Remote **monit**oring of axial spondyloarthritis in specialist healthcare services (ReMonit)

The ReMonit study

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Protocol amendments in version 1.1:

Amend-ment No.	Date	Protocol Section Affected	Reason for amendment	Expected Impact on Study
1	01.11.21	Protocol Summary + 5.1.2 Usual Care	The text regarding the content of the conventional follow-up strategy (usual care) is revised to be more specific on the content of the face-to-face-visits.	None
2	01.11.21	Protocol Summary + 3.2.3 Intervention + 5. Study Intervention	The text is revised to clarify that the physical activity tracker data is collected for the purpose of research, that this data is not monitored by the project group and that is not included in the evaluation of intervention compliance.	None
3	01.11.21	1.3 Schedule of Activities	Medication review is added to the schedule of activities for clarification of the content of the face-to-face-visits.	None
4	01.11.21	2.3.4 Objectives and endpoints	The secondary objectives were further divided into secondary and additional objectives to be more clear.	None
5	01.11.21	5.1.4 Patient-initiated care arm	Table 2 regarding indication for the HPs to contact a patient in the Remote monitoring study arm was updated to be more clear on which situations that leads to a “yellow flag” or a “red flag”.	None
6	01.11.21	Protocol Summary + 3. Overall Design + 8. Statistical Considerations	The definition of the primary endpoint was amended to be more clear. «The proportion of low disease activity…» was replaced with «The point prevalence of low disease activity..»	None
7	01.11.21	9.5.17 Patient satisfaction with remote monitoring or patient-initiated care	We have replaced the instrument Telehealth Usability Questionnaire (TUQ) with Service User Technology Acceptability Questionnaire (SUTAQ) since the SUTAQ is translated into Norwegian and validated.	None
8	01.11.21	References	The reference for the eHealth Literacy Questionnaire (eHLQ) was corrected.	None

Study organization

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Table of content

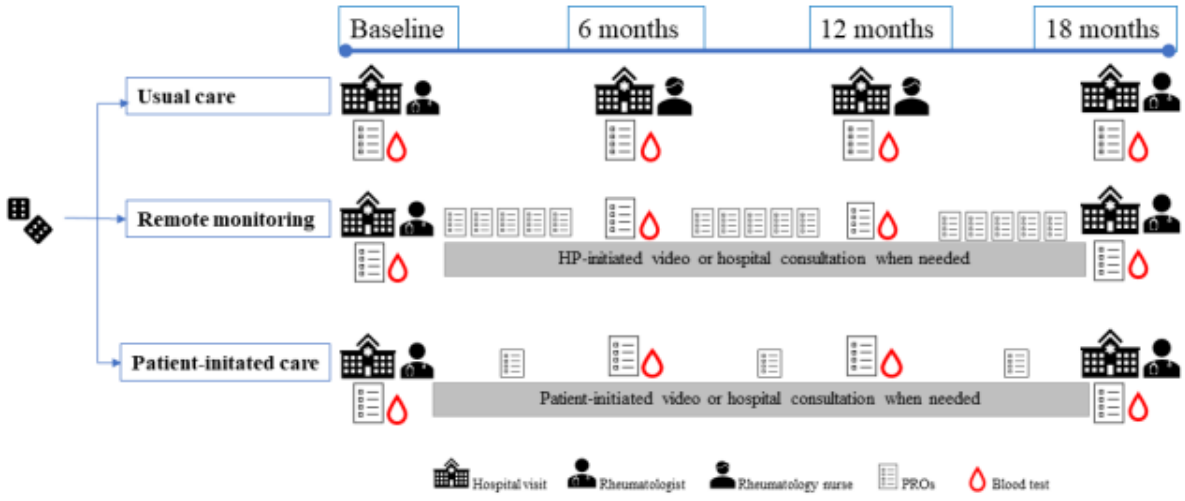
1 Protocol Summary

1.1 Synopsis

Study title	**Re**mote **monit**oring of axial spondyloarthritis in specialist healthcare services (ReMonit)
Study Period	Estimated date of first patient enrolled: September 7th 2021 Anticipated recruitment period: September 7th 2021 - May 31st 2022 Estimated date of last patient completed: November 30th 2023
Intervention Duration/ Follow-up	18 months
Main objective	To determine if two, new follow-up strategies for patients with axial spondyloarthritis (axSpA) are non-inferior in maintaining low disease activity over time compared to the conventional follow-up strategy with regular hospital visits.
Main Inclusion Criteria	• Adult (>18 years of age) • Clinical diagnosis of axSpA • Fulfillment of diagnostic ASAS criteria for axSpA • Stable medical treatment with tumour necrosis factor inhibitors (TNFi) the last 6 months • Inactive or low disease activity (ASDAS<2.1) at inclusion
Endpoints	*Primary endpoint:* The point prevalence of low disease activity (defined as ASDAS <2.1) at the 6-, 12- and 18-months follow-ups. *Secondary endpoints:* Individual and composite disease activity measures, patient global assessment of disease activity, general pain, joint pain, safety profile, adverse events, use of analgesics and antibiotics, health care resource use and societal costs related to consultations, health related quality of life, and patient satisfaction with care
Number of patients	240 patients (80+80+80)
Study Design	A single-site three-arm, parallel-group, non-inferiority follow-up strategy study, in which patient participants are randomized 1:1:1 to: a. Usual care: conventional follow-up strategy with pre-scheduled visits at the hospital every 6th month with a review of disease-related concerns, blood test results, joint examination, medication use, and adverse events or b. Remote monitoring: hospital health professionals (HPs) perform remote monitoring of frequent PROs and blood test results or c. Patient-initiated care: no pre-scheduled visits or remote monitoring

	The treatment target, applicable to all arms, is that the patients consider their symptoms to be absent or mild and that their medication is effective. The patients in all three study arms are instructed to contact the hospital should they experience significant symptom worsening and consider that a consultation with HP is indicated. The HP will then evaluate and schedule a visit when needed.
Intervention	Two, new follow-up strategies will be implemented and evaluated: b) Remote monitoring: patients will self-report symptoms and register blood tests using an app on their smartphone or tablet. HPs will remotely monitor patient data and schedule a consultation when needed. c) Patient-initiated care: there will be no pre-scheduled visits or remote monitoring. This way more responsibility is placed on the patients to contact the hospital should they experience significant symptom worsening. When needed, the HP will schedule a consultation.
Efficacy assessments	• Disease activity: Individual and composite disease activity measures at all three follow-ups • Safety profile, adverse events, use of analgesics, prescribed antibiotics • Patients' satisfaction, pain, sleep, and health related quality of life • Number of consultations in specialist or primary healthcare, costs and time for travelling, and time off work • Work participation/sick leave
Safety assessments	Physical examination and vital signs, laboratory tests, record of adverse events and serious adverse events

1.2 Schema



1.3 Schedule of Activities

Procedure	**Screening**		**Intervention Period** [remote monitoring/visits]				**Extra visits and early discontinuation**
		Baseline	Every month	6th month follow-up	12th month follow-up	18th month Study end	
Inclusion and exclusion criteria	X						
Fulfilment ASAS criteria[1]	X						
Physical examination incl. heart and lungs	X						
Informed consent	X						
Safety laboratory tests[2]		X		X	X	X	X
CRP and ESR		X	(X[3])	X	X	X	X
Clinical examination of disease activity, incl. enthesitis (heel), peripheral arthritis		X		X[4]	X[4]	X	X
Vital signs[5]		X					
Medical history		X					
Demography		X					
Lifestyle		X					
Patient global assessment		X	X[6]	X	X	X	X
Patient-reported outcomes		X	X[6]	X	X	X	X
Medication review		X		X	X	X	X
Randomization		X					
Adverse event review				X	X	X	X
Reason for discontinuation[7]							X

[1] The ASAS criteria include: Sacroilitis on imaging, HLA-B27 and SpA features (see 9.5.1)

[2] Patients using biologic medication, including the tumour necrosis factor inhibitors (TNFis), are instructed to take safety laboratory tests each 3rd month. For the "Usual care" arm, the patients will take blood tests at the 6th month visit at the hospital and take an additional blood test between these visits, which normally is prescribed and monitored by their general practitioner. For the "Remote monitoring" and "Patient-initiated care" arms, the patients are instructed to take blood tests each 3rd month, which normally is prescribed and monitored by their general practitioner. Patients, who normally take the 3-month blood tests at the hospital due to convenience, may continue this practice. Each 6th month the patients in the two latter arms will be requested to upload a photo of the blood test results into the MyDignio app.

[3] Only for the subgroup n=15 in the "Remote monitoring" arm that receive a home-based CRP instrument

[4] At 6 and 12 months only in the "Usual care" arm

[5] Pulse, blood pressure, body weight and height

[6] Patients in the "Remote monitoring" arm will complete a brief questionnaire each month, and patients in the "Patient-initiated care" only each 3rd month. Longer questionnaires will be completed by all study arms each 6th month.

[7] Only at "Early discontinuation" visit

Abbreviations: CRP: C-Reactive Protein, ESR: Erythrocyte Sedimentation Rate, HLA-B27: Human Leucocyte Antigen B27

2 Introduction

This protocol outlines an 18-months, non-inferiority randomized, controlled trial with three parallel arms to determine if two, new follow-up strategies for patients with axial spondyloarthritis (axSpA) are non-inferior in maintaining stable, low disease activity over time compared to the conventional follow-up regimen with regular hospital visits.

2.1 Study Rationale

The rapid development of technology and innovations for collecting patient-reported outcomes (PROs), remote patient monitoring, and medical decision support tools have opened an era for more personalized, and potentially better, treatment strategies for chronic diseases. Remote monitoring has shown consistent positive outcomes in chronic conditions like cardiovascular and respiratory disease[1]. It may also be effective for the management of inflammatory rheumatic diseases[2,3], but remote monitoring has not yet been formally tested or utilized in the management of people with rheumatic diseases in Norway. These are serious, chronic diseases affecting the working age population with follow-up management taking place in specialist healthcare. Hence, utilizing remote monitoring to improve management of care can have beneficial effects for both individuals and the society. Recently, the Norwegian Directorate of Health, the Norwegian Directorate of eHealth and the Norwegian Medicines Agency delivered a report to the Ministry of Health and Care Services on how to facilitate implementation and dissemination of patient remote monitoring. Remote monitoring is a strategic priority in a recently published plan for the specialist healthcare services in Norway ("Nasjonal helse- og sykehusplan") for achieving a sustainable healthcare sector[4].

The COVID-19 pandemic has resulted in a rapid implementation of digital technology in the healthcare sector in general. While adopting and implementing new innovations may have several beneficial effects, the research evidence on remote monitoring of patients with rheumatic diseases is very limited[2,3]. There is a need to determine whether remote monitoring for this patient group is equally effective in maintaining a stable, low disease activity as traditional outpatient visits at the hospital. The medical treatment of axSpA has been revolutionized during the last two decades, after the introduction of biologic medication, including the tumour necrosis factor inhibitors (TNFis). These drugs improve

symptoms and substantially inhibit inflammation in the majority of patients regardless of disease duration[5,6]. However, adherence to medication is only moderate over the long term[7]. Since non-optimal adherence compromises therapeutic efficacy and may lead to complications, unnecessary treatment switches and heightened costs, optimization of adherence should be integrated in new care models[7,8]. It is currently unknown if digital remote monitoring may increase, or decrease, adherence to medical treatment.

In June 2020, a quality assurance study on video consultations at Division of Rheumatology and Research at Diakonhjemmet Hospital was conducted. This included an electronic patient survey (n=139) and focus group interviews (7 nurses, 7 rheumatologists). Both the patients and the health professionals (HPs) reported high satisfaction with video consultations and considered video consultation to be suitable for follow-up care, also in a non-pandemic situation. The study further revealed that axSpA would be the optimal patient group for testing remote monitoring since this is a predominantly young population with a large proportion reaching a low disease activity state. Furthermore, for axSpA, the prospects of potential joint damage in case of non-optimal treatment are much smaller compared to other rheumatic diseases, e.g., rheumatoid arthritis.

In this randomized, controlled trial (RCT), we will compare two, new follow-up strategies for axSpA patients with conventional outpatient follow-up. The purpose is to investigate whether axSpA patients with stable, low disease activity and stable medication can be remotely monitored, i.e. be scheduled for consultations only when they experience significant symptoms worsening. We will further investigate whether regular monitoring by HPs is unnecessary and if patients and HPS are equally adept to judge when a hospital visit is needed.

2.2 Background

AxSpA is a chronic inflammatory disease primarily affecting the sacroiliac joints and the spine, but inflammation in peripheral joints and at the site of muscle/tendon attachment are also frequent[9]. The prevalence of axSpA is from 9 to 30 per 10 000 in the general population[10]. The main symptoms, back pain and stiffness, may lead to limited mobility of the spine, fatigue and functional disability. The evolution of axSpA is marked by alternated periods of flares (disease activity worsening) and stable

disease activity. Assessments of flares are needed for evaluations of disease status and treatment efficacy[11]. Uncontrolled, the disease may lead to structural damage, employment obstacles and serious socio-economic load[12,13]. Current treatment guidelines propose a treat-to-target strategy aiming at minimal or low disease activity[14] and recommend a combination of pharmacological and non-pharmacological treatment modalities[15].

2.2.1 Pharmacological and non-pharmacological treatment of axial spondyloarthritis

Non-steroidal anti-inflammatory drugs (NSAIDs) and exercise represent the first line treatment of axial SpA, which often leads to reduced back-pain and stiffness. For patients with inadequate effects of NSAIDs and exercise, TNFis may be tested as the next step. TNFis improve symptoms and substantially inhibit inflammation in the majority of patients regardless of disease duration[5,6]. It is currently unknown if digital remote monitoring may increase, or decrease, adherence to medical treatment.

Physical activity and exercise are important parts of the treatment regimen as most patients experience a relief of symptoms by exercise[15]. While several studies have demonstrated beneficial effects of exercise on disease activity[16,17], high disease activity may also reduce the ability to be physically active due to pain, stiffness and fatigue[18]. A recent pilot study employing machine learning showed that episodes of reduced physical activity were associated with disease flares among patients with SpA and rheumatoid arthritis[19]. Thus, automatic monitoring may lead to early identification of flares[20]. This may pave the way for future remote monitoring of disease activity with great precision and minimal patient burden, but further testing is needed[19]. Compared to the general population, patients with axSpA have a higher risk of cardiovascular disease and cardiovascular mortality[21]. The increased risk is partly related to a higher prevalence of traditional risk factors[22], but the systemic, chronic inflammation is recognized as an independent risk factor[23]. Physical activity and exercise can reduce this risk[21].

2.2.2 Clinical assessment of axial spondyloarthritis

The disease course can be unpredictable, with periods of relatively lower disease activity interspersed with clinically significant worsening (disease flares) with up to 75% of patients reporting a current or past flare[24]. Ankylosing Spondylitis Disease Activity Score (ASDAS) is a common clinical measure of disease activity calculated from four PROs and C-reactive Protein (CRP). ASDAS <2.1 is regarded as an acceptable, low disease activity level[25], and an increase of ASDAS>0.9 is considered a clinical important

worsening[26]. Patients can also self-report their "global assessment of disease activity" on a 0-10 or 0-100 scale, and a flare has been defined as a relative change of ≥2 on a 0-10 scale[11].

2.2.3 Follow-up strategies in axial spondyloarthritis

SpA care is resource demanding since it requires long-term treatment with regular monitoring and costly drug treatments. A recent study from UK showed that 93% of patients with axSpA were reviewed by a rheumatologist at least once a year, and 23% were reviewed three or more times a year[27]. In Norway, patients with axSpA on biologic medication have traditionally been followed by rheumatologists at the out-patient clinic with a 3-month interval in the beginning, and thereafter ideally every 6th month.

Since the conventional outpatient follow-up regimen is scheduled using standardized time intervals and not based on the disease activity in the individual patient, the visit may not occur when it is needed the most (e.g., when severe flares or adverse effects occurs). In addition, for patients with axSpA with stable, low disease activity, several visits could likely be postponed. A study on outpatient visits among patients with rheumatoid arthritis showed that 30% of the visits led to no examinations or other actions, and 42% of visits were considered unnecessary by the rheumatologist[28].

A previous RCT showed that patients with rheumatoid arthritis and psoriasis arthritis were able to self-monitor their blood tests and disease activity leading to a 50% reduction in hospital visits while maintaining acceptable disease activity and psychosocial well-being[29]. Patient interviews revealed that they described usual care as burdensome and inefficient use of time for those in employment, and that being able to self-monitor and initiate their own personalized care increased patient empowerment[30]. In Denmark a PRO–based remote monitoring follow-up strategy for tight control of disease activity was recently compared with conventional outpatient follow-up in an RCT among patients with rheumatoid arthritis. The Danish follow-up strategy with PROs every 3-4 months and a telephone call from a nurse or rheumatologist, achieved similar disease control as usual care follow-up; with less visits per year[31] and a possible cost-saving impact[32].

2.3 Benefit/Risk Assessment

2.3.1 Risk Assessment

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Missed detection of no efficacy of medical treatment or underreporting of symptoms ("Remote monitoring" and "Patient-initiated care" arms)	In theory, less hospital visits may have negative effects like non-adherence to treatment, under-reporting of symptoms and that patients develop tolerance for high disease activity levels	Frequent patient self-reporting in combination with patient-registered blood test results every 6th month should allow for detection of loss of efficacy, underreporting or increasing tolerance levels.
Missed detection of clinically important side-effects/adverse events ("Remote monitoring" and "Patient-initiated care" arms)	If patients underreport or fail to complete the self-reporting or register blood test results, important side-effects or adverse events may not be detected	Patients repeatedly failing to complete the self-reports will be contacted.

2.3.2 Benefit Assessment

All participants may benefit from the frequent collection of self-reported outcomes, physical or digital visits and predefined treatment goals and therapy. Patients in the two, new follow-up arms may save time off from work and travel time as well as travel costs compared to standard care with hospital visits.

2.3.3 Overall Benefit: Risk Conclusion

For axSpA, the prospects of potential joint damage in case of non-optimal treatment are much smaller compared to other inflammatory rheumatic diseases, e.g., rheumatoid arthritis. Given the close monitoring in the remote monitoring group with frequently brief self-reporting of disease activity and symptoms as well as blood test results, we consider that a significant worsening of the disease activity is likely to be detected and that treatment to minimize the impact in patient outcomes will be initiated when needed. The patient-initiated care arm is instructed to contact the hospital if they experience symptoms worsening or adverse events.

2.3.4 Objectives and endpoints

Objectives	Endpoints
Primary	
Assess if two, new follow-up strategies are non-inferior compared to conventional follow-up with hospital visits in terms of maintaining low disease activity	Disease activity (ASDAS) at 6, 12 and 18 months
Secondary	
Compare additional measures of clinical efficacy between the treatment arms	Efficacy measures outlined in section 7.2 at each time point
Compare the safety of the two, new follow-up strategies in axSpA with the conventional follow-up strategy	Safety profile and adverse events throughout the study + doses of analgesics + prescribed antibiotics
Assess if the patients and HPs are equally adept to judge the need for consultation	Comparing the proportions that are scheduled for a visit when a serious disease activity worsening (flare) occurs
Additional	
Evaluate cost effectiveness of remote monitoring in axSpA	Health related quality of living, health care utilization and costs related to the societal perspective (e.g. work participation) as outlined in section 7.4. at each, or a combination, of time points.
Examine fluctuations in disease activity and physical activity level over time	Self-reported disease activity every month, blood tests every 6th month, and monthly CRP for a subgroup of participants. Physical activity data from wearing an activity tracker in the two, new follow-up strategy arms
Examine if flares can be detected based on changes in monitored physical activity level	Physical activity tracker data (steps per day and minutes with moderate and high intensity activity levels) and measures of disease activity
Investigate barriers and facilitators for remote monitoring among HPs and patients	Questionnaire at baseline among HPs and patients
Investigate the HPs' and patients' perspectives and satisfaction with remote monitoring	Semi-structured interviews of 10-15 patients and their treating rheumatologist and/or nurse
Investigate HPs' and patients' experiences with video consultations, as compared to hospital visits and telephone consultations, and the impact of self-reporting on the follow-up care	Semi-structured interviews and observations of 10-15 patients and their treating rheumatologist and/or nurse
Investigate the optimal frequency of collecting patient self-reported outcomes based on HPs' experiences in clinical decision making, patients' preferences, and disease activity fluctuation data	Semi-structured interviews of 10-15 patients and their treating rheumatologist and/or nurse. Comparing observed fluctuations in diseases activity with the frequency of patient self-reporting

3 Study Design

3.1 Overall Design

- Randomised
- Single-blind
- Parallel group
- Non-inferiority
- Treatment strategy: conventional follow-up with hospital visits vs. remote monitoring vs patient-initiated care
- Study intervention assignment: 1:1:1 central computer randomisation
- Patients with axSpA > 18 years of age and low disease activity (ASDAS<2.1)
- Primary end point: the point prevalence of low disease activity at the 6-, 12- and 18-month follow-ups
- Duration of study: 18 months

3.2 Scientific Rationale for Study Design

The study is designed to investigate if two, new follow-up strategies for patients with axSpA are non-inferior to the conventional follow-up strategy with hospital visits for maintaining a stable, low disease activity. Hence, a randomized, controlled design is required to provide a valid comparison. A non-inferiority design is chosen as the two, new follow-up strategies are likely to be less resource-intensive, but they may still not be inferior compared to conventional follow-up for maintaining a stable, low disease activity. Based on data from the NOR-DMARD database (ClinicalTrials.gov NCT01581294), 88% of the patients remained at a stable, low disease activity level (ASDAS >2.1) after two-year follow-up, hence, superiority may be difficult to achieve.

3.2.1 Conventional treatment target

The protocol adheres to current treatment recommendations to ensure appropriate care for patients and to ensure generalizability of results[14,15]. The goal of treating the patient with axSpA is to maximize long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalization of function and social participation[15]. This implies that the patients consider that their symptoms are absent or mild and that their medication is effective.

3.2.2 Primary outcome measure

The primary outcome for this trial is the point prevalence of low disease activity (defined as ASDAS< 2.1) at the 6-, 12- and 18-monts follow-ups.

Ankylosing Spondylitis Disease Activity Score (ASDAS) is a common clinical measure of disease activity calculated from four PROs and CRP (or ESR if CRP is not available). The formula for calculating $ASDAS_{CRP}$ = 0.12 × back pain + 0.06 × duration of morning stiffness + 0.11 × patient global + 0.07 × peripheral pain/swelling + 0.58×Ln(CRP + 1)). The formula for calculating $ASDAS_{ESR}$ = 0.08 x back pain + 0.07 x duration of morning stiffness + 0.11 x patient global + 0.09 x peripheral pain/swelling + 0.29 x √(ESR).

There is a defined cut-off for low disease activity which allows using the ASDAS score as a target, and ASDAS <2.1 is regarded as an acceptable, low disease activity level[25]. ASDAS is also a continuous measure, which makes it appropriate to assess potential changes in disease activity, and an increase of ASDAS>0.9 is considered a clinical important worsening[26].

3.2.3 Intervention

The remote monitoring study arm includes implementing remote monitoring and remote care using the Dignio platform and software allowing for remote collection of PROs, patient monitoring and triaging by using the clinicians' dashboard and asynchronous chat, as outlined in 5.1.3 and 5.1.4.

The patients in the "Patient-initiated care" arm will have no remote monitoring and no pre-scheduled hospital visits but will be instructed to contact the hospital should they experience significant symptom worsening and consider that a consultation with a health professional is indicated.

In a substudy, the patients in the two intervention arms will be asked to wear wrist bands/smart watches during daytime for physical activity tracking, but this data will not be monitored and will only be collected for the purpose of research. A subgroup of 10-15 participants will use a CRP instrument for home-based measurements.

3.2.4 Participant Input into Design

Patient research partners, Tale Gjøvik and Sarah Hakim, are included in the project group. They have provided input on the relevance of the research question, the feasibility of the study design from a patient perspective and written information to patients. They will continue their involvement for the continuation of the study.

3.3 End of Study Definition

A participant is considered to have completed the study if he/she has completed all phases of the study including the last visit. The study period is 18 months, with a possible extension to 36 months, which will be decided by the study project group. The end of the study is defined as the date of the last visit of the last participant in the study.

4 Study Population

4.1 Inclusion Criteria

Participants are eligible to be included in the study only if all the following criteria apply:

- Male or female >18 years of age at screening
- Patients with a diagnosis of axSpA who fulfil the diagnostic ASAS criteria for axSpA (see Appendix 9.4)
- Stable medical treatment with TNFi the last 6 months
- Inactive or low disease activity (ASDAS<2.1) at inclusion
- Capable of understanding the Norwegian language and of signing an informed consent form

4.2 Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical conditions:

- Major co-morbidities, such as severe malignancies, severe diabetes mellitus, severe infections, uncontrollable hypertension, severe cardiovascular disease (NYHA class III or IV), severe respiratory diseases, and/or cirrhosis.
- Indications of active tuberculosis (TB)
- Pregnant or nursing

Diagnostic assessments:

- Abnormal renal function, defined as serum creatinine >142 µmol/L in female and >168 µmol/L in male, or glomerular filtration rate (GFR) <40 mL/min/1.73 m2
- Abnormal liver function (defined as Alanine Transaminase (ALT) >3x upper normal limit), active or recent hepatitis
- Leukopenia and/or thrombocytopenia

Other:

- Severe psychiatric or mental disorders, alcohol abuse or other substance abuse, language barriers or other factors which makes adherence to the study protocol impossible

4.3 Lifestyle Considerations

Female patients planning pregnancy within the study period will not be recruited as this will induce a different follow-up pattern not compatible with this study design. No lifestyle changes are otherwise required for participation in the study.

4.4 Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomly assigned to study intervention. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened.

5 Study Intervention

5.1 Study intervention

The ReMonit study is a randomized, controlled study with three parallel arms, and the design is illustrated in Figure 1. AxSpA patients are randomized 1:1:1 to either:

a. Usual care: conventional follow-up strategy with pre-scheduled visits at the hospital every 6th month with a review of disease-related concerns, blood test results, joint examination, medication use, and adverse events

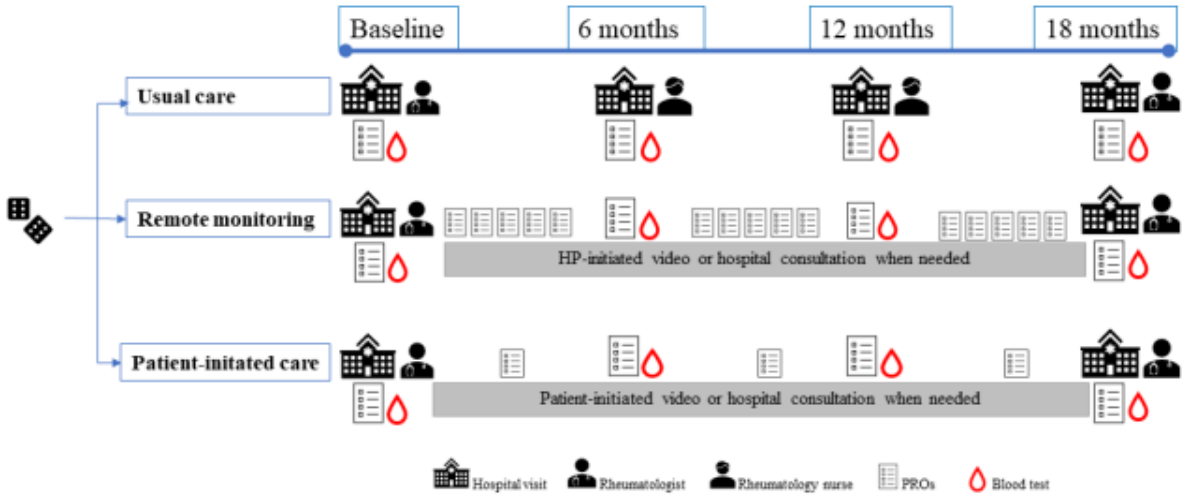
or

b. Remote monitoring: hospital health professionals (HPs) perform remote monitoring of frequent PROs and blood test results

or

c. Patient-initiated care: no pre-scheduled visits or remote monitoring

Figure 1: Illustration of the ReMonit study design.



5.1.1 Medical treatment for all three arms

The medical treatment will be the same for all three study arms and will follow the current treatment recommendations for axSpA[15]. At inclusion, all patients will have low disease activity. The treatment target for all three study arms is that the patients consider their symptoms to be absent or mild and that their medication is effective. The treatment will be individualized by the treating physician according to signs

and symptoms of the disease and patient characteristics. If TNFi therapy fails, switching to another TNFi alternative or an anti-IL-17 therapy may be considered.

All included patients will be on stable medical treatment with TNFi for the last 6 months. Patients will be instructed to use NSAIDs should they experience minor worsening of symptoms, but if the patients experience significant symptom worsening and suspect a severe disease worsening (flare) or adverse events, they will be instructed contact the hospital (Table 1). A visit will be arranged within two weeks to allow for examination and documentation of disease status. Concomitant medication will be recorded in the CRF, with particular attention to registration of use of NSAIDs, oral or injected glucocorticoid, and analgesics for residual pain (paracetamol or opioids).

Patients in all three study arms will be instructed to take blood tests for assessment of safety and side effects each 3rd month as prescribed and monitored by their general practitioner. Patients, who normally take these 3-month blood tests at the hospital due to convenience, may continue this practice.

5.1.2 Usual care arm

Patients in the "Usual care" arm will be treated according to current conventional follow-up regimen with regular hospital visits. In the ReMonit study this includes prescheduled face-to-face visits with an experienced rheumatology nurse at 6 and 12 months and with a rheumatologist at 18 months (study end), with a review of disease-related concerns, blood test results, joint examination as well as recording medication use, and adverse events.

5.1.3 Remote monitoring arm

The patients in this study arm will download the app, MyDignio, on their smartphone or tablet and receive a brief introduction on the use of MyDignio from the study coordinator. MyDignio app will be used for reporting PROs, displaying results (histograms) for PROs over time, and for asynchronous (chat) communication with HPs. The patients will receive a SMS reminder for "tasks" (e.g., self-reporting PROs or uploading a photo with blood test results each 6th month) according to the planned time points as outlined in 7.2- 7.3. The patients will receive an automatic reminder when a task is uncompleted.

A subgroup of patients (n= 10-15) will use a CPR instrument for home-based monthly self-measurements of CRP. The patients will register the CRP value in the MyDignio app.

The patients will be asked to wear a wrist band/smart watch for physical activity monitoring over 12 months. They will be instructed to wear this activity tracker at least 10 hours during daytime, but they can wear the water-resistant tracker all day and night should they want to. The number of steps and mean pulse levels will be collected per minute for research purposes.

A study coordinator/nurse will once daily (Monday to Friday) log on to the digital platform, Dignio Prevent, to monitor the PROs and respond to potential patient messages/questions. By setting acceptable maximum and minimum values for the outcomes (see table 2), a triaging functionality in the Dignio Prevent software will aid the study coordinator/nurse in highlighting PROs or measurements that needs attention. The software will also indicate if the patient misses one or more self-reports or measurement registrations.

The patients can send a message to the HP through the app, and HPs can reply or call the patient to investigate if there is a need to schedule a visit. The software uses a standardized application program interface, and all communication through the software is encrypted and in compliance with current legislation.

5.1.4 Patient-initiated care arm

Patients in this arm will also download the app, MyDignio, on their smartphone or tablet and receive a brief introduction from the study coordinator. The app will be used to collect PROs. Patients are instructed to contact the hospital if they need an evaluation regarding medication, symptoms worsening or adverse events. The patients will receive a SMS reminder for “tasks” (e.g. self-reporting or uploading a photo with blood test results each 6 months) according to the planned time points as outlined in 7.2-7.3. The patients will receive an automatic reminder if the task is not completed.

Table 1: Indication for unscheduled/extra visits for all three study arms

Indication	Definition	Action
Significant worsening	Patient-reported significant symptoms worsening	The HP excludes other potential reasons for the experienced worsening. If there is a need for changing medication, a physical examination or blood test, a visit will be scheduled within two weeks
Significant adverse effects	Safety laboratory test results showing adverse effects or patient-reported adverse events	Schedule a visit within two weeks

Table 2: Indication for the HPs to contact a patient in the Remote monitoring study arm

Indication	**Definition**	**Action**
Significant worsening	Yellow flag: BASDAI ≥4 in the monthly PRO reporting Red flag: BASDAI ≥8 in the monthly PRO reporting	The study nurse contacts the patient to evaluate if a hospital visit is needed
The patient has requested to be contacted by HP	The patient sends a message in MyDignio app asking to be contacted by HP	The study nurse contacts the patient to evaluate if a hospital visit is needed

[1] PGA: Patient Global Assessment of disease activity

5.2 Measures to Minimize Bias: Randomization and Blinding

Eligible patients will be allocated in a 1:1:1 ratio between the three study arms. A statistician and a secretary, not involved in patient screening or enrollment, will provide a computer-generated block randomization list, and prepare sealed, opaque envelopes containing information on study arm assignment. Details of block size and allocation sequence generation will be provided in a separate document unavailable to those who enroll patients or assign treatment. The study does not include blinding of participant and treating health care personnel.

5.3 Study Intervention Compliance

Compliance to treatment will be assessed as the proportion of completed self-reports at all time points for self-reporting and the proportion who register their blood test results at 6- and 12-months. Full

compliance is defined as completion of ≥80% of all frequent self-reports and 100% of all half-year self-reports and blood test results. Partial compliance is less than full, but ≥60% completed frequent self-reports, and 2 half-year self-report and blood test result registered. Low compliance is <60% completed frequent self-reports, and only 1 half-year self-report and 1 blood test result registered.

Full compliance to medical treatment is defined as taking the treatment as prescribed, partial compliance is less than 100% but more than 70% compliant to prescribed treatment, and low compliance is less than 70% compliant. Reason for non-compliance (lack of efficacy/adverse events/concurrent medical condition/patient wish/other) will be assessed.

6 Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal

6.1 Discontinuation of Study Intervention

Patients who for some reason withdraw from following the treatment protocol will be asked to continue follow-up in the study.

6.2 Participant Discontinuation/Withdrawal from the Study

Patients have the right to withdraw from the study at any time for any reason. In the case that a patient decides to prematurely withdraw from the study, he or she should be asked if they can still be contacted for further information, so that a final evaluation can be made with an explanation of why the patient is withdrawing from the study, including assessment of possible adverse events. Although a subject is not obliged to give his or her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights. If possible, at the last visit of the patient all assessments of the" Early discontinuation of study visit" will be done.

6.3 Lost to Follow up

A participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits or to complete self-reports and is unable to be contacted by the study site. If a participant in the "Usual care" arm fails to return to the clinic for a required study visit, the study coordinator must attempt to contact the participant and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether the participant wishes to and/or should continue in the study. If a participant in any of the two, new follow-up strategy arms fail to report the half-year self-reports and register blood test results, the study coordinator must attempt to contact the participant and counsel the participant on the importance of maintaining the self-report schedule and ascertain whether the participant wishes to and/or should continue in the study. Before a participant is deemed lost to follow up, the coordinator must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These

contact attempts should be documented in the participant's medical record. Should the participant continue to be unreachable, he/she will be considered to have withdrawn from the study.

7 Study Assessments and Procedures

Study procedures and their timing are summarized in the Schedule of Activities. Adherence to the study design requirements, including those specified in the Schedule of Activities, is essential and required for study conduct.

7.1 Study visits

7.1.1 Screening

All screening evaluations as outlined in the Schedule of Activities must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management and obtained before signing of the informed consent form may be used for screening purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the Schedule of Activities. Laboratory measures preformed < 14 days prior to screening can be used.

7.1.2 Assignment of intervention and subject numbering

Eligible patients will be assigned a unique patient identification number. Once assigned, this number cannot be reused for another patient. The patients will be randomized 1:1:1 to the three arms as described in section 5.1.

7.1.3 Baseline visit

At the baseline visit all assessments outlined in 7.2. and 7.3 except AE/SAE will be assessed. In addition, the following data will be recorded:

- Demography: age, sex, education, work status
- General medical history: previous and current comorbidities and previous and current medications
- Disease specific medical history: symptom duration, date of diagnosis, current and previous SpA-features (peripheral arthritis, enthesitis), SpA associated disease (uveitis, psoriasis, inflammatory bowel disease), family history of SpA and SpA associated diseases.
- Fulfilment of ASAS criteria including HLA B27, X-ray and/or MRI findings on sacroiliac (SI) joints and spine as documented in the patient journal
- Lifestyle factors: tobacco use and physical activity last seven days (frequency, intensity, and duration)
- Patient satisfaction with care
- Self-efficacy/confidence related to using smartphone, tablet, computer, app's, secure login and digital health serviced: 6 items with response categories: Never used, Very bad, Bad, Neither good nor bad, Good, Very good
- eHealth literacy (20 items from 4 domains from the eHealth Literacy Questionnaire (eHLQ) [33]: 1) using technology to process health information, 2) ability to actively engage with digital services, 3) feel safe and in control, 4) motivated to engage with digital services. Response options range from 1 (strongly disagree) to 4 (strongly agree).

7.1.4 Regular visits

Assessments are as outlined in the Schedule of Activities and in section 7.2.

7.1.5 Unscheduled visits

HPs can freely schedule additional visits as required according to clinical judgement. If patients in any of the three study arms suspects a disease worsening or AE, he or she should contact the hospital and be seen there within two weeks as the latest. Unscheduled visit will, if possible, include all assessments of a regular visit.

7.1.6 End of study visit

The end of the study visit will be performed at 18 months and will include a formal end of study assignment in the eCRF. The patients will self-report their satisfaction with care.

7.1.7 Withdrawal visit

A withdrawal visit (early discontinuation) will include all assessments of a regular visit in addition to an assessment of reason for withdrawal and time of withdrawal.

7.2 Efficacy assessments

7.2.1 Patient-reported outcome measures

At Baseline (after screening, but before the randomization), patient demographics and PROs be collected using a digital device at the hospital.

Every 6. month, patients will receive a link a digital survey ("Nettskjema" (Services for sensitive data (TSD), University of Oslo)). Collection of a few PROs from patients will be done monthly for the Remote monitoring arm and every third month for the Patient-initated care arm using the MyDignio app. The participants in these two intervention arm will also report blood test results every 6. month using the MyDignio app.

- **Patient global assessment of disease activity** (PGA) (Visual Analogue Scale, NRS 0-10) (All arms: Baseline, 6-, 12- and 18-months) (Remote monitoring arm: each month) (Patient-initiated care arm: each 3rd month)
- **Patient-reported flares** (All arms: 6-, 12- and 18-months) (Remote monitoring arm: each month) (Patient-initiated care arm: each 3rd month)
  If the patient responds "yes" or "uncertain" to the question if they have experienced a significant worsening of symptoms (reflecting a flare in disease activity), they will be asked which date the flare occurred and the number of days it lasted.
- **Bath Ankylosing Spondylitis Disease Activity Index** (BASDAI) (All arms: Baseline, 6-, 12- and 18-months) (Remote monitoring arm: each month if disease worsening) (Patient-initiated care arm: each 3rd month if disease worsening)
  BASDAI is a 6 item questionnaire (NRS 0-10) used to assess disease activity in ankylosing spondylitis[34]. The score is the sum (of the first four individual questions and the mean of questions five and six) divided by five.
- **Bath Ankylosing Spondylitis Functional Index** (BASFI) (Baseline)
  BASFI is a 10 item questionnaire (NRS 0-10) used to assess disease activity in ankylosing spondylitis[34]. The score is the sum of each individual question divided by 10.
- **Patient-reported pain (general)** Single item (NRS 0-10) (Baseline, 6-, 12- and 18-months)

- **Patient-reported joint pain** Single item (NRS 0-10) (Baseline, 6-, 12- and 18-months)
- **Patient-reported global change in disease activity.** Single item with seven-point response scale ranging from "Much worse" to "Much better" (6-, 12- and 18-months)
- **Patient-reported global change in activity impairment.** Single item with seven-point response scale ranging from "Much worse" to "Much better" (6-, 12- and 18-months)
- **Euro Quality of Life 5 Dimensions 5 Levels** (EQ5D-5L) (Baseline, 6-, 12- and 18-months)
  EQ-5D is a utility instrument for measurement of health related quality of life[35] and is applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status.
- **Work Productivity and Activity Impairment (WPAI)** – item no. 6 on activity Impairment (NRS 0-10) (Baseline, 6-, 12- and 18-months).
- **Questions on physical activity from the HUNT study** (Baseline, 6-, 12- and 18-months) The HUNT questionnaire consists of 3 questions assessing frequency, intensity, and duration of physical activity in the past 7 days [36].
- **Sleep disturbance** (Baseline, 6-, 12- and 18-months) 1 item from the Pittsburgh Sleep Quality Index measuring sleep disturbance due to pain with four-point response categories ranging from "Not during the past month" to "Three or more times a week"[37].
- **Patient satisfaction with care** (Baseline, 6-, 12- and 18-months)
  Satisfaction with the care provided (from patient experience questionnaires) includes one item with five point response options ranging from “Very satisfied” to “Very dissatisfied” [38].
- **Medication use** (Baseline, 6-, 12- and 18-months)
  Questions on whether the patient has taken the TNFi medication as instructed, and if NSAIDs, glucocorticoid (oral or injections) or analgesics have been used.
- **Time and costs related to consultations** (Baseline)
  The time being absent from work and potential travel costs related to consultations will be registered.

7.2.2 Clinical examination/assessment

Clinical assessments will be performed as outlined for each element below. If possible, assessments of individual patients will be performed by the same assessor. Training in clinical examination will be provided for all assessors

- **General clinical examination** (baseline visit)
- **Heel enthesitis and peripheral arthritis assessment** (all visits)

Assessment of heel enthesitis is done by palpating with sufficient pressure to blanch the anterior part of the examiner’s fingernail and scored as yes/no. For assessment of peripheral arthritis, the following joints are examined for tenderness and swelling: proximal interphalangial joints (1-5, metacarpophalangial joints (1-5), wrists, elbows, shoulders, knees, ankles, metatarsophalangial joints. Both tenderness and swelling are scored as yes/no.

7.2.3 Laboratory assessment

Assessment of inflammatory markers will be performed prior to each hospital visit by the hospital laboratory and includes ESR (mm/hr) and CRP (mg/L). All patients will be instructed to take standard care blood samples (hemoglobin, red blood cells, white blood cells with differential count, platelets, creatinine, and alanine transaminase) as a safety procedure when using TNFi as prescribed and monitored by their general practitioner. Patients, who normally take these blood tests at the hospital due to convenience, may continue this practice. Patients in the "Remote monitoring" and the "Patient-initiated care" arms are instructed to report blood test results each 6th month in the MyDignio app. These blood tests will in addition be used to assess clinical safety (see 7.3.3). A small subgroup in the Remote monitoring group will receive a CRP-instrument and be asked to measure their CRP monthly and register the value in the MyDignio app.

7.2.4 Composite measures of disease activity

- **Ankylosing Spondylitis Disease Activity Score** (**ASDAS)** (Baseline, 6-, 12- and 18-months)

  The ASDAS score is a 6-item composite measure of 4 PROs and CRP or ESR:
  $\underline{ASDAS_{CRP}:}$ 0.12 x back pain + 0.06 x duration of morning stiffness + 0.11 x patient global + 0.07 x peripheral pain/swelling + 0.58 x Ln(CRP+1).
  $\underline{ASDAS_{ESR}}$: 0.08 x back pain + 0.07 x duration of morning stiffness + 0.11 x patient global + 0.09 x peripheral pain/swelling + 0.29 x √(ESR).
  $ASDAS_{CRP}$ is preferred, but the $ASDAS_{ESR}$ can be used in case CRP data are not available. CRP in mg/L; all patient assessments on a 10 cm scale. ASDAS <2.1 is regarded as an acceptable, low disease activity level[25]. ASDAS is also a continuous measure, which makes it appropriate to assess potential changes in disease activity, and an increase of ASDAS>0.9 is considered a clinical important worsening[26].
- **Bath Ankylosing Spondylitis Disease Activity Index** (BASDAI) (Baseline, 6-, 12- and 18-months)
  BASDAI is a 6 item questionnaire (NRS 0-10) used to assess disease activity in ankylosing spondylitis[34]. The score is the sum (of the first four individual questions and the mean of questions five and six) divided by five.

7.3 Safety assessments

Planned time points for all safety assessments are provided in the Schedule of Activities.

7.3.1 Physical Examinations

- General clinical examination (baseline visit)

7.3.2 Vital signs

- Pulse and blood pressure (baseline visit)
- Height and weight (baseline visit)

7.3.3 Clinical Safety Laboratory Assessments (every 3rd month and all visits)

- Haemoglobin, red blood cells, white blood cells with differential count and platelet count
- Glomerular filtration rate (GFR) and creatinin
- Alanine transaminase (ALT)

7.3.4 Adverse Events (AEs), Serious Adverse Events (SAEs), and Other Safety Reporting

The definitions of adverse events (AEs) and serious adverse events (SAEs) as well as the method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in Appendix 3.

7.3.5 Time Period and Frequency for Collecting AE and SAE Information

All AEs and SAEs will be collected from the start of intervention until the final follow-up visit at the time points specified in Schedule of Activities. Medical occurrences that begin before the start of study intervention, but after obtaining informed consent, will be recorded as Medical History/Current Medical Conditions, not as AEs. All SAEs, including updates, will be recorded and reported to the sponsor or designee immediately, as indicated in Appendix 3. Investigators are not obligated to actively seek information on AEs or SAEs after conclusion of the study participation.

7.3.6 Method of Detecting AEs and SAEs

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and non-leading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

7.3.7 Follow-up of AEs and SAEs

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up.

7.3.8 Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities are met. The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical

investigation. The sponsor will comply with regulatory requirements relating to safety reporting to the regulatory authority, Institutional Review Board and Independent Ethics Committee.

7.3.9 Pregnancy

Details of all pregnancies in female participants will be collected after the start of study intervention and until end of the study. If a pregnancy is reported, the investigator will record pregnancy information on the appropriate form and submit it to the sponsor. While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be reported as an AE or SAE. Abnormal pregnancy outcomes are considered SAEs and will be reported as such. The participant will be followed to determine the outcome of the pregnancy and any post-study pregnancy-related SAE considered reasonably related to the study intervention by the investigator will be reported to the sponsor. Further participation in the study will be determined by the treating physician and principal investigator.

7.4 Health Economics

Use of health care (costs) will be captured by the following registers: The Norwegian Patient Register (hospital services), The Norwegian Prescription Register (pharmaceuticals), Norway Control and Payment of Health Reimbursement - KUHR database (primary care services), Statistics Norway's database on social benefits (FD Trygd). We will assign unit costs to each type of service by means of the diagnosis-related group (DRG) pricing system, and the price list of the Norwegian Medicines Agency. The patients will be asked about costs related to consultations, e.g., transport costs, time use, work absenteeism, need for support. We will also register the time study coordinator/nurse and rheumatologist spend on remote monitoring, telephone calls, replies to patient messages on the Dignio platform and similar. For each patient we will estimate one-year costs based on register data for utilization of health care and the unit costs. The mean quality adjusted life years (QALYs) and costs in the three arms will be used to estimate an incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB).

8 Statistical Considerations

8.1 Statistical Hypotheses

Statistical hypothesis (non-inferiority test):

Null hypothesis: The point prevalence of low disease activity (ASDAS<2.1) in both "Remote monitoring" and "Patient-initiated care" is more than 15 percentage points lower than in "Usual care" arm at any follow-up time point.

Alternative hypothesis: The point prevalence of low disease activity (ASDAS<2.1) in "Remote monitoring" / "Patient-initiated care" is at most 15 percentage points lower than in "Usual care" arm at any follow-up time point.

8.2 Sample Size Determination

Randomly assigning 80 participants to each of the three study arms will give approximately 80% power to conclude that at least one of the alternative follow-up strategies is non-inferior to conventional follow-up, using a 15% non-inferiority margin. This controls for multiple testing at the 5% level and assumes an analysis based on a logistic mixed model. We will additionally test the non-inferiority of "Patient-initiated care" to "Remote monitoring" using the same 15% margin. This test will be done only if "Patient-initiated care" is shown to be non-inferior to conventional care (a hierarchical test), and thus will not inflate the 5% false positive rate.

8.3 Analysis Sets

Population	Description
Enrolled	The Enrolled set will include all patients who have provided informed consent and have been included into the study data base.
Intention to Treat Set	The Intention to Treat (ITT) Set will include all patients randomly assigned to a study arm irrespective of post randomization occurrences.
Full Analysis Set	The Full Analysis Set (FAS) will be defined as all patients randomly assigned to a study arm and that have started the allocated intervention defined as having completed at least one assessment of the primary endpoint at 6, 12 or 18 months. The FAS will form the primary analysis set of the study and will be used for primary non-inferiority analyses.
Completer Analysis Set	The Completer Analysis Set will include all randomized patients having started the allocated intervention and not withdrawn during the study.
Per Protocol Analysis Set	The Per Protocol Analysis Set (PPS) will include all randomized patients meeting the study entry criteria who followed the study protocol with no major protocol deviations.

8.4 Statistical Analyses

The statistical analysis plan (SAP) will be finalized prior to un-blinding and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints including primary and key secondary endpoints.

8.4.1 General Considerations

- Efficacy (both primary and secondary endpoints) and safety analyses will include data from all randomised patients who started the allocated intervention by attending at least one completed questionnaire and blood test result after randomisation (FAS), and robustness analyses will be performed in the PPS.
- Demographics, baseline characteristics, efficacy and safety variables will be summarised using descriptive statistics.
- All efficacy analyses will be presented with the results from the hypothesis testing (by p-value) in addition to estimates and 95% confidence limits of the treatment effect. For the primary variables specifically, this will be the estimated mean probability with corresponding 95% confidence limits.

8.4.2 Primary Endpoint

The primary endpoint is defined as the point prevalence of with low disease activity (defined as ASDAS <2.1) at the 6-, 12- and 18-months follow-ups.

The probability of being in low disease activity for repeated measures per individual will be used to estimate a risk difference across the three study arms. The primary variables will be analyzed using logistic regression mixed models with allocated study arm as primary explanatory variable. Other pre-specified covariates included in sensitivity analyses include age, gender, disease features. The SAP will detail these procedures, as well as alternative and further supportive evaluations, such as analyses including unbalanced baseline predictors or modifications of the regression model in case validity assumptions are not met. The primary analysis will be performed in the FAS. The primary endpoint will be evaluated by the p-value and confidence interval of the hypothesis test from the regression analysis.

In case the null hypothesis is not rejected, the new, follow-up strategies will be considered worse or inferior to usual care with hospital follow-up visits.

8.4.3 Secondary Endpoint

Between-group comparisons will be performed for secondary efficacy endpoints.

The between-group comparisons for secondary endpoints will be tested as for the primary endpoint where applicable and additional analyses will be performed based on the following methods (but not limited to):

- Continuous secondary variables will be subject to repeated measures mixed models or appropriate non-parametric alternatives
- Binary response variables will be analyzed using logistic regression (possibly adjusting for within-subject dependencies by mixed model approaches) or other appropriate tests, e.g., chi-square/Mantel-Haenszel test

Unless otherwise specified, all statistical hypotheses will be tested as the primary endpoint, i.e., with an assessment of non-inferiority based on the p-value of the group differences.

8.4.4 Safety Analysis

Rates and type of adverse events and serious adverse events in all three study arms will be reported.

9 Supporting Documentation and Operational Considerations

9.1 Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

9.1.1 Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, ICH Good Clinical Practice (GCP) Guidelines and applicable laws and regulation.

The protocol, protocol amendments, informed consent form and Investigator Brochure must be reviewed and approved to the institutional review board and independent ethics committee before the study is initiated. Any amendments to the protocol will require approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for providing written summaries of the status of the study to the relevant authorities in accordance with their requirements and notify them of any significant safety findings. The investigator is also responsible for providing oversight of the conduct of the study at the site and adherence to relevant regulations.

9.1.2 Informed Consent Process

The investigator or his/her representative will explain the nature of the study to the participant and answer all questions regarding the study. Participants must be informed that their participation is voluntary. Participants will be required to sign a statement of informed consent that meets the requirements of local regulations. Participants must be re-consented to the most current version of the informed consent form during their participation in the study and a copy must be provided to the participant.

9.1.3 Data Protection

Participants will be assigned a unique identifier by the sponsor. The participant must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant who will be required to give

consent for their data to be used as described in the informed consent. The participant must be informed that his/her medical records may be examined by auditors or other authorized personnel appointed by the sponsor, institutional review board, independent ethics committee or regulatory authorities.

9.1.4 Dissemination of Clinical Study Data

Study design and results will be registered at the US National Institutes of Health's website www.clinicaltrials.gov. Trial results will be disseminated through non-promotional, peer-reviewed publications. Access to analyzable datasets from the clinical study can be granted through a secure system, following an independent assessment of the scientific merit of a rigorously defined research question from a third party.

9.1.5 Data Quality Assurance

All participant data relating to the study will be recorded on electronic case report file (eCRF). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF. Guidance on completion of CRFs will be provided in investigator brochure and eCRF. The investigator must permit study-related monitoring and regulatory reviews, audits and inspections. The investigator must provide direct access to source data documents. Monitoring details are provided in the monitoring plan and contracts. The sponsor or designee is responsible for the data management of this study including quality checking of the data and the sponsor assumes accountability for actions delegated to other individuals. Records and documents, including signed informed consent forms, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion. No records may be destroyed or transferred to another location or party during the retention period without the written approval of the sponsor.

9.1.6 Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator's site. Data entered in the eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. Definition of what constitutes source data can be found in the investigator brochure. Study monitors will perform ongoing source data verification to confirm that data entered into the eCRF by authorized site personnel are accurate, complete, and verifiable from source

documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and all applicable regulatory requirements.

9.1.7 Study and Site Start and Closure

Study start

The study start date is the date on which the clinical study will be open for recruitment of participants.

Study Termination

The sponsor or designee reserves the right to terminate the study at any time for any reason at the sole discretion of the sponsor. Reasons for the early closure of a study by the sponsor or investigator may include but are not limited to: Failure of the investigator to comply with the protocol, the requirements of the institutional review board, independent ethics committee or local health authorities, the sponsor's procedures, or GCP guidelines, inadequate or no recruitment or total number of participants included earlier than expected.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, independent ethics committee and institutional review board and the regulatory authorities of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

9.1.8 Publication Policy

Authorship will be determined by mutual agreement and in line with International Committee of Medical Journal Editors authorship requirements.

9.2 Appendix 2: Clinical Laboratory Tests

The tests detailed in Table 6 will be performed at the hospital laboratory for any hospital visit including the standardized preplanned 6. month visits for the "Usual care" arm, unscheduled visits, early discontinuation visits and at study end visit. Patients will be instructed to take blood tests each 3rd month. The patient's general practitioner will be responsible for these blood tests in the two, new follow-up strategy arms. If there are safety issues or adverse events, the general practitioner will contact HPs at the hospital. Patients, who normally take the 3-month blood tests at the hospital due to convenience, may continue this practice. Every 6th month the patients in the two intervention arms will take a photo of the laboratory test results and upload this in the MyDignio app. For the "Remote monitoring" study arm, the laboratory test results will be monitored each 6th month, whereas for the "Patient-initiated care", the laboratory test results will only be used for research purposes after the 18-month follow-up. Additional tests may be performed at any time during the study as determined necessary by the medical doctor or required by local regulations. Medical doctors must document their review of each laboratory safety report.

Table 6: Protocol-Required Safety Laboratory Tests

Laboratory Tests	Parameters
Hematology	Hemoglobin Red blood cells White blood cell count with Differential: Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils Platelet Count
Clinical Chemistry	Creatinine Glomerular filtration rate Alanine transaminase

9.3 Appendix 3: AEs and SAEs: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

9.3.1 Definition of AE

AE Definition
An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.
Events Meeting the AE Definition
• Any abnormal laboratory test results or other safety assessments, including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. • Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition. • New conditions detected or diagnosed after study intervention even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either TNFi or a concomitant medication. Intentional overdose taken with possible suicidal/self-harming intent should be reported regardless of sequelae. • The signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfil the definition of an AE or SAE.

Events NOT Meeting the AE Definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition. • Medical or surgical procedure: the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

9.3.2 Definition of SAE

An SAE is defined as any serious adverse event that, at any dose:
a. Results in death
b. Is life-threatening The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
d. Results in persistent or significant disability/incapacity The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect
f. Other situations: Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations such as significant medical events that may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.

9.3.3 Recording and Follow-Up of AE and/or SAE

AE and SAE Recording
• When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation related to the event and record all relevant AE/SAE information. • The investigator will attempt to establish a diagnosis based on signs, symptoms, and/or other clinical information, and whenever possible, this diagnosis will be documented as the AE/SAE.
Assessment of Intensity
The investigator will assess the intensity for each AE/SAE according to the following categories: • Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities. • Moderate: An event that causes sufficient discomfort to interfere with normal everyday activities. • Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

Assessment of Causality
• The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE/SAE and must document this review in the medical notes. • A “reasonable possibility” of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than it not being ruled out. Clinical judgment and the Product Information is applied to determine the relationship. Alternative causes (e.g. underlying disease, concomitant therapy, other risk factors) and temporal relationship of the event to study intervention will be considered and investigated.

Follow-up of AEs and SAEs
• The investigator is obligated to perform or arrange for any supplemental evaluations as medically indicated to elucidate the nature and/or causality of the AE or SAE as fully as possible. • New or updated information will be recorded in the originally submitted documents.

9.4 Appendix 5: ASAS Classification criteria for Axial Spondyloarthritis

<table>
<tr><th colspan="2">In patients with ≥3 months history of back pain and age of onset <45 years</th></tr>
<tr><td>Sacroiliitis on imaging* and ≥1 SpA feature

OR

HLA B27 and ≥2 SpA features</td><td>SpA- features
Inflammatory back pain
Arthritis
Enthesitis (heel)
Uveitis
Dactylitis
Psoriasis
Inflammatory bowel disease
Good response to NSAIDs
Family history of SpA
HLA B27
Elevated CRP</td></tr>
<tr><td colspan="2">Sacroiliitis on imaging
Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
Definite radiographic sacroiliits according to the modified New York criteria</td></tr>
</table>

9.5 Appendix 6: Patient-reported outcomes

9.5.1 Patient global assessment

Vi ber deg vennligst vurdere aktiviteten i din revmatiske sykdom i løpet av den siste uken. Når du tar alle symptomer med i betraktning, hvordan synes du tilstanden er? *

Angi på en skala fra 0 (Bra, ingen symptomer) til 10 (Svært dårlig)

9.5.2 Pain assessment

Hvor mye smerte har du hatt i løpet av den siste uken? *

Angi på en skala fra 0 (Ingen smerter) til 10 (Uutholdelige smerter)

9.5.3 Joint pain assessment

Hvordan vil du beskrive de leddsmertene du vanligvis har hatt den siste uken? *

Angi på en skala fra 0 (Ingen smerter) til 10 (Uutholdelige smerter)

9.5.4 Patient reported flare

Har du sykdomsoppbluss (klar forverring) av din revmatiske sykdom nå?

- ☐ Nei
- ☐ Ja
- ☐ Usikker

Hvis du svarte «Ja» eller «usikker», hvilken dato startet forverringen? __.__.20__

Omtrent hvor mange dager varte forverringen/har forverringen vart? _____dager

9.5.5 BASDAI

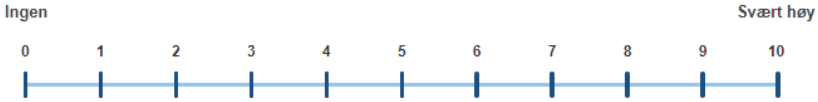
Sykdomsaktivitet (BASDAI)

Spørsmålene nedenfor gjelder hvordan du følte deg den siste uken.

1.Hvordan vil du beskrive den generelle graden av utmattelse/tretthet du har erfart? *

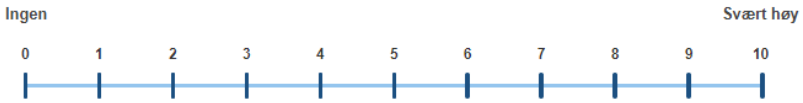
2.Hvordan vil du beskrive den generelle graden av smerter i nakke-, rygg og eller hofter i forbindelse med din revmatiske sykdom? *

4.Hvordan vil du beskrive den generelle graden av ubehag du har på eventuelle steder som gjør vondt ved berøring eller trykk? *



3.Hvordan vil du beskrive det generelle nivået av smerte/hevelse du har hatt i ANDRE LEDD enn nakken, ryggen eller hoftene? *

5.Hvordan vil du beskrive den generelle graden av stivhet du har opplevd om morgenen fra det tidspunktet du våkner? *



6.Hvor lenge varer morgenstivheten fra det tidspunktet du våkner? *

9.5.6 **BASFI**

Angi hvordan du greide følgende aktiviteter den siste uken:.

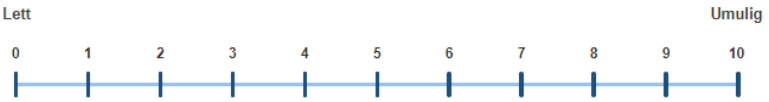
1. Ta på strømper eller strømpebukser uten assistanse eller ved bruk av hjelpemiddel (for eksempel strømpe-påtrekker)?

2. Bøye deg forover fra midjen for å plukke opp en penn fra gulvet uten å bruke et hjelpemiddel

3. Nå opp til en høythengende hylle uten bruk av hjelpemidler (for eksempel gripetang).

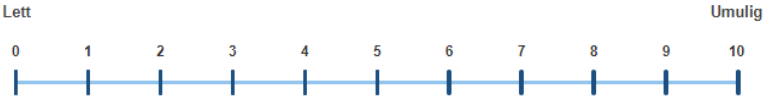
4. Reise deg fra en spisebordsstol uten armlener eller annen hjelp

5. Reise deg opp fra liggende stilling på gulvet uten hjelp?

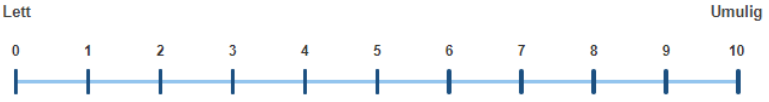


6. Stå oppreist uten støtte i 10 min. uten å få ubehag

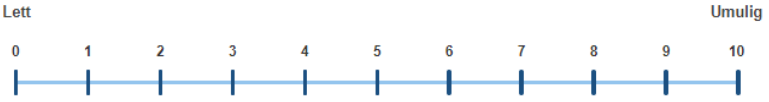
7. Gå opp 12-15 trappetrinn uten å bruke rekkverk eller gåstøtte. En fot på hvert trinn



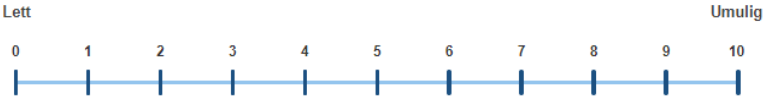
8. Se deg over skulderen uten å vri kroppen



9. Utføre fysisk krevende aktiviteter (for eksempel fysioterapiøvelser, hagearbeid eller sport).



10. Utføre en hel dags aktiviteter enten hjemme eller på arbeid



9.5.7 EQ-5D-5L

EQ-5D-5L.

Klikk på den ENE boksen som best beskriver helsen din I DAG.

GANGE *

- ○ Jeg har ingen problemer med å gå omkring
- ○ Jeg har litt problemer med å gå omkring
- ○ Jeg har middels store problemer med å gå omkring
- ○ Jeg har store problemer med å gå omkring
- ○ Jeg er ute av stand til å gå omkring

PERSONLIG STELL *

- ○ Jeg har ingen problemer med å vaske meg eller kle meg
- ○ Jeg har litt problemer med å vaske meg eller kle meg
- ○ Jeg har middels store problemer med å vaske meg eller kle meg
- ○ Jeg har store problemer med å vaske meg eller kle meg
- ○ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *

(f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- ○ Jeg har ingen problemer med å utføre mine vanlige gjøremål
- ○ Jeg har litt problemer med å utføre mine vanlige gjøremål
- ○ Jeg har middels store problemer med å utføre mine vanlige gjøremål
- ○ Jeg har store problemer med å utføre mine vanlige gjøremål
- ○ Jeg er ute av stand til å utføre mine vanlige gjøremål

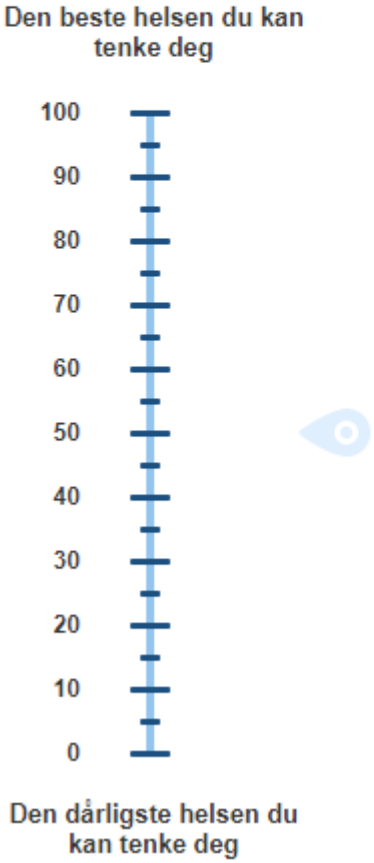
SMERTER / UBEHAG *

- ○ Jeg har verken smerter eller ubehag
- ○ Jeg har litt smerter eller ubehag
- ○ Jeg har middels sterke smerter eller ubehag
- ○ Jeg har sterke smerter eller ubehag
- ○ Jeg har svært sterke smerter eller ubehag

ANGST / DEPRESJON *

- ○ Jeg er verken engstelig eller deprimert
- ○ Jeg er litt engstelig eller deprimert
- ○ Jeg er middels engstelig eller deprimert
- ○ Jeg er svært engstelig eller deprimert
- ○ Jeg er ekstremt engstelig eller deprimert

- Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.
- Denne skalaen er nummerert fra 0 til 100.
- 100 betyr den beste helsen du kan tenke deg.
  0 betyr den dårligste helsen du kan tenke deg.
- Vennligst klikk på skalaen for å angi hvordan helsen din er I DAG.



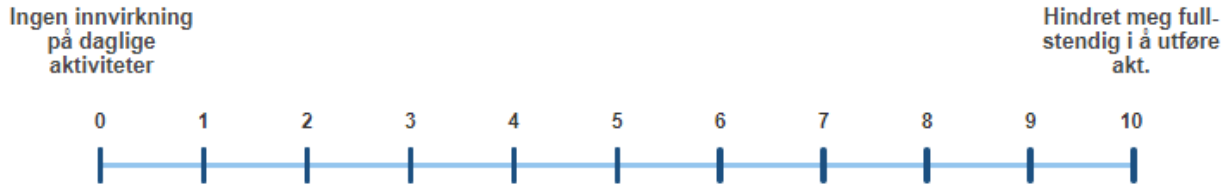
9.5.8 **WPAI item no. 6**

Hvor stor innvirkning hadde din revmatiske sykdom på din evne til å utføre vanlige, daglige aktiviteter, utenom arbeid i løpet av de siste 7 dagene? *

Med vanlige aktiviteter mener vi de vanlige aktivitetene du utfører, f.eks. husarbeid, handling, omsorg for barn, trening, studering, osv.

Hvis din revmatiske sykdom innvirket bare litt på dine aktiviteter, velger du et lavt tall. Velg et høyere tall hvis din revmatiske sykdom hadde stor innvirkning på dine aktiviteter.

Tenk kun på hvor stor innvirkning din revmatiske sykdom hadde på din evne til å utføre dine normale daglige aktiviteter, utenom arbeid.



9.5.9 **Patient-reported global change in disease activity**

Sammenliknet med for 6 måneder siden, hvordan er din sykdomsaktivitet nå?

☐ Mye verre ☐ Verre ☐ Litt verre ☐ Uforandret ☐ Litt bedre ☐ Bedre ☐ Mye bedre

9.5.10 **Patient-reported global change in activity impairment**

Sammenliknet med for 6 måneder siden, hvordan er din evne til å utføre vanlige, daglige aktiviteter, utenom arbeid, nå?

☐ Mye verre ☐ Verre ☐ Litt verre ☐ Uforandret ☐ Litt bedre ☐ Bedre ☐ Mye bedre

9.5.11 **Physical activity**

Mosjon/ fysisk aktivitet

Med mosjon mener vi at du f.eks går tur, går på ski, svømmer eller driver trening/idrett.

1.Hvor ofte driver du mosjon?

Ta et gjennomsnitt

- ○ Aldri
- ○ Sjeldnere enn en gang i uka
- ○ En gang i uka
- ○ 2-3 dager i uka
- ○ Omtrent hver dag

2. Hvor hardt mosjonerer du?

ⓘ Dette elementet vises kun dersom alternativet «En gang i uka», «Omtrent hver dag» eller «2-3 dager i uka» er valgt i spørsmålet «1.Hvor ofte driver du mosjon?»

Ta et gjennomsnitt

- ○ Tar det rolig uten å bli andpusten eller svett
- ○ Tar det så hardt at jeg blir andpusten og svett
- ○ Tar meg nesten helt ut

3.Hvor lenge holder du på hver gang?

ⓘ Dette elementet vises kun dersom alternativet «En gang i uka», «Omtrent hver dag» eller «2-3 dager i uka» er valgt i spørsmålet «1.Hvor ofte driver du mosjon?»

Ta et gjennomsnitt

- ○ Mindre enn 15 minutter
- ○ 15-29 minutter
- ○ 30 min - 1 time
- ○ Mer enn 1 time

9.5.12 Patient satisfaction with care

Hvor fornøyd er du alt i alt med den behandlingen du har fått for din revmatiske sykdom?

☐	☐	☐	☐	☐
Svært fornøyd	Fornøyd	Både og	Misfornøyd	Svært misfornøyd

9.5.13 Medication use

De siste 6 månedene, har du tatt medisin for din revmatiske sykdom som avtalt?

- ☐ Nei
- ☐ Ja

Hvis nei: Hvor mange ganger har du ikke tatt medisinen de siste 6 månedene? _____

De siste 6 månedene, har du fått kortison (injeksjon i ledd eller som tablett)?

- ☐ Nei
- ☐ Ja

Hvis ja: Hva var årsaken til at du fikk kortison: _____

De siste 6 månedene, har du brukt NSAIDs (betennelsesdempende medikamenter)?

- ☐ Nei
- ☐ Ja

Hvis ja: De siste 6 månedene, har du da brukt…

- ☐ NSAIDs som en kur over en periode?
- ☐ Enkelte NSAIDs tabletter nå og da?

Hvis ja: Hvilken NSAIDs type (navn) brukte du? _____

Hvis ja: Hvor mange milligram tok du per dag? _____

Hvis ja: Hvor mange dager brukte du NSAIDs?

- ○ Mindre enn 1 dag per uke
- ○ 1-3 dager per uke
- ○ 4-5 dager per uke
- ○ Mer enn 5 dager per uke
- ○ Hver eneste dag

Hvis ja og som en kur: Hvilken dato startet du en NSAIDs kur? __.__.___

Hvis ja og som en kur: Hvilken dato stoppet du en NSAIDs kur? __.__.___

De siste 6 månedene, har du brukt andre smertestillende medikamenter (andre enn betennelsedempende/NASAIDs)?

- ☐ Nei
- ☐ Ja

Hvis ja, Oppgi navn på medikament, hvor mange milligram du brukte per dag og antall dager:
_____

9.5.14 **Time use and costs related to consultations**

1) *Hvis du er i lønnet arbeid:* Hva må du gjøre for å få fri fra arbeidet for å dra til Diakonhjemmet Sykehus

Lønnet fravær fra arbeid	☐
Ulønnet fravær fra arbeid	☐
Jobber inn tiden senere/avspaserer	☐
Var utenfor arbeidstiden	☐
Tok ut ferie	☐
Andre ordninger	☐

*Hvilken annen ordning må du gjøre for å få fri?*_____

2) Omtrent hvor lang tid bruker du på å reise til Diakonhjemmet Sykehus (én vei)?
Oppgi antall minutter:_____

3) Omtrent hvor lang er reiseveien til Diakonhjemmet Sykehus (én vei)?
Oppgi antall kilometer (km) én vei. _____

4) Hva slags transportmiddel bruker du vanligvis for å reise til Diakonhjemmet Sykehus?
Dersom du brukte flere typer transportmiddel, sett kryss for transportmiddelet du bruker lengst (i form av distanse). *(Sett ett kryss)*

Går/sykler	☐
Privat bil	☐
Buss/T-bane/tog	☐
Taxi	☐
Fly	☐
Annet:	☐

Hvilket annet transportmiddel brukte du?: _____

5) *Hvis bil*: Kjører du bil selv eller blir kjørt?

Kjører bil selv ☐ Blir kjørt ☐

6) *Hvis du blir kjørt:* Må vedkommende ta seg fri fra arbeidet? Nei ☐ Ja ☐

9.5.15 **Digital self-efficacy**

Mestring av digitale tjenester og teknologi

Vurder dette på en skala fra "Svært dårlig" til "Svært godt". Sett kryss ved «Aldri prøvd» dersom du ikke har brukt tjenesten eller teknologien.

Hvor godt mestrer du:

	Aldri prøvd	Svært dårlig	Dårlig	Verken eller	Godt	Svært godt
Smarttelefon	○	○	○	○	○	○
Nettbrett	○	○	○	○	○	○
Datamaskin	○	○	○	○	○	○
Å bruke app'er	○	○	○	○	○	○
Innlogging med ID-porten (MinID, BankID, BankID på mobil, BuyPass)	○	○	○	○	○	○
Digitale helsetjenester (f.eks. e-konsultasjon, videokonsultasjon, Helsenorge.no)	○	○	○	○	○	○

9.5.16 **eHealth literacy**

20 items from 4 domains of the eHLQ[33]: 1) using technology to process health information, 2) ability to actively engage with digital services, 3) feel safe and in control, 4) motivated to engage with digital services. Response options for all items range from 1 (strongly disagree) to 4 (strongly agree). The instrument cannot be shown due to license requirements.

9.5.17 Patient satisfaction with remote monitoring or patient-initated care

22 items in the Service User Technology Acceptability Questionnaire (SUTAQ)[39] reported at the 18-months follow-up. While the remote monitoring arm will report all 22 items, the patient-initiated care arm will report on 3 of the 22 items (no. 1, 10 and 11). The usual care arm will not report on this questionnaire.

9.6 Appendix 8: Abbreviations and Definitions

AE	Adverse event
ALT	Alanine Transaminase
ASAS	Assessment of SpondyloArthritis International Society
ASDAS	Ankylosing Spondylitis Disease Activity Score
AxSpA	Axial spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
CIOMS	Council for International Organizations of Medical Sciences
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case report file
CRP	C-reactive protein
EQ5D	Euro Quality of Life 5 dimensions
ESR	Erythrocyte Sedimentation Rate
FAS	Full analysis set
GCP	Good clinical practice
GFR	Glomerular Filtration Rate
HLA-B27	Human Leucocyte Antigen B27
HP	Health professional
ICER	Incremental Cost-Effectiveness Ratio
ITT	Intention to treat
MRI	Magnetic Resonance Imaging

NSAIDs	Non-steroidal anti-inflammatory drugs
NYHA	New York Heart Association
PGA	Patient global assessment
PPS	Per protocol set
PRO	Patient-reported outcomes
QALY	Quality Adjusted Life Years
RCT	Randomized controlled trial
SAE	Serious Adverse Event
SAP	Statistical analysis plan
SI-joints	Sacroiliac joints
SpA	SpondyloArthritis
TB	Tuberculosis
TNFi	Tumor Necrosis Factor inhibitor
VAS	Visual analogue scale
WPAI	Work Productivity and Activity Impairment
X-ray	Conventional radiography

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