and technique acquisition; social integration and support; health service navigation), each scored 1–4, where higher values reflect better self-management (note: emotional wellbeing is reverse-scored). The heiQ demonstrates sound internal consistency, construct validity, and responsiveness across chronic-disease and rheumatology settings [49,50]. The primary endpoint is the between-group difference in least-squares means (LS-means) for the heiQ "skill and technique acquisition" score at 12 months from baseline, reported with two-sided 95% confidence intervals and p values (superiority defined as $p<0.05$).

Key secondary outcomes and endpoints

Secondary outcomes are the following PROMs:

- Self-management skills measured by seven of the heiQ domains: health-directed activity; positive and active engagement in life; emotional wellbeing; self-monitoring and insight; constructive attitudes and approaches; social integration and support, and health service navigation [49,50]. The corresponding endpoints is the between-group difference in least squares means from the 6 heiQ domains after 12 months. Endpoints in the extension study are the between-group difference in least squares means in heiQ domain 1, 2, 3, 4, 5, 6, 7, and 8 after 24 months.
- Anxiety and depression measured by the Hospital Anxiety and Depression Scale (HADS), that has good reliability and factorial validity across medical populations, including rheumatology [51,52]. The

corresponding endpoint is the between-group difference in least squares means from HADS after 12 months. Endpoint in the extension study is between group difference in HADS 24 months after baseline.

- Fatigue measured by the Bristol Rheumatoid Arthritis Fatigue Numeric Rating Scale (BRAF-NRS), that is validated, including Danish versions, with good construct validity and responsiveness [53], and VAS-fatigue (0-100). The corresponding endpoint is the between-group difference in least squares means from VAS and BRAF-NRS after 12 months. Endpoint in the extension study is between group difference in VAS and BRAF-NRS 24 months after baseline.
- Pain self-efficacy measured by the Arthritis specific Self-Efficacy measurement tool (ASES-pain). The scale has established internal consistency and predictive validity in arthritis [54,55]. The corresponding endpoint is the between-group difference in least squares means from ASES-pain after 12 months. Endpoint in the extension study is between group difference in ASES-pain 24 months after baseline.
- Pain Intensity measured by VAS (0-100), a simple, reliable single-item measures with strong convergent validity in IA [56,57]The corresponding endpoint is the between-group difference in least squares means from VAS after 12 months. Endpoint in the extension study is between group difference in VAS 24 months after baseline.
- Patient global assessment measured by VAS-Global, which is validated within rheumatology [58]. The corresponding endpoint is the between-group difference in least squares means from VAS after 12 months. Endpoint in the extension study is between group difference in VAS 24 months after baseline.
- Medication adherence will be measured by the Compliance Questionnaire Rheumatology (CQR)-5-item scale, that has acceptable reliability and criterion validity for identifying non-adherence [59,60] The corresponding endpoint is the between-group difference in least squares means from CQR after 12 months. Endpoint in the extension study is between group difference in CQR 24 months after baseline.
- Health Related Quality of Life measured by European Quality of Life (EQ5D-5L), that has validity supported across rheumatic diseases; Danish value set applied [61,62]. The corresponding endpoint is

the between-group difference in least squares means from EQ5D-5L after 12 months. Endpoint in the extension study is between group difference in EQ5D-5L 24 months after baseline.

- Loneliness will be measured by the Three Item Loneliness Scale, a short scale validated for measuring loneliness [63]. The corresponding endpoint is the between-group difference after 12 months. Endpoint in the extension study is between group difference 24 months after baseline.
- Physical function measured by Modified Health Assessment Questionnaire (MD-HAQ) , is well-validated and responsive across rheumatology) [64]. The corresponding endpoint is the between-group difference in least squares means from MD-HAQ after 12 months. Endpoint in the extension study is between group difference in MD-HAQ 24 months after baseline.

Other secondary outcomes and endpoints

- Disease activity measured by the percentage improvement from baseline using various composite scores depending on the rheumatic diagnoses. For RA: Disease Activity Score in 28 joints (DAS28) [65], for axSpA: the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [66], and for PsA: the Disease Activity index for Psoriatic Arthritis (DAPSA) [67].These indices have established reliability, construct validity, and responsiveness in their target populations, and are analyzed as between-group LS-means differences at 12 months; the extension study repeats these analyses at 24 months.

All primary and secondary outcomes will be measured at baseline (t=0 months), 12 months after baseline. The extension study will report all outcomes, presenting the long-term effect and sustainability at 24 months from baseline.

Analysis methods for primary and secondary outcomes {27}

The primary study

Descriptive statistics for baseline characteristics will be reported in a Table 1 format; reported separately for each treatment group. These descriptive statistics will summarize the characteristics of participants at baseline, including demographic information and outcome variables relevant to the trial. Descriptive statistics and measures will be presented as means with standard deviations or medians with interquartile ranges depending on the empirical data distribution. Categorical variables will be presented as absolute counts and proportions (percentages). No statistical significance tests will be conducted for baseline characteristics.

The primary endpoint will be based on the between-group difference in heiQ 'skill and technique acquisition' at 12 months, estimated as the difference between least squares means. In our main analyses, estimations of between-group differences for all continuous outcomes will be conducted after 12 months. The primary endpoint will be analyzed using analysis of covariance (ANCOVA), adjusting for baseline values, trial site, and IA diagnosis as covariates.

The analyses of the secondary endpoints will be performed and interpreted in sequence until one of the analyses fails to show the statistically significant difference, or until all analyses have been completed at a statistical significance level of 0.05 ($P<0.05$). All analyses in the statistical hierarchy will be based on the treatment policy estimand (the primary estimand, i.e., the ITT principle), which quantify the average treatment effect regardless of adherence to treatment or initiation of rescue interventions between baseline and month 12. Key assumptions for statistical tests, including normality of residuals in ANCOVA, will be assessed using studentized residuals scattered against the predicted values, and other graphical methods (e.g., Q-Q plots, histograms). If assumptions are violated, alternative methods such as nonparametric tests (e.g., Wilcoxon rank-sum test) or transformation of variables will be considered.

The extension study

Given the availability of repeated measures in the extension study, missing data will be addressed implicitly using repeated-measures mixed-effects models. The primary and key secondary (continuous) outcomes will be analyzed using linear mixed-effects models (LMMs) with repeated measures, incorporating: Treatment group (2 levels: intervention, control), time (0, 12, and 24 months after baseline [3 levels]), group × time interaction, baseline values of the respective outcome as a covariate, and stratification factors:diagnosis (3 levels)

This approach ensures that all intergroup differences at each timepoint are adjusted for baseline levels, thereby minimizing random variation. Least squares means (LSMs) and their standard errors will be reported

for each group, with between-group differences presented as adjusted LSM differences with two-sided 95% CIs and P values. Superiority will be defined as $P < 0.05$.

Methods in analysis to handle missing data {28}

The main analyses will be based on the ITT population, i.e., including all randomized patients with a baseline measure available [57]. The ITT principle asserts the effect of a treatment policy (that is, the planned treatment regimen), rather than the actual treatment given (i.e., it is independent of treatment adherence) [9]. Accordingly, participants allocated to a treatment group (NISMA and Control, respectively) will be followed up, assessed, and analyzed as members of that group, irrespective of their adherence to the planned course of treatment (i.e., independent of withdrawals and cross-over phenomena).
A multiple imputation approach will be used in which missing data are imputed from month 12 measurements from participants in the same treatment group. A series of complete data sets will be generated and analyzed, and the results will be combined using the Rubin formula [58] to obtain overall estimates. For continuous outcomes, all between-group differences 95% CIs for continuous outcomes will be based on the least square means, adjusted for baseline levels and stratifying factors to minimize random variation [59].
Continuous outcome measures will be analyzed using analysis of covariance, with randomized treatment, trial site, and type of IA diagnoses as factors, and baseline (pre-exposure) value as a covariate. Categorical end points will be analyzed using logistic regression, with the same factors and covariates.

Methods for additional analyses (e.g., subgroup analyses) {29}

This item does not apply as no additional analyses are planned.

Adverse Event Reporting and Harms {30}

This is a non-drug intervention trial incorporating educational elements, behavioral therapies, and self-efficacy training strategies — all of which are standard components of routine clinical practice for many healthcare professionals (HPs). While the intervention is considered low risk, participants will be monitored throughout the 12-month period to identify any unintended events and ensure their safety.

HPs delivering the intervention will continuously observe participants for potential adverse events during both individual and group sessions. Any adverse events reported by participants or observed by the HPs will

be documented. Serious adverse events (SAEs), defined as events resulting in hospitalization, significant disability, or life-threatening conditions, will be promptly reported to the Research Ethics Committee [60].

The number and percentage of participants who discontinue the trial, including those who withdraw specifically due to adverse events, will be recorded for each treatment arm. Additionally, the number and percentage of serious adverse events, deaths (if applicable), and the frequency of each type of adverse event will be presented for both groups. Given the exploratory nature of this reporting, no formal statistical testing will be conducted on adverse events.

Although the intervention is non-pharmacological and designed to support participants, some adverse events may still occur. Potential adverse events include emotional distress, particularly when discussing sensitive topics such as crisis management and role adjustments. Some participants may experience increased anxiety or frustration, especially if they perceive slow progress or feel overwhelmed by goal-setting and behavior changes. Group sessions could provoke social discomfort for those unaccustomed to sharing personal experiences in a group setting. Additionally, participants might experience fatigue or cognitive strain, especially when balancing the intervention with the demands of managing their condition. In rare cases, increased physical or emotional effort during self-management activities could temporarily worsen symptoms such as pain or fatigue.

The intervention is designed to minimize these risks through a person-centered approach, ensuring that HPs — trained in Acceptance and Commitment Therapy (ACT) techniques — can provide appropriate emotional support and guide participants in managing their responses and setting realistic, achievable goals.

Statistical software {31}

All analyses will be executed using SAS Enterprise Guide version 8.3.

Table 1. Participant characteristics

Outcome	Intervention Group	Control Group	Total Population
Demographics			
Age			
Female sex, N (%)			
Hospital (trial site)			
Cohabitant, N (%)			
On sick leave, N (%)			
School level above high school, N (%)			
Lifestyle			
Smoking Present, N (%) Previous or never, N (%)			
Alcohol, ≥10 units/week, N (%)			
Clinical variables			
Diagnoses RA axSpA PsA			
Pharmacological treatment of arthritis (DMARDs)			
Use of pain medication			
Use of glucocorticoids			
Co-morbidity*			
Primary Outcome			
Self-management skills and technique HeiQ[1] Domain 6: Skill and technique acquisition			
Key Secondary Outcomes			
Self-management skills by HeiQ[1] Domain 1: Health-directed activities Domain 2: Positive and active engagement in life Domain 3: Emotional distress Domain 4: Self-monitoring and insight Domain 5: Constructive attitudes and approaches Domain 7: Social integration and support Domain 8: Health service navigation			
Medication adherence by CQR-5-item scale[2]			
Anxiety and depression by HADS[3] Anxiety Depression			
Fatigue by BRAF-NRS[4] VAS[5]-fatigue			
Pain intensity by VAS[5]-pain			
Pain self-efficacy by ASES-pain[6]			
Global assessment by VAS[5]-global			
Physical function by MD-HAQ[7]			
Quality of life by EQ5D-5L[8]			
Loneliness by Three-Item Loneliness Scale			
Other Secondary Outcomes			
Disease activity by condition DAS28[9] for RA BASDAI[10] for axSpA			

DAPSA[11] for PsA			
Acute phase reactant value by C-reactive protein			

Footnotes: *Diabetes, hypertension, myocardial infarction, chronic obstructive pulmonary disease, cancer, osteoarthritis, osteoporosis, asthma, depression, or anxiety.
[1] Health Education Impact Questionnaire (HeiQ), [2] Compliance Questionnaire Rheumatology (CQR), [3] Hospital Anxiety and Depression Scale (HADS), [4] Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS), [5] Visual Analog Scale (VAS), [6] Arthritis Self-Efficacy Scale (ASES), [7] Modified Health Assessment Questionnaire (MD-HAQ), [8] EuroQol 5 Dimensions 5 Levels (EQ5D-5L), [9] Disease Activity Score 28 (DAS28), [10] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), [11] Disease Activity in Psoriatic Arthritis (DAPSA)

Table 2. Outcomes after 12 months (end of intervention) in the ITT-population†

Outcome	Intervention Group	Control Group	Between group difference	*p*-value
Primary Outcome				
Self-management skills and technique HeiQ[1] Domain 6: Skill and technique acquisition				
Key Secondary Outcomes				
Self-management skills by HeiQ[1] Domain 1: Health-directed activities Domain 2: Positive and active engagement in life Domain 3: Emotional distress Domain 4: Self-monitoring and insight Domain 5: Constructive attitudes and approaches Domain 7: Social integration and support Domain 8: Health service navigation				
Medication adherence by CQR-5-item scale[2]				
Anxiety and depression by HADS[3] Anxiety Depression				
Fatigue by BRAF-NRS[4] VAS[5]-fatigue				
Pain intensity by VAS[5]-pain				
Pain self-efficacy by ASES-pain[6]				
Global assessment by VAS[5]-global				
Physical function by MD-HAQ[7]				
Quality of life by EQ5D-5L[8]				
Loneliness by Three-Item Loneliness Scale				
Other Secondary Outcomes				
Disease activity by condition DAS28[9] for RA BASDAI[10] for axSpA DAPSA[11] for PsA				
Acute phase reactant value by C-reactive protein				

Footnotes:

[1] Health Education Impact Questionnaire (HeiQ), [2] Compliance Questionnaire Rheumatology (CQR), [3] Hospital Anxiety and Depression Scale (HADS), [4] Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS), [5] Visual Analog Scale (VAS), [6] Arthritis Self-Efficacy Scale (ASES), [7] Modified Health Assessment Questionnaire (MD-HAQ), [8] EuroQol 5 Dimensions 5 Levels (EQ5D-5L), [9] Disease Activity Score 28 (DAS28), [10] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), [11] Disease Activity in Psoriatic Arthritis (DAPSA)

†ITT= Intention To Treat → Missing data will be imputed from retrieved patients of the same randomized treatment and the results will be combined using Rubin's rules.

Table 3. Safety, Harms, and Adverse Events assessed from baseline to end of intervention

Outcome	Intervention, N=??	Control, N=??	Difference between groups (95% CI)
Discontinuations, no. (%):			
Total discontinuations			
Discontinuations due to adverse events			
Serious Adverse Events (SAEs), no. (%):			
Hospitalization			
Significant disability			
Life-threatening event			
Deaths, no. (%):			
Frequency and percentage of each AE type:			
Emotional distress			
Increased anxiety or frustration			
Social discomfort			
Fatigue or cognitive overload			
Temporary worsening of symptoms			

Appendix 1. Outcomes after 12 months in the PP-population†

Outcome	Intervention Group	Control Group	Between group difference
Primary Outcome			
Self-management skills and technique HeiQ[1] Domain 6: Skill and technique acquisition			
Secondary Outcomes			
Self-management skills by HeiQ[1] Domain 1: Health-directed activities Domain 2: Positive and active engagement in life Domain 3: Emotional distress Domain 4: Self-monitoring and insight Domain 5: Constructive attitudes and approaches Domain 7: Social integration and support Domain 8: Health service navigation			
Medication adherence by CQR-5-item scale[2]			
Anxiety and depression by HADS[3] Anxiety Depression			
Fatigue by BRAF-NRS[4] VAS[5]-fatigue			
Pain intensity by VAS[5]-pain			
Pain self-efficacy by ASES-pain[6]			
Global assessment by VAS[5]-global			
Physical function by MD-HAQ[7]			
Quality of life by EQ5D-5L[8]			
Loneliness by Three-Item Loneliness Scale			
Other Secondary Outcomes			
Disease activity by condition DAS28[9] for RA BASDAI[10] for axSpA DAPSA[11] for PsA			
Acute phase reactant value by C-reactive protein			

Footnotes:

[1] Health Education Impact Questionnaire (HeiQ), [2] Compliance Questionnaire Rheumatology (CQR), [3] Hospital Anxiety and Depression Scale (HADS), [4] Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS), [5] Visual Analog Scale (VAS), [6] Arthritis Self-Efficacy Scale (ASES), [7] Modified Health Assessment Questionnaire (MD-HAQ), [8] EuroQol 5 Dimensions 5 Levels (EQ5D-5L), [9] Disease Activity Score 28 (DAS28), [10] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), [11] Disease Activity in Psoriatic Arthritis (DAPSA)

†PP= Per Protocol. Missing data will be imputed from retrieved patients of the same randomized treatment and the results were combined using Rubin's rules.

Appendix 2. Outcomes after 12 months in the ITT-population. Missing data will be replaced using non-responder imputation

Outcome	Intervention Group	Control Group	Between group difference
Primary Outcome			
Self-management skills and technique HeiQ[1] Domain 6: Skill and technique acquisition			
Secondary Outcomes			
Self-management skills by HeiQ[1] Domain 1: Health-directed activities Domain 2: Positive and active engagement in life Domain 3: Emotional distress Domain 4: Self-monitoring and insight Domain 5: Constructive attitudes and approaches Domain 7: Social integration and support Domain 8: Health service navigation			
Medication adherence by CQR-5-item scale[2]			
Anxiety and depression by HADS[3] Anxiety Depression			
Fatigue by BRAF-NRS[4] VAS[5]-fatigue			
Pain intensity by VAS[5]-pain			
Pain self-efficacy by ASES-pain[6]			
Global assessment by VAS[5]-global			
Physical function by MD-HAQ[7]			
Quality of life by EQ5D-5L[8]			
Loneliness by Three-Item Loneliness Scale			
Other Secondary Outcomes			
Disease activity by condition DAS28[9] for RA BASDAI[10] for axSpA DAPSA[11] for PsA			
Acute phase reactant value by C-reactive protein			

Footnotes:

[1] Health Education Impact Questionnaire (HeiQ), [2] Compliance Questionnaire Rheumatology (CQR), [3] Hospital Anxiety and Depression Scale (HADS), [4] Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS), [5] Visual Analog Scale (VAS), [6] Arthritis Self-Efficacy Scale (ASES), [7] Modified Health Assessment Questionnaire (MD-HAQ), [8] EuroQol 5 Dimensions 5 Levels (EQ5D-5L), [9] Disease Activity Score 28 (DAS28), [10] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), [11] Disease Activity in Psoriatic Arthritis (DAPSA)

Abbreviations

ACT: Acceptance and Commitment Therapy
ASES-pain: Arthritis specific Self-Efficacy measurement tool
axSpA: Axial Spondyloarthritis
BASDAI: Bath Ankylosing Spondylitis Disease Activity Index
BRAF-NRS: Bristol Rheumatoid Arthritis Fatigue Numeric Rating Scale
CQR-5-item scale: Compliance Questionnaire Rheumatology
DAS28: Disease Activity Score in 28 joints
DAPSA: Disease Activity index for Psoriatic Arthritis
DMARDs: disease-modifying anti-rheumatic drugs
EQ5D: European Quality of Life
EULAR: European Alliance of Associations for Rheumatology
HPs: health professionals
IA: Inflammatory arthritis
ITT: Intention to Treat
LHL: Luise Holberg Lindgren
MHAQ: Modified Health Assessment Questionnaire
PP: Per protocol
PsA: Psoriatic Arthritis
QoL: quality of life
RA: Rheumatoid Arthritis
SCT: Social Cognitive Theory
SD: standard deviation
VAS-Global: Patient global assessment measured by visual analog Scale.

References

[1] Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. Nat Rev Dis Primer 2018;4:18001. https://doi.org/10.1038/nrdp.2018.1.

[2] Bohn R, Cooney M, Deodhar A, Curtis JR, Golembesky A. Incidence and prevalence of axial spondyloarthritis: methodologic challenges and gaps in the literature. Clin Exp Rheumatol 2018;36:263–74.

[3] Gladman D, Antoni C, Mease P, Clegg D, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64:ii14–7. https://doi.org/10.1136/ard.2004.032482.

[4] Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. Lancet Lond Engl 2018;391:2273–84. https://doi.org/10.1016/S0140-6736(18)30830-4.

[5] Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Res 2018;6:1–14. https://doi.org/10.1038/s41413-018-0016-9.

[6] Hetland ML. Psoriatic arthritis: still room for improvement. The Lancet 2020;395:1463–5. https://doi.org/10.1016/S0140-6736(20)30800-X.

[7] Innala L, Sjöberg C, Möller B, Ljung L, Smedby T, Södergren A, et al. Co-morbidity in patients with early rheumatoid arthritis - inflammation matters. Arthritis Res Ther 2016;18. https://doi.org/10.1186/s13075-016-0928-y.

[8] Løppenthin K, Esbensen BA, Østergaard M, Ibsen R, Kjellberg J, Jennum P. Morbidity and mortality in patients with rheumatoid arthritis compared with an age- and sex-matched control population: A nationwide register study. J Comorbidity 2019;9:2235042X19853484. https://doi.org/10.1177/2235042X19853484.

[9] Detry MA, Lewis RJ. The intention-to-treat principle: how to assess the true effect of choosing a medical treatment. JAMA 2014;312:85–6. https://doi.org/10.1001/jama.2014.7523.

[10] Duarte C, Ferreira RJO, Santos EJF, da Silva JAP. Treating-to-target in rheumatology: Theory and practice. Best Pract Res Clin Rheumatol 2022;36:101735. https://doi.org/10.1016/j.berh.2021.101735.

[11] Murray K, Turk M, Alammari Y, Young F, Gallagher P, Saber T, et al. Long-term remission and biologic persistence rates: 12-year real-world data. Arthritis Res Ther 2021;23:25. https://doi.org/10.1186/s13075-020-02380-z.

[12] Khabbazi A, Gadakchi L, Moslemi M, Khalaji A, Esalatmanesh K, Ziarati Yazdeli A, et al. Prevalence and predictors of long-term remission in rheumatoid arthritis in real-world practice: a longitudinal study. Clin Rheumatol 2023;42:1537–44. https://doi.org/10.1007/s10067-023-06548-1.

[13] Ferreira RJO, Landewé RBM, Silva JAP da. Definition of Treatment Targets in Rheumatoid Arthritis: Is It Time for Reappraisal? J Rheumatol 2021;48:1763–6. https://doi.org/10.3899/jrheum.210050.

[14] Ishida M, Kuroiwa Y, Yoshida E, Sato M, Krupa D, Henry N, et al. Residual symptoms and disease burden among patients with rheumatoid arthritis in remission or low disease activity: a systematic literature review. Mod Rheumatol 2018;28:789–99. https://doi.org/10.1080/14397595.2017.1416940.

[15] Ajeganova S, Huizinga T. Sustained remission in rheumatoid arthritis: latest evidence and clinical considerations. Ther Adv Musculoskelet Dis 2017;9:249–62. https://doi.org/10.1177/1759720X17720366.

[16] Sun X, Li R, Cai Y, Al-Herz A, Lahiri M, Choudhury MR, et al. Clinical remission of rheumatoid arthritis in a multicenter real-world study in Asia-Pacific region. Lancet Reg Health West Pac 2021;15:100240. https://doi.org/10.1016/j.lanwpc.2021.100240.

[17] Madsen M, Jensen KV, Esbensen BA. Men's experiences of living with ankylosing spondylitis: a qualitative study. Musculoskeletal Care 2015;13:31–41. https://doi.org/10.1002/msc.1082.

[18] Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Boström C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis 2015;74:954–62. https://doi.org/10.1136/annrheumdis-2014-206807.

[19] White A, McKee M, Richardson N, Visser R d., Madsen SA, Sousa BC d., et al. Europe's men need their own health strategy. BMJ 2011;343:d7397–d7397. https://doi.org/10.1136/bmj.d7397.

[20] CLARKE LH, BENNETT E. 'You learn to live with all the things that are wrong with you': gender and the experience of multiple chronic conditions in later life. Ageing Soc 2013;33:342–60. https://doi.org/10.1017/S0144686X11001243.

[21] Dures E, Bowen C, Brooke M, Lord J, Tillett W, McHugh N, et al. Diagnosis and initial management in psoriatic arthritis: a qualitative study with patients. Rheumatol Adv Pract 2019;3. https://doi.org/10.1093/rap/rkz022.

[22] Kristiansen TM, Primdahl J, Antoft R, Hørslev-Petersen K. Everyday Life with Rheumatoid Arthritis and Implications for Patient Education and Clinical Practice: A Focus Group Study: Everyday Life with Rheumatoid Arthritis. Musculoskeletal Care 2012;10:29–38. https://doi.org/10.1002/msc.224.

[23] Sumpton D, Kelly A, Tunnicliffe DJ, Craig JC, Hassett G, Chessman D, et al. Patients' Perspectives and Experience of Psoriasis and Psoriatic Arthritis: A Systematic Review and Thematic Synthesis of Qualitative Studies. Arthritis Care Res 2020;72:711–22. https://doi.org/10.1002/acr.23896.

[24] Nikiphorou E, Santos EJF, Marques A, Böhm P, Bijlsma JW, Daien CI, et al. 2021 EULAR recommendations for the implementation of self-management strategies in patients with inflammatory arthritis. Ann Rheum Dis 2021;80:1278–85. https://doi.org/10.1136/annrheumdis-2021-220249.

[25] Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns 2002;48:177–87. https://doi.org/10.1016/s0738-3991(02)00032-0.

[26] Holman HR, Lorig K. Perceived self-efficacy in self-management of chronic disease. Self-Effic. Thought Control Action, Washington, DC, US: Hemisphere Publishing Corp; 1992, p. 305–23.

[27] Lorig KR, Holman H. Self-management education: history, definition, outcomes, and mechanisms. Ann Behav Med Publ Soc Behav Med 2003;26:1–7. https://doi.org/10.1207/S15324796ABM2601_01.

[28] Prochaska JO, DiClemente CC. The transtheoretical approach. Handb. Psychother. Integr. 2nd Ed, New York, NY, US: Oxford University Press; 2005, p. 147–71. https://doi.org/10.1093/med:psych/9780195165791.003.0007.

[29] Dures E, Hewlett S. Cognitive-behavioural approaches to self-management in rheumatic disease. Nat Rev Rheumatol 2012;8:553–9. https://doi.org/10.1038/nrrheum.2012.108.

[30] Novak M, Costantini L, Schneider S, Beanlands H. Approaches to Self-Management in Chronic Illness. Semin Dial 2013;26:188–94. https://doi.org/10.1111/sdi.12080.

[31] Nolte S, Osborne RH. A systematic review of outcomes of chronic disease self-management interventions. Qual Life Res Int J Qual Life Asp Treat Care Rehabil 2013;22:1805–16. https://doi.org/10.1007/s11136-012-0302-8.

[32] Nolte S, Elsworth GR, Newman S, Osborne RH. Measurement issues in the evaluation of chronic disease self-management programs. Qual Life Res Int J Qual Life Asp Treat Care Rehabil 2013;22:1655–64. https://doi.org/10.1007/s11136-012-0317-1.

[33] Warsi A, LaValley MP, Wang PS, Avorn J, Solomon DH. Arthritis self-management education programs: a meta-analysis of the effect on pain and disability. Arthritis Rheum 2003;48:2207–13. https://doi.org/10.1002/art.11210.

[34] Warsi A, Wang PS, LaValley MP, Avorn J, Solomon DH. Self-management education programs in chronic disease: a systematic review and methodological critique of the literature. Arch Intern Med 2004;164:1641–9. https://doi.org/10.1001/archinte.164.15.1641.

[35] Hansen CW, Esbensen BA, de Thurah A, Christensen R, de Wit M, Cromhout PF. Outcome measures in rheumatology applied in self-management interventions targeting people with inflammatory Arthritis A systematic review of outcome domains and measurement instruments. Semin Arthritis Rheum 2022;54:151995. https://doi.org/10.1016/j.semarthrit.2022.151995.

[36] Lindgren LH, de Thurah A, Aadahl M, Hetland ML, Kristensen S, Esbensen BA. Newly Diagnosed with Inflammatory Arthritis (NISMA) – Development of a Complex Self-management Intervention (accepted for publication) n.d.

[37] Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008;337. https://doi.org/10.1136/bmj.a1655.

[38] Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ 2021;374:n2061. https://doi.org/10.1136/bmj.n2061.

[39] Create a blocked randomisation list | Sealed Envelope n.d. https://www.sealedenvelope.com/simple-randomiser/v1/lists (accessed February 25, 2025).

[40] REDCap. GCP-Enhederne n.d. https://gcp-enhed.dk/forsoegsdokumenter/case-report-form/ecrf/redcap/ (accessed February 25, 2025).

[41] Francis KL, Matthews BL, Van Mechelen W, Bennell KL, Osborne RH. Effectiveness of a community-based osteoporosis education and self-management course: a wait list controlled trial. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA 2009;20:1563–70. https://doi.org/10.1007/s00198-009-0834-0.

[42] Crotty M, Prendergast J, Battersby MW, Rowett D, Graves SE, Leach G, et al. Self-management and peer support among people with arthritis on a hospital joint replacement waiting list: a randomised controlled trial. Osteoarthritis Cartilage 2009;17:1428–33. https://doi.org/10.1016/j.joca.2009.05.010.

[43] Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis 2023;82:19–34. https://doi.org/10.1136/ard-2022-223296.

[44] Banerjee A, Hendrick P, Bhattacharjee P, Blake H. A systematic review of outcome measures utilised to assess self-management in clinical trials in patients with chronic pain. Patient Educ Couns 2018;101:767–78. https://doi.org/10.1016/j.pec.2017.12.002.

[45] Osborne R, Elsworth G, Whitfield K. The Health Education Impact Questionnaire (heiQ): An outcomes and evaluation measure for patient education and self-management interventions for people with chronic conditions. Patient Educ Couns 2007;66:192–201. https://doi.org/10.1016/j.pec.2006.12.002.

[46] Hughes LD, Done J, Young A. A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) successfully identifies low adherence to DMARDs. BMC Musculoskelet Disord 2013;14:286. https://doi.org/10.1186/1471-2474-14-286.

[47] Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002;52:69–77. https://doi.org/10.1016/s0022-3999(01)00296-3.

[48] Primdahl J, Esbensen BA, Pedersen AK, Bech B, de Thurah A. Validation of the Danish versions of the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaires (BRAFs). Scand J Rheumatol 2021:1–9. https://doi.org/10.1080/03009742.2020.1869301.

[49] Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain 1986;27:117–26. https://doi.org/10.1016/0304-3959(86)90228-9.

[50] Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17:45–56. https://doi.org/10.1016/0304-3959(83)90126-4.

[51] Brady TJ. Measures of self-efficacy: Arthritis Self-Efficacy Scale (ASES), Arthritis Self-Efficacy Scale-8 Item (ASES-8), Children's Arthritis Self-Efficacy Scale (CASE), Chronic Disease Self-Efficacy Scale (CDSES), Parent's Arthritis Self-Efficacy Scale (PASE), and Rheumatoid Arthritis Self-Efficacy Scale (RASE). Arthritis Care Res 2011;63:S473–85. https://doi.org/10.1002/acr.20567.

[52] Areskoug-Josefsson K, Ekdahl C, Jakobsson U, Gard G. Swedish version of the multi dimensional health assessment questionnaire - Translation and psychometric evaluation. BMC Musculoskelet Disord 2013;14:178. https://doi.org/10.1186/1471-2474-14-178.

[53] Sørensen J, Davidsen M, Gudex C, Pedersen K, Brønnum-Hansen H. Danish EQ-5D population norms. Scand J Public Health 2009;37:467–74. https://doi.org/10.1177/1403494809105286.

[54] Disease Activity Scores (DAS and DAS28) | Arthritis-health n.d. https://www.arthritis-health.com/glossary/disease-activity-scores-das-and-das28 (accessed February 2, 2023).

[55] https://danskreumatologi.dk/nbv/sygdomme/ra/ n.d.

[56] Smolen JS, Schoels M, Aletaha D. Disease activity and response assessment in psoriatic arthritis using the Disease Activity index for PSoriatic Arthritis (DAPSA). A brief review. Clin Exp Rheumatol 2015;33:S48-50.

[57] Christensen R, Ranstam J, Overgaard S, Wagner P. Guidelines for a structured manuscript: Statistical methods and reporting in biomedical research journals. Acta Orthop 2023;94:243–9. https://doi.org/10.2340/17453674.2023.11656.

[58] Little RJA, Rubin DB. Statistical Analysis with Missing Data. John Wiley & Sons; 2019.

[59] Vickers AJ, Altman DG. Statistics notes: Analysing controlled trials with baseline and follow up measurements. BMJ 2001;323:1123–4. https://doi.org/10.1136/bmj.323.7321.1123.

[60] Bivirkninger n.d. https://nationaltcenterforetik.dk/videnskab/vejledninger/bivirkninger (accessed December 14, 2022).