




# BMJ Open NET-RMDs study: networks of fatigue and pain in rheumatic and musculoskeletal diseases – protocol for an international cross-sectional study

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## ABSTRACT

**Introduction** Fatigue and pain are the main symptoms of rheumatic and musculoskeletal diseases (RMDs). Healthcare professionals have a primary role in helping patients to manage both these symptoms, which are part of a complex network of co-occurring factors including sleep problems, psychological distress, social support, body weight, diet, inactive lifestyle and disease activity. The patterns of relationships (networks) between these factors and these symptoms, fatigue and pain, are largely unknown. The current proposal aims to reveal them using network estimation techniques. We will also consider differences in networks for subgroups of people with (1) different RMDs and (2) different clusters (profiles) of biopsychosocial factors.

**Methods and analysis** Adults with at least one RMD will be recruited to this online cross-sectional observational project. To provide a complete overview, a large sample size from different countries will be included. A brief online survey, using 0–10 numeric rating scales will measure, for the past month, levels of fatigue and pain as well as scores on seven biopsychosocial factors. These factors were derived from literature and identified by interviews with patients, health professionals and rheumatologists. Using this input, the steering committee of the project decided the factors to be measured giving priority to those that can be modified in self-management support in community health centres worldwide. Network estimation techniques are used to detect the complex patterns of relationships between these biopsychosocial factors, fatigue and pain; and how these differ for subgroups of people with different RMDs and profiles.

**Ethics and dissemination** Ethical approval of national Institutional Review Boards was obtained. The online survey includes an information letter and informed consent form. The findings will be disseminated via conferences and publications in peer-reviewed scientific journals, while public media channels will be used to inform people with RMDs and other interested parties.

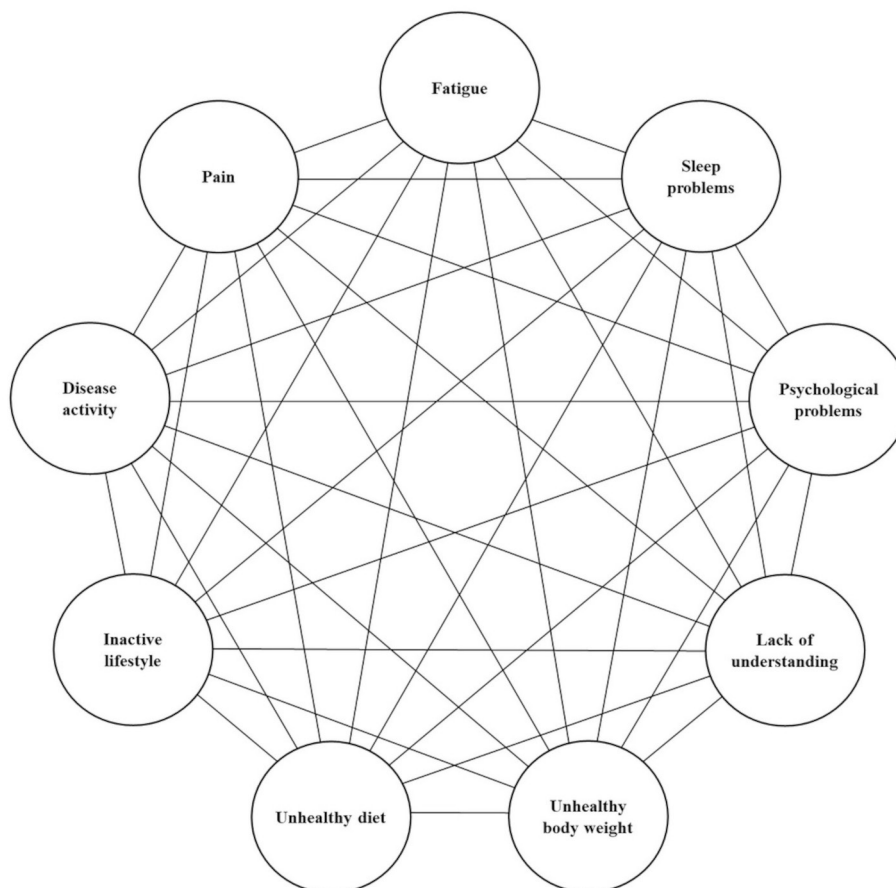
## INTRODUCTION

Fatigue and pain are the predominant symptoms for patients with rheumatic and musculoskeletal diseases (RMDs).<sup>1</sup> Health

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This international study was developed by researchers and people with rheumatic and musculoskeletal diseases (RMDs) from different countries and stands out by its feasibility and potential scalability.
- ⇒ A strength of this protocol is that it acknowledges the multifaceted nature of fatigue and pain in RMDs by using a network approach including multiple biopsychosocial factors.
- ⇒ This protocol allows to examine how patterns of associations between biopsychological factors involved in fatigue and pain differ between people with different RMDs and biopsychosocial profiles.
- ⇒ The low respondent burden assures a large sample size, but the use of single-item measures and self-reported RMD diagnosis could reduce the validity of the study.
- ⇒ Additional limitations of the study are that its cross-sectional design precludes inferring causality and the observed associations between subjects cannot be generalised to associations within a subject.

professionals in rheumatology are ideally placed to provide comprehensive, evidence-based support for managing fatigue and pain. Based on existing literature,<sup>2,3</sup> the European Alliance of Associations for Rheumatology pain management task force proposed a network model of pain postulating that any type of pain encompasses multiple and mutually interacting biological, psychological and social factors that include but are not limited to physical (dis)ability, psychological resilience and vulnerability, social factors, sleep quality, obesity and disease activity.<sup>1</sup> Unhealthy diet habits may also affect pain.<sup>4</sup> Similarly, fatigue is defined as a multifaceted symptom that can be conceptualised as a network model.<sup>5,6</sup> The aim of the current proposal is to offer a taxonomy of network models in subgroups of patients with an RMD and in subgroups of



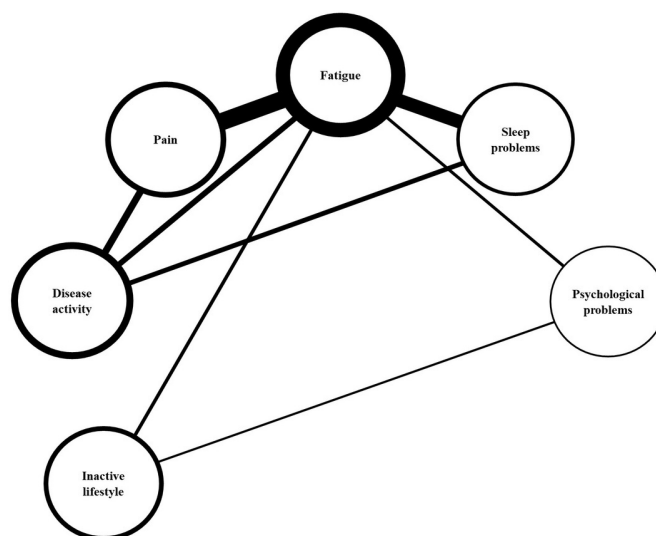
**Figure 1** The baseline network model for analyses: every factor (circle, node) is associated (line, edge) with every other factor.

patients according to their specific profile of biopsychosocial factors. These models will inform clinical practice about factors of fatigue and pain that appear to be the most important ones in specific subgroups.

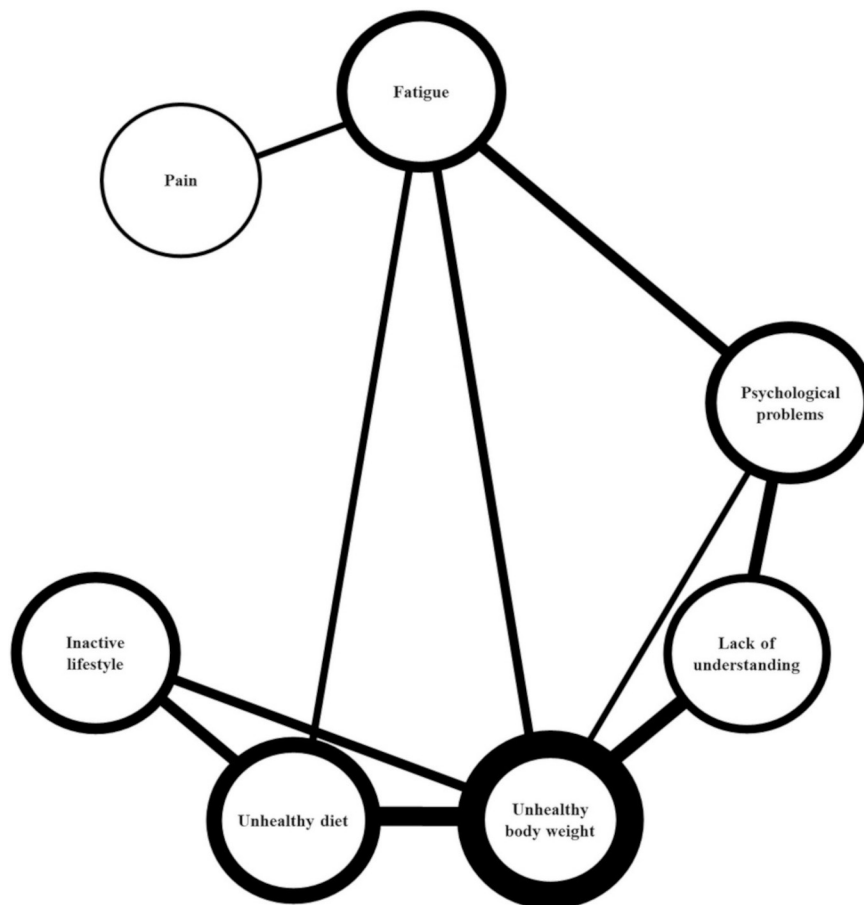
Figure 1 presents the baseline network model in our study. Every included factor (circle, node) is associated (line, edge) with every other factor. A guiding idea of our study is that the importance of these distinct factors differs between subgroups.<sup>7,8</sup> Figures 2 and 3 show examples of networks that could result from our study. As simulated in figures 2 and 3, the complex associations of biopsychosocial factors including fatigue and pain may be represented as a network in which the thickness of lines (edges) between circles (nodes) indicate the strengths of associations between variables.<sup>9,10</sup> The associations shown are partial correlation networks that estimate the association between two factors while adjusting for all other factors in the network. For example, the simulation in figure 2 shows that the patients appraise fatigue to be the most severe problem (thickest line of the circle). Moreover, the associations of fatigue with both pain and sleep problems are particularly strong. Also, disease activity appears a factor of importance, because of its associations with fatigue, pain and sleep problems as well as with fatigue through its associations with pain and sleep problems. Finally, inactive lifestyle and psychological problems are associated with fatigue. Figure 3 shows another simulated

model of a subgroup in which particularly unhealthy body weight and diet are the main problems.

The networks as shown in the figures 2 and 3 indicate the potential importance of specific factors in the model for a specific subgroup. For instance, if the results of



**Figure 2** A simulated network model of a subgroup in which fatigue is appraised to be the most severe problem and especially pain, sleep problems and disease activity appear important.



**Figure 3** A simulated network model of a subgroup in which particularly unhealthy body weight and diet are considered severe and are directly and indirectly associated with fatigue and several other factors.

figure 2 are found for a specific group, it might suggest including disease activity, sleep problems and pain in the management plan of fatigue. However, it is not possible to make inferences beyond a model of (partial) correlations for at least two reasons. First, the associations are adjusted for all other factors in the model. Thus, the results depend on the specific factors that are included in the model. For instance, included behavioural factors may steal variance from each other and reduce correlations of all behavioural factors. Second, the associations between factors may not be interpreted causally as direct influences or indirect mediators; associations may reflect a different directionality for members in the group and they can be due to (third) factors that are not included in the model.

To give a comprehensive overview of these network models measurements from a large sample including different RMDs are required. From the perspective of clinical usability, these measurements should involve factors that are modifiable by self-management interventions or interventions led by health professionals in rheumatology. Key factors that were identified in previous studies or in interviews with patients, health professionals and rheumatologists are fatigue, pain, sleep problems, psychological problems, lack of understanding, unhealthy body weight, unhealthy diet, inactive lifestyle and disease

activity (eg,<sup>1 5 11</sup>). Within psychological factors, those that are representative of factors that can be targeted in classical cognitive-behavioural management and in third generation therapies are considered important (eg, self-efficacy and acceptance, respectively).<sup>12</sup>

Using the nine biopsychosocial factors, including fatigue and pain, network models will be determined for the more common RMDs. We will also explore network models for specific subgroups characterised by profiles of biopsychosocial factors. We will use a clustering technique to derive profiles, which could identify subgroups characterised by, for instance, (1) severe disease activity and pain, (2) unhealthy body weight and diet or (3) severe scores on all the variables. To conduct this proposal in a large sample is viable because (1) the internet will be used to collect data online, (2) only a single (cross-sectional) measurement will be taken for each person and (3) only a brief questionnaire will be employed.

This study is observational and exploratory. Although it is the first study that examines network models in RMDs, some tentative hypotheses can be derived from the existing literature. First, in people with an inflammatory RMD, disease activity and sleep disturbance (because sleep is also affected by inflammation and medication) will have a stronger correlation with fatigue and pain than in people with fibromyalgia or osteoarthritis.<sup>13</sup> Second,

fatigue, sleep problems, inactive lifestyle and psychological problems have a key role in the network.<sup>5</sup> Third, the severity of the factors (level of scores) differs between patients, also between patients within a specific RMD.

### Objective

The aim is to identify network models of nine biopsychosocial factors including fatigue, pain, sleep problems, psychological problems, lack of understanding, unhealthy body weight, unhealthy diet, inactive lifestyle and disease activity in (1) specific RMDs and in (2) subgroups of patients, across all RMDs, characterised by different profiles of biopsychosocial factors.

## METHODS AND ANALYSIS

### Design

This observational cross-sectional study, in adult patients with RMDs, assesses fatigue, pain and seven biopsychosocial factors that are related to fatigue and pain in the short-term (eg, sleep) or long-term (eg, obesity), as well as demographic (eg, gender and age) and clinical variables (eg, diagnosis) that are needed to characterise the participants.

### Participants and procedure

We will only recruit participants from countries in which ethical approval has been obtained. The inclusion criteria for participating are: (1) to have been diagnosed with at least one RMD and (2) to be 18 years of age or older. It will be assessed who diagnosed the disease (a professional or self-diagnosis). Because data of participants who self-diagnosed their disease may be less valid, we will exclude them from analyses. However, as this procedure may especially exclude participants with low socioeconomic status and low access to healthcare, we will examine demographics of these excluded participants and whether their inclusion in sensitivity analyses does affect the results.

We aim for a minimum of 150 participants in each subgroup with a single (without comorbid RMD) diagnosis of fibromyalgia, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, spondyloarthritis, Sjögren's syndrome, psoriatic arthritis, systemic sclerosis or a single other rheumatic disease. The link to participate in our study will be circulated via websites and journals of national and regional associations of people with RMDs and via social media networks (eg, Facebook, Instagram and Twitter). The complete survey can be found as online supplemental material. Data collection was started in April 2021 and will be finished in December 2022.

### Measurements

To guarantee a sufficiently large sample size, the questionnaire should be brief. Moreover, the two primary variables (fatigue and pain) and the seven other network variables should be measured using the same response scale. Therefore, all nine variables were measured on single-item 0–10 numeric scales. Items reflected the core

construct without content overlap with other constructs (eg, for depression we measured depressed mood, but not fatigue, physical inactivity or sleep problems). Previous studies have evidenced the validity of single-item scales to measure depression,<sup>14</sup> anxiety<sup>15</sup> or sleep quality.<sup>16</sup>

### Primary variables

The two main variables are fatigue and pain, measured by 0 (no fatigue/pain) to 10 (the worst fatigue/pain) numeric rating scales.<sup>17</sup> These variables are *not* considered outcome variables. In a network model with cross-sectional associations, any variable can be a determinant or an outcome of another variable and both variables can be associated because of other variables.

### Other network variables

Based on the literature and interviews with people with RMDs, health professionals in rheumatology and rheumatologists, the inclusion of biopsychosocial factors that are associated with fatigue and pain were considered. The criteria to include these factors were that (1) the content of the factors should not overlap with other factors, (2) associations of the factor with fatigue and pain have been observed, which might indicate that the factor could directly or indirectly modulate fatigue and pain or be modulated by fatigue and pain and (3) the factor should be modifiable through education or commonly available therapies.

The steering committee of this project agreed on the inclusion of the following seven factors reflecting broad categories (eg, psychological problems) or a specific aspect of a broader category (eg, lack of understanding as part of social problems): sleep problems, psychological problems, lack of understanding, unhealthy body weight, unhealthy diet, inactive lifestyle and disease activity. A graphical representation of fatigue, pain and the other seven factors considered to build the network models is shown in [figure 1](#). Similar to the measurement of fatigue and pain, each of these seven factors is measured by one item using a 0 (the most favourable score) to 10 (the most unfavourable score) numeric rating scales and asking for the degree (eg, inactive lifestyle) or severity (disease activity) the factor was experienced during the last month. Thus, both the format and the direction (negative pole on the right) of fatigue, pain and the seven other network variables is the same, which makes it possible to fit and examine the nine variables in one network model.

### Participants' characteristics

Demographic and disease characteristics are included.

Demographic variables: country of residence, ethnicity, age, gender, education (the highest degree completed), marital status and work status. Diagnostic information:

- ▶ The RMD diagnosis. The following categories are used (multiple answers are allowed): fibromyalgia, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus (SLE), spondyloarthritis/Bechterew's disease, Sjögren's syndrome, psoriatic arthritis, scleroderma/

- systemic sclerosis, mixed connective tissue disease and any other RMD(s). The latter requires that the participants write the name of the disease(s). The participants also specify whether or not each of the conditions is the primary/most incapacitating disease.
- ▶ Who diagnosed the RMD(s). The following categories are used (single answer question): a medical specialist such as a rheumatologist, a general practitioner, another health professional (such as a nurse, physical therapist or psychologist), I made the diagnosis myself or another person. The latter requires that the participant writes the role of the person who made the diagnosis.
  - ▶ Disease duration (time since diagnosis).
  - ▶ Comorbidities. Participants report whether they have any other disease. If they have other disease(s), the following categories will be used (multiple answers will be allowed): (1) persistent physical symptoms (eg, chronic fatigue syndrome/myalgic encephalomyelitis, irritable bowel syndrome, somatoform disorder/somatic symptom disorder or chronic pain in the body (not migraine), (2) psychiatric or psychological problems (eg, schizophrenia, depression, anxiety, personality disorder, job burnout or an addiction that needs treatment), (3) a pulmonary disease (emphysema, chronic obstructive pulmonary disease, asthma, bronchitis), (4) diabetes or severe obesity, (5) chronic skin condition, (6) neurological disorder (eg, epilepsy, dementia, Parkinson's disease, migraine), (7) cancer, (8) cardiovascular diseases (eg, high blood pressure, stroke or other cerebrovascular accidents, myocardial infarction), (9) stomach, liver, gastrointestinal tract, kidney or other organ disease, (10) hereditary disease (eg, Huntington, Ehlers-Danlos) or (11) any other disease(s). The latter requires that the participants write the name of the disease(s).

The aforementioned items comprise the basic version of the survey. Participants that are willing to complete the full survey also answer the following questions:

- ▶ Disability. The following items are adapted from the Health Assessment Questionnaire Disability Index<sup>18</sup> (5-point Likert scale): 'During the last month, I could perform activities such as dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities' (Cannot be done at all ... Can be done without any difficulty) and the International Fitness Scale<sup>19</sup>: 'Compared with people who are the same age as me, my general physical fitness during the last month was ...' (Very poor...very good).
- ▶ COVID-19 disease status and quarantined time. Participants select one of the following options: (1) never tested positive or never suffered from COVID-19, (2) tested positive/suffered from COVID-19 at some point or (3) currently tested positive/suffering from COVID-19. They also report how much time they have been quarantined at home.
- ▶ Menopausal status: premenopause, menopause transition or postmenopause.

- ▶ Medication. Participants report (yes/no/not sure) whether they are currently taking any of the following medications on a regular basis for:
  - Rheumatic conditions: Non-steroidal anti-inflammatory drugs (NSAIDs), biological drugs, Janus kinase inhibitors, prednisone (or similar), methotrexate (or similar) or any other drug for rheumatic condition. The latter requires that the participants write the name of the drug.
  - Pain medication: Paracetamol, pain alleviating medication other than NSAIDs or paracetamol (acetaminophen).
  - Psychological problems: Drugs for depression, anxiety or schizophrenia.
  - Sleep problems: Other medication for sleeping.

### Concurrent validity variables

To be able to examine whether the seven single-item biopsychosocial network variables give an adequate reflection of the underlying constructs (concurrent validity), a minimum of two questions representing each of the seven network variables were added to the second part of the questionnaire. The subset of two variables will also give an indication of the reliability. Items were selected by the steering committee based on (1) factor loadings of items in the original questionnaire and (2) differentiation between items avoiding overlap with other variables.

### Sleep problems

- ▶ Sleep quality and day sleeping patterns (the adapted item 1 from the Insomnia Severity Index<sup>20</sup> summarising its contents and an additional item asking for unrefreshing (non-restorative) sleep, because this is a problem which is often associated with RMDs. Participants respond on 5-point Likert scales (none ... very severe) to the following two adapted questions: 'In general, how severe were your sleeping problems during the last month?' and 'During the last month, to what extent did you wake up tired in the morning?'

### Psychological variables

- ▶ Depression and anxiety: Using the two overarching constructs of the Hospital Anxiety and Depression Scale,<sup>21</sup> patients note how depressed and anxious they generally felt in the last month in two separate Visual Analogues Scales (Not at all...extremely). Single-item scales have demonstrated validity to measure depression<sup>14</sup> and anxiety.<sup>15</sup>
- ▶ Negative affect: Choosing items that are distinctive from other items (eg, fatigue), items 2 and 15 on negative affect valence<sup>22</sup> were adapted and answered in a 5-point Likert scale: 'To what extent you generally felt': (1) distressed (Not at all...Extremely) and (2) nervous (Not at all...extremely) during the last month?.
- ▶ Positive affect: Choosing items that reflect psychological status and are distinctive from other items, items 9 and 11 on positive affect valence<sup>22</sup> were adapted and

answered in a 5-point Likert scale: 'To what extent you generally felt' (1) enthusiastic (Not at all...Extremely) and (2) inspired (Not at all...Extremely) during the last month?.

- ▶ Satisfaction with life: Participants answer the following two questions (5-point Likert scales): 'How satisfied have you generally felt with your life during the last month?' ((Very) Dissatisfied...(Very) Satisfied) adapted from the single-item questionnaire<sup>23</sup> and 'During the last month, I considered myself to be...' ((Very) unhappy....(very) happy)) adapted from item 1 from.<sup>24</sup>
- ▶ Acceptance: Two items (items 2 and 5) with the first and third highest loading of the Acceptance and Action Questionnaire-II<sup>25</sup> were selected to avoid overlap with negative and positive affect measurements. These items were adapted and answered on a 5-point Likert scale: 'During the last month, my painful experiences and memories made it difficult for me to live a life that I would have valued' (Not at all...All the time) and 'During the last month, my painful memories have prevented me from having a fulfilling life' (Not at all...All the time).
- ▶ Catastrophising thoughts: The three items (items 2, 11 and 13) with the highest loading for each construct (rumination, magnification and helplessness) of the catastrophising scale<sup>26</sup> were adapted and answered on a 5-point Likert scale: 'During the last month, I felt I couldn't go on' (Not at all...All the time). 'During the last month, I kept thinking about how badly I wanted the pain or fatigue to stop' (Not at all...All the time), and 'During the last month, I wondered whether something serious may happen' (Not at all...All the time).
- ▶ Soothing/Compassion: A characteristic self-kindness item (item 12) and self-judgement item (item 1) from the self-compassion scale were adapted and answered on a 5-point Likert scale<sup>27</sup>: 'During the last month, when I went through a very hard time, I gave myself the caring and tenderness I needed' (Never ... Very often/Always) and 'During the last month, I was disapproving and judgemental about my own flaws and inadequacies' '(Never ... Very often/Always). Two items were chosen to reflect the two overarching factors.<sup>28</sup>

### Social support

- ▶ Invalidation (Discounting): Two high loading items (items 2 and 6) from the 3\*I<sup>29</sup> were adapted and answered on a 5-point Likert scale: 'My family, colleagues at work, or medical professionals think I should be tougher' (Never... Very often/Always) and 'My family, colleagues at work, or medical professionals make me feel like I am an exaggerator' (Not at all...Very often/Always).
- ▶ Social support: Items 2 and 5 from the multidimensional scale of perceived social support<sup>30</sup> were adapted. This questionnaire makes a distinction between 'a

special person', 'my family' and 'my friends'. Considering that the quality of social support is considered more important than the quantity of social support, two high loading items of 'a special person' were selected and answered on a 5-point Likert scale: 'There is a special person with whom I can share my joys and sorrows' (strongly disagree...strongly agree) and 'I have a special person who is a real source of comfort to me' (strongly disagree...strongly agree).

- ▶ Loneliness: Two items (items 16 and 5) with the highest corrected item-total correlations from the UCLA Loneliness Scale<sup>31</sup> were adapted and answered on a 5-point Likert scale: 'During the last month, how often have you felt that there were people who really understand you?' (Never...Very often/Always) and 'During the last month, how often did you feel part of a group of friends?' (Never...Very often/Always).

### Body weight

- ▶ Body weight and height (to compute body mass index).

### Diet

- ▶ Food: Items 4 and 5 from the Mediterranean Diet Adherence Screener used in the PREDIMED study<sup>32</sup> were adapted: 'How many pieces of fruit (including fresh-squeezed juice) did you consume per day during the last month?' '(Less than one piece/one piece/two pieces/three pieces/four pieces/five or more pieces) and 'How many servings of red meat, hamburger, or sausages did you consume per day during the last month? A full serving is 100–150 g (4–6 oz)' '(Less than one serving/one serving/two servings/three servings/four or more servings). Also, patients answer on a 5-point Likert scale 'In general, how healthy was your diet during the last month?' (poor...excellent). The selection of these two items were based on evaluating positive (ie, fruit consumption) and negative (ie, red meat consumption) aspects of the participants' diet. Additionally, the research team appraised that these two items are relatively easy to recall.

### Inactive lifestyle

Items were chosen to reflect leisure-time physical activity and sedentary behaviour as well as physical activity during work, because these are differently associated with health.<sup>33 34</sup>

- ▶ Leisure-time physical activity: Participants respond to the following two questions: (1) 'In the past week' and (2) 'In a normal week', 'on how many days have you done a total of 30 min or more of physical activity'. This may include activities of low intensity (eg, slow walking) to high intensity (eg, cycling for recreation or to get to and from places), but 'should not include housework or physical activity that may be part of your job'; adapted from a single-item measure.<sup>35</sup> Participants will provide a number of days/week.

- ▶ Physical activity during work: Patients choose one of the following options to describe their main activity during working hours (adapted from item 111 from<sup>36</sup>): ‘Mainly sitting during working hours’, ‘Mainly standing during working hours with little movement’, ‘Walking, lifting some weights, and frequent movement’, ‘Tasks that require great physical effort’ or ‘Not applicable’.
- ▶ Sedentary time: Participants respond to the following adapted question from the single question of the Global Physical Activity Questionnaire<sup>37</sup>: ‘This question is about sitting or lying during your leisure time (but NOT including work or sleeping time). How many hours do you usually spend sitting or lying (reclining) on a normal day during your leisure time?’ (number of hours/day).

#### Disease activity

- ▶ Because diseases have different indicators of disease activity, we asked for a global indication that could hold for all diseases. Common disease activity (as compared with patients with a similar disease) and current disease activity (as compared with one’s own common disease activity) are assessed on a 5-point Likert scale ranging from ‘lower’ (1) to ‘higher’ (5). Participants also report whether or not they consider to be in a flare (sudden worsening of symptoms) at that moment (‘No, my symptoms are the same, as usual’ or ‘Yes, my symptoms have suddenly worsened’).

#### Scalability of the project

Regarding the participants, data collection involves only a cross-sectional measurement via a brief electronic survey. Time burden depends on whether participants decide to complete the full survey (around 20 min) or the basic survey (around 10 min). Slight modifications of the original scale were incorporated to allow similar response formatting across items of the electronic survey (eg, most questions were referred to the last month when a time frame was needed and were adapted to a 5-point Likert scale). We do recognise the limitations of this approach in terms of reliability. However, our approach has the advantage of ensuring the inclusion of a large number of participants and reducing the burden that research imposes on them.

The steering committee of the project includes researchers from Ireland, the Netherlands, Portugal, Spain and the UK. The project is recruiting participants from all these countries. In addition, researchers (including people with RMDs as research partners) from other countries are welcome to implement this project in their local communities. Table 1 shows how the steering committee will support them. To adapt the study to other cultures, meeting(s) with local patients, healthcare providers or researchers may be organised to ensure inclusion of any variable which is found to be of particular relevance to the local culture of the researcher and is expected to be related to fatigue or pain.

#### Sample size

Power and sample size requirements are understudied in the data driven techniques involved in the present proposal. One suggestion is that a minimum sample size of three times the number of edges to be computed in network analyses is required.<sup>38</sup> With nine variables (nodes) in the model, this would be a minimum of 108 participants for the 36 associations  $((9 \times 8) / 2)$  to be calculated. By aiming for a minimum of 150 participants for each patient subgroup with the most prevalent RMD, we thus feel this project is adequately powered to fulfil its aims. As the sample size has the potential to impact network estimations, we will perform a set of sensitivity analyses in which we repeat all analyses in equal subgroups of randomly selected patients with a specific RMD.

#### Data analyses

The network analyses are performed in the free software statistical environment R (<http://cran.r-project.org>). To reveal the complex patterns of relationships between the seven biopsychosocial factors, fatigue and pain, a network is estimated using the R package *mgm*,<sup>39</sup> which estimates a network model by performing regularised generalised regressions for each variable, estimating edges connected to that variable. When one or two scores are missing, we will impute them using the *mice* package.<sup>40</sup>

To determine profiles, a hierarchical cluster analysis with Ward’s method will be conducted to get an indication of the optimal number of clusters (profiles). Visual inspection of the dendrogram will indicate the number of clusters that could be considered. Next, an optimisation clustering (ie, *k*-means cluster analysis) will be performed to parsimoniously allocate participants to clusters. The number of clusters will be decided by practical considerations (the least frequent cluster should include a minimum of 15% of the total sample<sup>41</sup>) and by interpretability of mean factor scores within clusters.<sup>7,8</sup> By using this combination of interpretability and hierarchical and *k*-means cluster analyses, the developed cluster solution minimises within-group variability and maximises between-group differences.<sup>42</sup>

The package network comparison test<sup>43</sup> is used to test whether the networks differ for subgroups of people with different RMDs and profiles. In ancillary analysis, we will test whether findings are affected by demographic variables, gender, age, education level, number of comorbidities and self-diagnosis. Patients with multiple RMDs will be analysed as separate groups. The number of participants with non-RMD comorbidities will be described.

#### Patient and public involvement

A patient representative (MV) has been involved in the design of this study, is part of the steering committee that defined the research question and outcomes of the study and will take part in the analyses and report of the study. A rheumatologist assisted with specifications of the pharmacological questions and comorbidities.

**Table 1** Conditions to be a national leader of the present research in countries from which representatives are not included in the steering committee of the project (listed in chronological order)

Task to be performed by the interested researcher	Support provided by the steering committee*	Type of requirement	Expected date for the task to be completed†
Apply for and obtain ethical approval by an appropriate local institutional review board	Ethical application and letter of ethical approval by Utrecht University	Compulsory	As soon as possible after the steering committee approves participation
Meeting(s) with patients or healthcare providers to include a variable of interest for networks models of pain or fatigue.	Examples of questions and minutes from previous meetings	Strongly advised	Meeting(s) are carried out in months 2 and 3
Transcultural (forward–backward) translation process <sup>45</sup> of the survey	Written directions explaining the procedure	Compulsory	Months 4 and 5
Corroboration that the electronic implementation of the survey as completed by the steering committee is correct	Electronic implementation of the survey and storage of the data, expenses are covered by the funder of the study	Compulsory	Month 6
Circulation of the link to the electronic survey via patients associations and, if possible, other complementary ways such as healthcare providers	Examples of successful experiences and approaches followed in other countries	Compulsory	Month 7 to month 19
Provide feedback in at least a scientific manuscript led by members of the steering committee	Members of the steering committee write at least two scientific manuscripts on the network models for fatigue and pain	Advised	To be agreed
Prepare a communication to a conference or led a scientific manuscript	The specific support will depend on the needs of the local researcher (eg, statistical support)	Not required	To be agreed
To disseminate the findings of the project to policymakers, healthcare providers, people with rheumatic and musculoskeletal diseases or other sections of society	Examples of successful experiences. Additional support will be offered depending on the needs of the local researcher	Strongly advised	From month 20 until a date to be agreed
Applications for obtaining additional funding for addressing new questions	The specific support will depend on the needs of the local researcher (eg, identifying potential calls)	Not required	To be agreed

\*All the materials will be provided in the English language.

†The expected date is indicated in months after the ethical approval has been obtained.

Meetings with Dutch and Spanish patients, health professionals and rheumatologists were organised to choose the variables included in the study. The survey was reviewed by people with RMDs in Ireland and the UK. Patients are involved in the recruitment of participants as the link to the electronic survey is circulated via people with RMDs who lead local and national associations. Lastly, the main findings of the research will be communicated to patients with RMDs. The manuscripts presenting the findings of the study will be published open access when possible.

### Strengths and limitations

This study protocol has several strengths and limitations. First, multiple biopsychosocial factors are considered

in a study with large samples, allowing a better understanding of: (1) the multifaceted nature of fatigue and pain and (2) differences in associations between fatigue, pain and biopsychosocial factors. The collection of multiple variables requires short and efficient measurements that differ from longer, validated and ‘psychometrically superior’ tools. While short measures reduce the reliability, this is not necessarily at the cost of validity.<sup>44</sup> Most important, the inclusion of all items of a questionnaire (a potential ‘psychometrically superior’ approach), would increase the burden for participants and limit the scalability of the project. Similarly, the limitation of a self-reported diagnosis as an inclusion criterion allows to recruit a large sample size from several European



countries to adequately address the aims of the study and test the generalisability of the findings, making the study more realistic and feasible. Another strength is that comorbidities are assessed. However, taking into account of them as a covariate is a very conservative approach, because non-RMD comorbidities may actually be part of the RMD (eg, skin disease in SLE, ophthalmic problems in Sjögren's syndrome or heart damage due to rheumatic fever). Finally, although this study does not allow inferences beyond the cross-sectional design, the results can be used to design experimental and non-experimental single-case longitudinal studies to examine the directionality of effects in individual patients.

## ETHICS AND DISSEMINATION

Ethical approval from national Institutional Review Boards was obtained, which mainly involved the ethical board of the institution employing the researchers within each country. The first and second screens of the electronic survey are participant's information letter and the informed consent form. This is done according to the ethical guidelines of the Declaration of Helsinki (and updates). To date, the study has been already approved to be conducted in the Netherlands by the Ethics Committee of the Faculty of Social and Behavioural Sciences of Utrecht University (FETC19-058), in Spain by the Ethics Committee of the University of Granada (981/CEIH/2019) in UK by the Ulster University Research Ethics Committee (REC/20/0037), in Ireland by the Social Research Ethics Committee (SREC 2021-003) of University College Cork and in Portugal by the Ethics Committee of the Health Sciences Research Unit: Nursing (UICiSA:E) in Coimbra (#667-04/2020).

The findings of this research will be communicated to researchers, clinicians and patients internationally in at least two abstracts in conferences such as the European Congress of Rheumatology and two manuscripts in peer-reviewed journals, one of the works will focus on different RMDs and another on profiles of biopsychosocial factors. The findings will be widely communicated to society using mass media. Since our findings may have an impact on policy and healthcare practice, we will also present them to policymakers and healthcare providers. We will present our findings to patients with RMDs.

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**Dear reader,**

**You are invited to participate in a study examining factors that can influence symptom severity in rheumatic disease, in particular pain and fatigue. This research is being carried out in several countries across Europe including Portugal, Spain, the Netherlands, Ireland and the UK. This study is funded by the European Alliance of Associations for Rheumatology (EULAR). The project supervisor is Fernando Estévez-López.**

**We are interested in including people in this study who are 18 years of age or older and have been diagnosed with a rheumatic or musculoskeletal disease.**

**Participation in the study will take approximately 10 minutes (basic survey) or 20 minutes (full survey) depending on your preferences. Your data will be processed confidentially and your name will not be linked to the results.**

**If you have questions, please get in contact with:**

**Ciara M. Hughes (Ulster University) United Kingdom: [cm.hughes@ulster.ac.uk](mailto:cm.hughes@ulster.ac.uk)**

**Joseph G. McVeigh (University College Cork) Ireland: [joseph.mcveigh@ucc.ie](mailto:joseph.mcveigh@ucc.ie)**

**Thank you in advance for participating in this study.**

**Kind regards,**



## Section A: Consent

**A1. By completing and submitting the survey I am providing consent to use the information submitted for research purposes. My responses are anonymous and confidential. I can stop participation at any time.**

I provide consent to participate in this survey  
I do not provide consent to participate in this survey

## Section B:

**B1. Gender**

Male  
Female  
Other

**B2. Age**

## Section C:

**C1. Country**

England  
Ireland  
Northern Ireland  
Scotland  
Wales  
Other (please specify)

Other (please specify)



## Section D:

### D1. Marital Status

- In a relationship (married, cohabiting, living together)
- Separated/divorced
- Widowed
- Single
- Other (please specify)


Other (please specify)

### D2. What is the highest level of education you have completed?

- No school education
- Primary Education
- Secondary Education
- Further Education (e.g. Technical College)
- Higher Education (University)


### D3. Current employment status

- Self-employed or employed (paid) work for 16 hours or more per week
- Self-employed or employed (paid) work for less than 16 hours per week
- Volunteer work (unpaid)
- Sick leave
- Pandemic unemployment payment or other special arrangement due to the COVID-19 pandemic
- Homeworker (doing household or looking after children)
- Student
- Retired
- Disability pension
- Combination of employed and one of the other categories
- Other


### D4. Which of the following better describes your main activity during working hours?

- Mainly sitting during working hours
- Mainly standing during working hours with little movement
- Walking, lifting some weights, and frequent movement
- Tasks that require great physical effort
- Not applicable


## Section E:

### E1. In general, how severe would you rate your pain during the last month?

No pain at all	1	2	3	4	5	6	7	8	9	Very severe pain
□	□	□	□	□	□	□	□	□	□	□



**E2. In general, how severe would you rate your fatigue during the last month?**

No fatigue at all	1	2	3	4	5	6	7	8	9	Very severe fatigue
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	0

**E3. In general, how severe would you rate your sleep problems during the last month?**

No sleep problems at all	1	2	3	4	5	6	7	8	9	Very severe sleep problems
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	0

**E4. In general, how severe would you rate the severity of your disease during the last month?**

**This refers to your primary rheumatic disease. For example: severity of inflammatory activity in the case of rheumatoid arthritis or severity of pain in the case of osteoarthritis**

No disease activity at all	1	2	3	4	5	6	7	8	9	Very severe disease activity
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	10

**E5. In general, how inactive was your lifestyle during the last month?**

Not inactiv e at all	1	2	3	4	5	6	7	8	9	Very in activel
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	0

**E6. In general, how would you rate your experience of lack of understanding of your disease by others during the last month?**

**This refers to your condition not being recognized by others including nonacceptance, misunderstanding, disbelief, rejection or stigmatization**

No lack of understan ding at all	1	2	3	4	5	6	7	8	9	Very severe lack of under- standing
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	10

**E7. In general, how unhealthy was your diet during the last month?**

Not unhealth y at all	1	2	3	4	5	6	7	8	9	Very u nhealth y
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	10

**E8. In general, how unhealthy is your body weight?**

Not unhealth y at all	1	2	3	4	5	6	7	8	9	Severely unhealth y
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	10



**E9. In general, how severe would you rate your psychological problems during the last month?**

No psychologi- cal problems at all0	1	2	3	4	5	6	7	8	9	Very severe psychologi- cal problems10
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Section F:**

**F1. Weight**

Please select in which units you prefer to report your data:

lbs/pounds	<input type="checkbox"/>
kilograms	<input type="checkbox"/>

**F2. Enter here your weight in lbs**

--	--	--	--	--	--	--	--	--	--	--

**F3. Enter here your weight in kgs**

--	--	--	--	--	--	--	--	--	--	--

**F4. Height**

Please select in which units you prefer to report your data:

feet and inches	<input type="checkbox"/>
centimeters	<input type="checkbox"/>

**F5. Enter here your height in feet**

--	--	--	--	--	--	--	--	--	--	--

**F6. Enter here your height in inches**

--	--	--	--	--	--	--	--	--	--	--

**F7. Enter here your height in cm**

--	--	--	--	--	--	--	--	--	--	--

**Section G:**

**G1. Have you ever been diagnosed with any of the following rheumatic diseases?**

Fibromyalgia	<input type="checkbox"/>
Rheumatoid arthritis	<input type="checkbox"/>
Osteoarthritis	<input type="checkbox"/>
Systemic lupus erythematosus (SLE)	<input type="checkbox"/>
Spondyloarthritis/Bechterew's disease	<input type="checkbox"/>
Sjögren's syndrome	<input type="checkbox"/>



Psoriatic arthritis

Scleroderma / Systemic sclerosis

Mixed Connective Tissue Disease (MCTD)

Other rheumatic disease not included in this list (you can specify later)

## Section H:

**H1. Fibromyalgia: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes

No

**H2. Fibromyalgia:**

**Who diagnosed this disease?**

**If more than one answer is true for you, select the one with the lowest number assigned**

1. A medical specialist such as a rheumatologist
2. General practitioner
3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)
4. I made the diagnosis myself
5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)

**H3. Fibromyalgia: Disease duration (time since diagnosis)**

Less than 6 months

Between 6 months and 2 years

Between 2 and 5 years

Between 5 and 10 years

Between 10 and 20 years

More than 20 years





## Section I:

**I1. Rheumatoid Arthritis: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes   
No

**I2. Rheumatoid Arthritis Who diagnosed this disease? If more than one answer is true for you, select the one with the lower number assigned**

1. A medical specialist such as a rheumatologist
2. General practitioner
3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)
4. I made the diagnosis myself
5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)

**I3. Rheumatoid arthritis: Disease duration (time since diagnosis)**

- Less than 6 months
- Between 6 months and 2 years
- Between 2 and 5 years
- Between 5 and 10 years
- Between 10 and 20 years
- More than 20 years


## Section J:

**J1. Osteoarthritis: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes   
No



## J2. Osteoarthritis

**Who diagnosed this disease?**

**If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist
  2. General practitioner
  3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)
  4. I made the diagnosis myself
  5. Another person (please specify the role of the person who made the diagnosis)
5. Another person (please specify the role of the person who made the diagnosis)



## J3. Osteoarthritis: Disease duration (time since diagnosis)

- Less than 6 months
- Between 6 months and 2 years
- Between 2 and 5 years
- Between 5 and 10 years
- Between 10 and 20 years
- More than 20 years


## Section K:

**K1. Systemic Lupus Erythematosus: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes

No



**K2. Systemic Lupus Erythematosus Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist  
 2. General practitioner  
 3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)  
 4. I made the diagnosis myself  
 5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)

**K3. Systemic Lupus Erythematosus: Disease duration (time since diagnosis)**

- Less than 6 months  
 Between 6 months and 2 years  
 Between 2 and 5 years  
 Between 5 and 10 years  
 Between 10 and 20 years  
 More than 20 years


**Section L:**

**L1. Spondyloarthritis/Bechterew's disease: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes   
 No

**L2. Spondyloarthritis/Bechterew's disease Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist  
 2. General practitioner  
 3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)  
 4. I made the diagnosis myself  
 5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)



**L3. Spondyloarthritis/Bechterew's disease: Disease duration (time since diagnosis)**

- |                              |                          |
|------------------------------|--------------------------|
| Less than 6 months           | <input type="checkbox"/> |
| Between 6 months and 2 years | <input type="checkbox"/> |
| Between 2 and 5 years        | <input type="checkbox"/> |
| Between 5 and 10 years       | <input type="checkbox"/> |
| Between 10 and 20 years      | <input type="checkbox"/> |
| More than 20 years           | <input type="checkbox"/> |

## Section M:

**M1. Sjögren's syndrome: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

- |     |                          |
|-----|--------------------------|
| Yes | <input type="checkbox"/> |
| No  | <input type="checkbox"/> |

**M2. Sjögren's syndrome Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

- |  |                          |
|--|--------------------------|
| 1. A medical specialist such as a rheumatologist   | <input type="checkbox"/> |
| 2. General practitioner  | <input type="checkbox"/> |
| 3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist) | <input type="checkbox"/> |
| 4. I made the diagnosis myself   | <input type="checkbox"/> |
| 5. Another person (please specify the role of the person who made the diagnosis)                       | <input type="checkbox"/> |

5. Another person (please specify the role of the person who made the diagnosis)

**M3. Sjögren's syndrome: Disease duration (time since diagnosis)**

- |                              |                          |
|------------------------------|--------------------------|
| Less than 6 months           | <input type="checkbox"/> |
| Between 6 months and 2 years | <input type="checkbox"/> |
| Between 2 and 5 years        | <input type="checkbox"/> |
| Between 5 and 10 years       | <input type="checkbox"/> |
| Between 10 and 20 years      | <input type="checkbox"/> |
| More than 20 years           | <input type="checkbox"/> |

## Section N:

**N1. Psoriatic arthritis: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

- |     |                          |
|-----|--------------------------|
| Yes | <input type="checkbox"/> |
| No  | <input type="checkbox"/> |



## N2. Psoriatic Arthritis

**Who diagnosed this disease?**

**If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist
2. General practitioner
3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)
4. I made the diagnosis myself
5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)

## N3. Psoriatic arthritis: Disease duration (time since diagnosis)

- Less than 6 months
- Between 6 months and 2 years
- Between 2 and 5 years
- Between 5 and 10 years
- Between 10 and 20 years
- More than 20 years


## Section O:

**O1. Scleroderma/Systemic sclerosis: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes

No



**O2. Scleroderma/Systemic sclerosis Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist  
 2. General practitioner  
 3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)  
 4. I made the diagnosis myself  
 5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)

**O3. Scleroderma/Systemic sclerosis: Disease duration (time since diagnosis)**

- Less than 6 months  
 Between 6 months and 2 years  
 Between 2 and 5 years  
 Between 5 and 10 years  
 Between 10 and 20 years  
 More than 20 years


**Section P:**

**P1. Mixed Connective Tissue Disease (MCTD): Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes   
 No

**P2. Mixed Connective Tissue Disease (MCTD) Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist  
 2. General practitioner  
 3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)  
 4. I made the diagnosis myself  
 5. Another person (please specify the role of the person who made the diagnosis)


5. Another person (please specify the role of the person who made the diagnosis)



**P3. Mixed Connective Tissue Disease: Disease duration (time since diagnosis)**

- Less than 6 months
- Between 6 months and 2 years
- Between 2 and 5 years
- Between 5 and 10 years
- Between 10 and 20 years
- More than 20 years

**Section Q:**

**Q1. Have you ever been diagnosed with any other rheumatic disease not previously mentioned?  $\$(function() { \$("label[for=answercomment].control-label").text("If yes, please specify the name of the rheumatic disease(only one disease:"); });$**

- Yes
- No

**Q2. Other rheumatic disease: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

- Yes
- No

**Q3. Other rheumatic disease Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist
2. General practitioner
3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)
4. I made the diagnosis myself
5. Another person (please specify the role of the person who made the diagnosis)

5. Another person (please specify the role of the person who made the diagnosis)



**Q4. Other rheumatic disease: Disease duration (time since diagnosis)**

Less than 6 months	<input type="checkbox"/>
Between 6 months and 2 years	<input type="checkbox"/>
Between 2 and 5 years	<input type="checkbox"/>
Between 5 and 10 years	<input type="checkbox"/>
Between 10 and 20 years	<input type="checkbox"/>
More than 20 years	<input type="checkbox"/>

**Section R:**

**R1. Have you ever been diagnosed with any other rheumatic disease not previously mentioned?** `$(function() {`  
`$("label[for=answercomment].control-label").text("If yes, please specify the name of the rheumatic disease(only one):"); });`

Yes   
 No

**R2. Other rheumatic disease: Is this the primary/most incapacitating disease with which you have been diagnosed? Please answer the following questions for all diseases which you have been diagnosed with (not only your primary disease)**

Yes   
 No

**R3. Other rheumatic disease Who diagnosed this disease? If more than one answer is true for you, select the one with lowest number assigned**

1. A medical specialist such as a rheumatologist	<input type="checkbox"/>
2. General practitioner	<input type="checkbox"/>
3. Another health professional (such as a nurse, physiotherapist / physical therapist or psychologist)	<input type="checkbox"/>
4. I made the diagnosis myself	<input type="checkbox"/>
5. Another person (please specify the role of the person who made the diagnosis)	<input type="checkbox"/>

5. Another person (please specify the role of the person who made the diagnosis)

**R4. Other rheumatic disease: Disease duration (time since diagnosis)**

Less than 6 months	<input type="checkbox"/>
Between 6 months and 2 years	<input type="checkbox"/>
Between 2 and 5 years	<input type="checkbox"/>
Between 5 and 10 years	<input type="checkbox"/>
Between 10 and 20 years	<input type="checkbox"/>
More than 20 years	<input type="checkbox"/>





## Section S:

### S1. Please select other diseases that you have been diagnosed with

- Persistent physical symptoms (e.g. chronic fatigue syndrome/Myalgic Encephalomyelitis (ME/CFS), Irritable bowel syndrome (IBS), somatoform disorder, somatic symptom disorder, chronic pain in the body (not migraine))
- Psychiatric or psychological problems (e.g., schizophrenia, depression, anxiety, personality disorder, job burnout, or an addiction that needs treatment)
- A pulmonary disease (emphysema, COPD, asthma, bronchitis)
- Diabetes or severe obesity
- Chronic skin condition
- Neurological disorder (e.g., Epilepsy, Dementia, Parkinson's disease, migraine)
- Cancer
- Cardiovascular diseases (e.g., high blood pressure, stroke or other cerebrovascular accidents, myocardial infarction)
- Stomach, liver, gastrointestinal tract, kidney or other organ disease
- Hereditary disease (e.g., Huntington, Ehlers-Danlos)
- I have not been diagnosed with any other disease
- Other


Other

## Section T:

### T1.

**You have completed the first part of the survey**

**You can continue answering more questions to complete the full survey or you can finish your collaboration here.**

**Full survey will take approximately 10 more minutes.**

I would like to continue with the full survey

I would like to finish my participation now


## Section U:

### U1. COVID-19 disease status

Never tested positive or never suffered from COVID-19

Tested positive/suffered from COVID-19 at some point

Currently tested positive/suffering from COVID-19



**U2.** How much time have you been quarantined at home? *This includes time at home due to government policies, being infected or being in contact with someone infected*

Less than 2 weeks

2-4 weeks

4-8 weeks

8-12 weeks

12-16 weeks

More than 16 weeks

## Section V:

**V1.**

### Medication for rheumatic conditions

**Do you currently use anti-inflammatory (Nonsteroidal anti-inflammatory drugs NSAID) medication, such Ibuprofen, Naproxen or Celecoxib?**

Yes

No

Not sure

## Section W:

**W1.**

### Medication for rheumatic conditions

**Do you currently use a biologic drug, such as etanercept, adalimumab, golimumab, certolizumab, infliximab, rituximab, abatacept, tocilizumab, sarilumab, or a similar drug (which all have to be administered as injection or infusion)?**

Yes

No

Not sure

## Section X:

**X1.**

### Medication for rheumatic conditions

**Do you currently use targeted drugs (called JAK inhibitors), such as baricitinib, tofacitinib, and upadacitinib?**

Yes

No

Not sure

**Section Y:**

Y1.

**Medication for rheumatic conditions**

**Do you currently use a drug such as prednisone, prednisolone, or do you get on a regular or repeated basis injections or infusions with methylprednisolone or dexamethasone or a similar drug in the same category?**

Yes   
No   
Not sure

**Section Z:**

Z1.

**Medication for rheumatic conditions**

**Do you currently use medication such as methotrexate, sulfasalazine (salazopyrine), cloroquine, hydroxychloroquine, leflunomide, ciclosporin or gold injections?**

Yes   
No   
Not sure

**Section AA:**

AA1.

**Medication for rheumatic conditions**

**Do you currently use any other medication for your rheumatic condition?**

Yes   
No   
Not sure



## Section AB:

AB1.

### Pain medication

Do you currently use acetaminophen (paracetamol) as pain alleviating medication?

Yes   
 No   
 Not sure

AB2.

### Pain medication

Do you currently use pain alleviating medication other than NSAIDs or acetaminophen (paracetamol)? For example: tramadol, codeine, oxycodone or similar opioid drug, tricyclic antidepressant such as tryptizol, medication such as gabapentin or pregabalin, or over-the-counter (non-prescription) medication, such as cannabis and similar medications, glucosamine or, other complementary medicines?

Yes   
 No   
 Not sure

## Section AC:

AC1.

### Medication for psychological problems

Do you currently use other medication for psychological or psychiatric symptoms, such as drugs for depression, anxiety, or schizophrenia?

Yes   
 No   
 Not sure

## Section AD:

AD1.

### Medication for sleep problems

Do you currently use other medication that help you to sleep?

Yes   
 No   
 Not sure



## Section AE:

**AE1. Regarding your primary rheumatic disease, how do you feel the severity of your disease compares to other patients with a similar disease?**

Lower	<input type="checkbox"/>
A little bit lower	<input type="checkbox"/>
Average	<input type="checkbox"/>
A little bit higher	<input type="checkbox"/>
Higher	<input type="checkbox"/>

**AE2. Regarding your primary rheumatic disease, how do you feel the severity of your disease is, as compared to the severity you have experienced in the past?**

Lower	<input type="checkbox"/>
A little bit lower	<input type="checkbox"/>
Average	<input type="checkbox"/>
A little bit higher	<input type="checkbox"/>
Higher	<input type="checkbox"/>

**AE3. Would you consider yourself to be in a flare at the moment?**

No, my symptoms are the same as usual	<input type="checkbox"/>
Yes, my symptoms have suddenly worsened	<input type="checkbox"/>

## Section AF:

**AF1. How could you describe your current menstrual status?**

Premenopause (before menopause; having regular periods)	<input type="checkbox"/>
Menopause transition (changes in periods, but have not gone 12 months in a row without a period)	<input type="checkbox"/>
Postmenopause (after menopause)	<input type="checkbox"/>



## Section AG:

**AG1. In the past week, on how many days have you done a total of 30 minutes or more of physical activity during your leisure time?**

**This may include activities ranging from low intensity (for instance, slow walking) to high intensity (for instance, cycling for recreation or to get to and from places), but should not include housework or physical activity that may be part of your job**

--	--	--	--	--	--	--	--	--	--

**AG2. In a normal week, on how many days have you done a total of 30 minutes or more of physical activity during your leisure time?**

**This may include activities ranging from low intensity (for instance, slow walking) to high intensity (for instance, cycling for recreation or to get to and from places), but should not include housework or physical activity that may be part of your job**

--	--	--	--	--	--	--	--	--	--

## Section AH:

**AH1. This question is about sitting or lying during your leisure time (but NOT including work or sleeping time). How many hours do you usually spend sitting or lying (reclining) on a normal day during your leisure time?**

--	--

## Section AI:

**AI1. In general, how severe were your sleeping problems during the last month?:**

None	
Mild	
Moderate	
Severe	
Very Severe	



**AI2. During the last month, to what extent did you wake up tired in the morning?:**

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
Moderately	<input type="checkbox"/>
Quite a bit	<input type="checkbox"/>
Extremely	<input type="checkbox"/>

**Section AJ:**

**AJ1. How anxious have you generally felt during the last month?**

Not at all anxious 0	1	2	3	4	5	6	7	8	9	Extrem ely anxious 10
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**AJ2. How depressed have you generally felt during the last month?**

Not at all depre ssed 0	1	2	3	4	5	6	7	8	9	Extrem ely depre ssed 10
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Section AK:**

**AK1. To what extent have you generally felt nervous during the last month?**

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
Moderately	<input type="checkbox"/>
Quite a bit	<input type="checkbox"/>
Extremely	<input type="checkbox"/>

**AK2. To what extent have you generally felt distressed during the last month?**

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
Moderately	<input type="checkbox"/>
Quite a bit	<input type="checkbox"/>
Extremely	<input type="checkbox"/>

**AK3. To what extent have you felt enthusiastic during the last month?**

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
Moderately	<input type="checkbox"/>
Quite a bit	<input type="checkbox"/>
Extremely	<input type="checkbox"/>

**AK4. To what extent have you felt inspired during the last month?**

Not at all	<input type="checkbox"/>
A little	<input type="checkbox"/>
Moderately	<input type="checkbox"/>
Quite a bit	<input type="checkbox"/>
Extremely	<input type="checkbox"/>



## Section AL:

**AL1. How satisfied have you generally felt with your life during the last month?**

(Very) dissatisfied  
 Somewhat dissatisfied  
 Neither dissatisfied nor satisfied  
 Somewhat satisfied  
 (Very) satisfied


**AL2. During the last month, I considered myself to be...**

(Very) unhappy  
 Somewhat unhappy  
 Moderately happy  
 Somewhat happy  
 (Very) happy


## Section AM:

**AM1. During the last month, my painful memories have prevented me from having a fulfilling life**

Not at all  
 To a slight degree  
 To a moderate degree  
 To a great degree  
 All the time


**AM2. During the last month, my painful experiences and memories made it difficult for me to live a life that I would have valued**

Not at all  
 To a slight degree  
 To a moderate degree  
 To a great degree  
 All the time


## Section AN:

**AN1. During the last month, I kept thinking about how badly I wanted the pain or fatigue to stop**

Not at all  
 To a slight degree  
 To a moderate degree  
 To a great degree  
 All the time


**AN2. During the last month, I wondered whether something serious may happen**

Not at all  
 To a slight degree  
 To a moderate degree  
 To a great degree  
 All the time





**AN3. During the last month, I felt I couldn't go on**

Not at all  
To a slight degree  
To a moderate degree  
To a great degree  
All the time


## Section AO:

**AO1. During the last month, when I went through a very hard time, I gave myself the caring and tenderness I needed**

Never  
Rarely  
Sometimes  
Often  
Very often/Always


**AO2. During the last month, I was disapproving and judgmental about my own flaws and inadequacies**

Never  
Rarely  
Sometimes  
Often  
Very often/Always


## Section AP:

**AP1. My family, colleagues at work, or medical professionals think I should be tougher**

Never  
Rarely  
Sometimes  
Often  
Very often/Always


**AP2. My family, colleagues at work, or medical professionals make me feel like I am an exaggerator**

Never  
Rarely  
Sometimes  
Often  
Very often/Always


## Section AQ:

**AQ1. There is a special person with whom I can share my joys and sorrows**

Strongly disagree  
Mildly disagree  
Neutral  
Mildly agree  
Strongly agree




**AQ2. I have a special person who is a real source of comfort to me**

Strongly disagree	<input type="checkbox"/>
Mildly disagree	<input type="checkbox"/>
Neutral	<input type="checkbox"/>
Mildly agree	<input type="checkbox"/>
Strongly agree	<input type="checkbox"/>

## Section AR:

**AR1. During the last month, how often have you felt that there were people who really understand you?**

Never	<input type="checkbox"/>
Rarely	<input type="checkbox"/>
Sometimes	<input type="checkbox"/>
Often	<input type="checkbox"/>
Very often/Always	<input type="checkbox"/>

**AR2. During the last month, how often did you feel part of a group of friends?**

Never	<input type="checkbox"/>
Rarely	<input type="checkbox"/>
Sometimes	<input type="checkbox"/>
Often	<input type="checkbox"/>
Very often/Always	<input type="checkbox"/>

## Section AS:

**AS1. During the last month, I could perform activities such as dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities**

Cannot be done at all	<input type="checkbox"/>
Can be done with a lot of difficulty	<input type="checkbox"/>
Can be done with difficulty	<input type="checkbox"/>
Can be done with little difficulty	<input type="checkbox"/>
Can be done without any difficulty	<input type="checkbox"/>

**AS2. Compared to people who are the same age as me, my general physical fitness during the last month was ...**

Very poor	<input type="checkbox"/>
Poor	<input type="checkbox"/>
Average	<input type="checkbox"/>
Good	<input type="checkbox"/>
Very good	<input type="checkbox"/>



## Section AT:

**AT1. How many pieces of fruit (including fresh-squeezed juice) did you consume per day during the last month?**

- |                   |                          |
|-------------------|--------------------------|
| Less than 1 piece | <input type="checkbox"/> |
| 1 piece           | <input type="checkbox"/> |
| 2 pieces          | <input type="checkbox"/> |
| 3 pieces          | <input type="checkbox"/> |
| 4 pieces          | <input type="checkbox"/> |
| 5 or more pieces  | <input type="checkbox"/> |

**AT2. How many servings of red meat, hamburger, or sausages did you consume per day during the last month? A full serving is 100-150 g (4-6 oz)**

- |                     |                          |
|---------------------|--------------------------|
| Less than 1 serving | <input type="checkbox"/> |
| 1 serving           | <input type="checkbox"/> |
| 2 servings          | <input type="checkbox"/> |
| 3 servings          | <input type="checkbox"/> |
| 4 or more servings  | <input type="checkbox"/> |

**AT3. In general, how healthy was your diet during the last month?**

- |           |                          |
|-----------|--------------------------|
| Poor      | <input type="checkbox"/> |
| Fair      | <input type="checkbox"/> |
| Good      | <input type="checkbox"/> |
| Very good | <input type="checkbox"/> |
| Excellent | <input type="checkbox"/> |

## Section AU:

**AU1.**

**This is the end of the survey. All your answers have been registered.  
We do appreciate your participation.**

**Before finishing, would you like to provide feedback to the research team?**

**Any type of information that you find of interest is valuable for us.**



**Thank you very much for taking the time to complete this survey**