

2023 EULAR recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal diseases

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Abstract

OBJECTIVES

Fatigue is prevalent in people with inflammatory rheumatic and musculoskeletal diseases (I-RMDs) and recognised as one of the most challenging symptoms to manage. The existence of multiple factors associated with driving and maintaining fatigue, and the evidence about what improves fatigue have led to a multi-faceted approach to its management. However, there are no recommendations for fatigue management in people with I-RMDs. This lack of guidance is challenging for those living with fatigue and health professionals delivering clinical care. Therefore, our aim was to develop EULAR recommendations for the management of fatigue in people with I-RMDs.

METHODS

A multidisciplinary taskforce comprising 26 members from 14 European countries was convened, and two systematic reviews were conducted. The taskforce developed the recommendations based on the systematic review of evidence supplemented with taskforce members' experience of fatigue in I-RMDs.

RESULTS

Four overarching principles and four recommendations were developed. Overarching principles include health professionals' awareness that fatigue encompasses multiple biological, psychological and social factors which should inform clinical care. Fatigue should be monitored and assessed, and people with I-RMDs should be offered management options. Recommendations include offering tailored physical activity and/or tailored psychoeducational interventions and/or, if clinically indicated, immunomodulatory treatment initiation or change. Patient-centred fatigue management should consider the individual's needs and preferences, their clinical disease activity, comorbidities and other psychosocial and contextual factors through shared-decision-making.

CONCLUSIONS

These 2023 EULAR recommendations provide consensus and up-to-date guidance on fatigue management in people with I-RMDs.

KEYWORDS

Fatigue; rheumatic diseases; physical activity; psychoeducational interventions; health planning; shared decision-making; immunologic factors.

KEY MESSAGES

What is already known on this subject?

- Fatigue is a prevalent symptom in people with I-RMDs and challenging to manage because it is invisible, unpredictable and fluctuating.
- People with I-RMDs report that fatigue is often not addressed as part of their clinical care, and health professionals report that they do not know how best to support people.

What does this study add?

- The clinical care of people with I-RMDs can be enhanced through the monitoring of their fatigue and through offering tailored non-pharmacological interventions or, if clinically indicated by disease activity status, pharmacological treatments.
- Fatigue management should be addressed through shared decision-making and should consider the needs and preferences of people with I-RMDs, in conjunction with their clinical disease activity, comorbidities and psychosocial and contextual factors.

How might this impact on clinical practice?

- Routine assessment of fatigue in people with I-RMDs will become more common.
- Uptake of these recommendations will enhance patient-centred clinical care by managing a prevalent symptom that is a priority for people with I-RMDs.

INTRODUCTION

Inflammatory rheumatic and musculoskeletal diseases (I-RMDs) encompass several long-term conditions, including rheumatoid arthritis (RA), psoriatic arthritis, axial spondyloarthritis, systemic lupus erythematosus and Sjögren's syndrome, among others. Fatigue is prevalent in people with I-RMDs, and is one of the most challenging symptoms to cope with due to its invisible, pervasive and unpredictable nature.[1–4] Although there is no single conceptualisation or definition of fatigue, it is recognised that fatigue in I-RMDs is different to normal feelings of tiredness.[5] People with I-RMDs describe fatigue as overwhelming, intrusive, distressing and draining them of physical and mental energy.[6] It can impact all areas of their daily lives and can leave people feeling alone as they withdraw from social interactions and their lives become increasingly restricted.[7] Survey evidence with over 6,000 people with I-RMDs found that one out of every two was severely fatigued, scoring ≤ 35 on the SF-36 Vitality Scale.[8]

At an individual level, fatigue is strongly associated with a poor quality of life for people with I-RMDs.[9,10] At a societal level, fatigue in I-RMDs is associated with increased clinical care costs, primary care consultations, employment loss, and high levels of absenteeism, presenteeism and work disability.[11–13] People with I-RMDs report debilitating fatigue during flares and in low disease activity and remission states.[14–17] In those with early RA, one of the most common I-RMDs, fatigue is associated with perceived non-improvement in health in those with favourable treatment outcomes; and fatigue has been identified as one of the most important outcome domains in defining disease remission.[18,19] In rheumatology, people with I-RMDs and health professionals have identified access to fatigue interventions as an unmet need and priority.[20–22] Rheumatology health professionals recognise that fatigue is important, but few routinely offer advice, interventions or support to manage the symptom.[19,23,24]

Part of the challenge of providing support for fatigue in I-RMDs is that the causes and maintaining factors are unclear and multifaceted, and that there is no curative treatment. Research indicates that the immune system, the central and autonomic nervous systems and the neuroendocrine system might have a role in the induction and maintenance of fatigue in I-RMDs.[25] Evidence is also emerging that sleep, genetic susceptibility, metabolic disturbances and other biological and physiological mechanisms might contribute to fatigue.[26] However, this evidence is inconclusive. In addition, an array of other biopsychosocial and contextual variables are associated with fatigue in I-RMDs, including physical functioning and physical activity, comorbidities, pain, obesity, anxiety and depression, stress, and relationships and work roles.[27–29] Although the interrelationships between these diverse factors and fatigue are not clearly understood or defined, there is general agreement that fatigue in I-RMDs is likely to involve multiple biological, psychological and social mechanisms.[30] It has been proposed that these mechanisms can change over time and are likely to vary between people.[31] This body of evidence indicates that optimal fatigue management

requires a tailored, flexible and holistic approach. However, there are no recommendations to support people with I-RMDs and health professionals with fatigue management. Acknowledging this current lack of guidance, we convened a taskforce to develop EULAR recommendations for the management of fatigue in people with I-RMDs.

METHODS

We developed the recommendations following the 2014 updated EULAR standardised operating procedures.[32] The convenor (ED) and the methodologist (PMM) submitted a proposal to the EULAR Executive Committee (now designated EULAR Council). Once the proposal had been approved, PMM and ED set up a steering group with the two fellows (ES and BF) and invited the proposed taskforce members. The taskforce comprised 26 clinicians, academics, methodologists and experts by experience from 14 European countries. EULAR representatives from the health professionals committee, People with Arthritis/Rheumatism across Europe and EMerging Eular NETwork (EMEUNET) were included, and five members were recruited through an open call to EULAR countries via a competitive application process. Taskforce members were patient partners, nurses, physicians (rheumatology consultants and registrars), occupational therapists, psychologists and physiotherapists, all with personal and/or professional experience of fatigue in I-RMDs. The diverse, multidisciplinary taskforce reflects the complex nature of fatigue and the multi-faceted approach to its management. The recommendations were developed over two day-long meetings held online via MS Teams and co-facilitated by PMM and ED. As required by the EULAR SOP, all members disclosed their conflicts of interest upfront.

At the first meeting, taskforce members discussed which groups could benefit from fatigue management recommendations. These include people living with I-RMDs and those in their support systems, such as family, carers and friends; the multidisciplinary rheumatology team, which is often hospital-based; primary care physicians; health professionals in other clinical areas and settings, for example, community-based; healthcare funders, commissioners, insurers and providers; healthcare educators and trainers; charities and organisations that support people with I-RMDs; employers, educational institutions, and occupational health providers; and pharmaceutical companies.

The taskforce then formulated questions for the systematic literature review (SLR) that would provide the evidence to underpin the recommendations. The questions were:

- Which pharmacological interventions are efficacious in reducing fatigue (in a broad sense) in people with I-RMDs?
- Which non-pharmacological interventions are efficacious in reducing fatigue (in a broad sense) in people with I-RMDs?
- Which pharmacological and non-pharmacological interventions are safe in reducing fatigue in people with I-RMDs?

After the meeting, the steering group drafted a SLR protocol that was registered with PROSPERO (reference: CRD42021282899). As the initial searches returned large numbers of abstracts, the steering group decided to conduct two SLRs. ES led the review of non-pharmacological interventions, and BF led the review of pharmacological interventions. Both reviews were conducted according to the Cochrane Handbook proposed method and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.[33,34] The steering group drafted potential overarching principles (OAPs) and recommendations based on these results.

At the second taskforce meeting, ES and BF presented the results from the SLRs. The main findings included evidence that physical activity or exercise, psychoeducational interventions, and several pharmacological interventions are efficacious (and generally safe) in reducing fatigue in people with I-RMDs.[35,36] Physical activity or exercise was found to be efficacious in reducing fatigue, with a small effect size in RA (SMD=-0.23), a moderate effect size in SLE, and a large effect size in SpA (SMD=-0.94) (Ref no: 36). Psychoeducational interventions were also found to be efficacious in reducing fatigue in RA, showing a small effect size (SMD=-0.32). However, it is important to note that these effect sizes are challenging to interpret and compare due to the heterogeneity of studies in terms of inclusion criteria, intervention types, study design, and the number of studies included in the meta-analyses. PMM and ED then presented the steering group's potential OAPs and recommendations, one by one, which were modified through discussion and voting. OAPs and recommendations were edited live according to the comments made, followed by formal anonymised voting using the poll function in MS Teams. Consensus was reached if either $\geq 75\%$ of the members voted in favour of the recommendations in the first, $\geq 67\%$ in the second or $\geq 50\%$ in a third round. If multiple rounds of voting were necessary, a discussion took place in between voting rounds to refine the drafted statements.

After the meeting, the levels of evidence (LoE) and grades of recommendation (GoR) derived from the SLRs following the standards of the Oxford Center for Evidence Based Medicine were added by the steering committee to each of the recommendations.[37] Finally, each taskforce member anonymously indicated their level of agreement (LoA) through an online survey (numerical rating scale ranging from 0='do not agree at all' to 10='fully agree'). The mean and SD of the LoA, as well as the percentage of agreement ≥ 8 , are presented.

The taskforce also discussed important areas for future research on fatigue in I-RMDs that were not addressed in the current SLRs and where there is a lack of evidence. The draft of the manuscript was sent to all taskforce members for review. All authors and the EULAR Council approved the final manuscript.

RESULTS

The taskforce agreed on four OAPs and four recommendations (Table 1). These are based on evidence from the two SLRs, combined with the taskforce members' expert opinions. LoA was very high for all OAPs and recommendations, ranging from 9.4 to 9.9 average LoA on 0-10 scale, strengthening the validity and robustness of the agreed statements.

OVERARCHING PRINCIPLES

During the analysis of the evidence and expert discussion, the taskforce identified four key general themes across all recommendations. These were formulated and agreed as OAPs. They provide a set of crucial principles in managing fatigue in people with I-RMDs, reflecting state-of-the-art management.

1. Health professionals should be aware that fatigue encompasses multiple and mutually interacting biological, psychological and social factors.

This OAP provides a conceptual framework to inform health professionals' understanding of fatigue and their communication about this symptom with people with I-RMDs. It is important that the complexity of fatigue is recognised and that health professionals are aware of the potentially wide range of biopsychosocial factors that can drive and maintain fatigue and the implications of this for people's physical and mental health.[26,27,30,31] This awareness should facilitate discussions with people who have I-RMDs about which specific factors might be pertinent for them as individuals. People with I-RMDs have reported that being asked about their fatigue can be validating and make them feel less isolated; for some, it can be the first step to self-management.[38,39]

2. In people with I-RMDs, fatigue should be monitored, and management options should be offered as part of their clinical care.

Fatigue in I-RMDs is a prevalent, often non-resolving symptom that needs to be considered in the long term. Monitoring fatigue as part of clinical care acknowledges that the symptom is frequently present and has a detrimental impact on people with I-RMDs. In some settings, monitoring might comprise the completion of patient-reported outcome measures (PROMs) so that health professionals can gauge fatigue in people with I-RMDs at individual and population levels, for example, as part of national registries.[11,14,17,40–42]

Management options should be offered as part of clinical care. The taskforce recognises that various health professionals in different healthcare systems undertake responsibility for offering management options. In addition, not all fatigue management options are widely available and not all health professionals have the knowledge, skills and confidence to provide support. However, at a minimum, health professionals can provide information and signpost to resources, such as those provided by patient organisations. In multidisciplinary teams, health professionals can consider

referrals to colleagues who might be better placed to offer appropriate support.[43,44] Together, monitoring and offering management options should normalise fatigue which is likely to be helpful to people with I-RMDs.

3. Management of fatigue should be a shared decision between the person with an I-RMD and health and well-being professionals.

Patient-centred care includes listening to, informing and involving patients in ways that are meaningful and valuable to the individual, with the goal of empowering them to become active participants in their care. Shared-decision making is central to implementing patient-centred care. Therefore, as part of delivering patient-centred care in rheumatology, decisions about fatigue management need to be shared between the person with an I-RMD and the health professional.[45] This involves collaboration based on health professionals' expertise (e.g., knowledge about management options, including evidence, risks and benefits) and people with I-RMDs' expertise (e.g., knowledge of their preferences, circumstances, goals, values and beliefs). Shared decision-making should be undertaken to support people to make decisions about their fatigue management that are right for them at that time. Shared-decision-making allows people to choose the extent to which they want to collaborate with health professionals and includes acknowledging that some people prefer not to take an active role in making decisions. However, it is important that all people with I-RMDs are offered the opportunity to engage in shared- decision-making and that their needs and preferences determine the degree of collaboration.

As with the previous OAP, the taskforce discussed how healthcare systems differ in the care pathways available to people with I-RMDs and in who provides support for fatigue. The use of 'health and well-being professionals' reflects this breadth and includes a range of sources of support from multidisciplinary rheumatology teams to individual practitioners such as mental health therapists and/or fitness and exercise instructors. It is important to mobilise all available resources that might benefit people with I-RMDs and to recognise that elements of fatigue support might derive from shared decisions taken in both clinical and non-clinical settings.[46]

4. Management of fatigue should be based on the needs and preferences of people with I-RMDs, as well as their clinical disease activity, comorbidities and other individual psychosocial and/or contextual factors.

Current evidence suggests that fatigue may be caused and maintained by an array of biopsychosocial factors, which vary between and within individuals over time. This conceptualisation of fatigue underpins OAP1 and needs to be reflected in managing the symptom, which should be tailored to individuals with I-RMDs. Providing tailored fatigue management options includes considering the needs and preferences of people with I-RMDs, which will contribute to the shared decision-making underpinning OAP3. Management of fatigue also needs to be set in the context of

exploring which factors might be contributing to an individual's fatigue. This could include stress, disease activity, pain, sleep quality, comorbid long-term conditions, obesity, de-conditioning and low levels of physical activity, low mood and withdrawal and 'boom and bust' activity patterns, among others.[26,47]

RECOMMENDATIONS

1. Health professionals should incorporate regular assessment of fatigue severity, impact and coping strategies into clinical consultations.

Addressing fatigue should be part of usual clinical care for people with I-RMDs and incorporating regular assessment of fatigue is an important part of this process. People with I-RMDs have reported fatigue when their disease activity levels are high but also when they are in remission or low disease states, with fatigue being severe in about half of the cases.[27,48] Therefore, it is important to conduct regular assessments of fatigue over time and not make assumptions about when someone might be impacted by fatigue or when discussions about fatigue might be relevant. A strategic option for clinical practice may be to use a single-item instrument as a screening tool (e.g., BRAF NRS, RAID-F, among others), which could be supplemented by additional multidimensional assessments if significant levels of fatigue are identified by the screening tool.[49] It is important that responsibility for raising the issue of fatigue does not lie solely with the person with an I-RMD.

Not only might fatigue itself fluctuate over time, but how it affects people and how they respond can change. Central to this recommendation is that assessment should include not only the level or severity of fatigue but also the impact of the symptom on daily life and how someone is coping with it.[50,51] These assessments should inform the clinical consultations of people with I-RMDs and lead to discussions about management options.

2. As part of their clinical care, people with I-RMDs and fatigue should be offered access to tailored physical activity interventions and encouraged to engage in long-term physical activity.

According to the results of our SLR, there is evidence that supervised physical activity interventions can help reduce fatigue in people with I-RMDs. Existing EULAR recommendations on physical activity also emphasise its importance in disease management based on proven efficacy, feasibility and safety.[52] As such, tailored physical activity that considers a person's current sedentary and exercise behaviours; their disease activity, disease damage, comorbidities and disability; and their preferences and goals should be offered to people with I-RMDs and fatigue as part of their clinical care. However, there is also evidence of the benefits of unsupervised physical activity outside clinical care settings.[53–56] Therefore, long-term physical activity as a lifestyle change should be encouraged. There was consensus in the taskforce that the role of health professionals is to engage in shared decision-making about options and to facilitate access to physical activity interventions.

3. As part of their clinical care, people with I-RMDs and fatigue should be offered access to structured and tailored psychoeducational interventions.

There is evidence that psychoeducational interventions can help reduce fatigue in people with I-RMDs. This evidence is for structured, time-limited interventions. Typically, these go beyond information provision alone and explore the thoughts, feelings (physical and emotional) and behaviours of the person with an I-RMD in relation to their fatigue. As with recommendation 2, the role of health professionals is to engage in shared decision-making with the person with an I-RMD and fatigue and to facilitate access to psychoeducational interventions. It cannot be assumed that people with I-RMDs have achieved optimal benefits from participating in a single 'one-off' psychoeducational intervention or that helpful behaviour changes will be maintained for a certain length of time. Therefore, access to psychoeducational interventions should be discussed periodically and should be needs-based and not restricted based on previous offers and/or uptake. Fatigue-specific and/or other biopsychosocial and contextual factors can change over time, both within and between people with I-RMDs and fatigue. As such, psychoeducational interventions might be helpful to people at different points in their I-RMD trajectory.

4. The presence or worsening of fatigue should trigger evaluation of inflammatory disease activity status and consideration of immunomodulatory treatment initiation or change, if clinically indicated.

There is evidence that pharmacological interventions that reduce disease activity are also efficacious in reducing fatigue in people with I-RMDs, especially biologic agents.[35] These interventions are indicated and licensed to treat high disease activity levels, and recommendation 4 needs to be understood within the context of regulatory restrictions. A level of fatigue can always be present for some people with I-RMDs. However, if someone's fatigue is distressing and impactful or it worsens, this should trigger an evaluation of their disease activity. This evaluation might be more than calculating an individual's disease activity score and include procedures such as Magnetic Resonance Imaging (MRI) of their sacroiliac joints or spine to assess the presence of inflammatory/acute lesions or an ultrasound of their joints to check for synovitis. If high levels of (inflammatory) disease activity are present and are subsequently treated by starting and/or changing an immunomodulatory drug, fatigue will likely decrease. This includes disease modifying antirheumatic drugs such as biologics and other drugs such as prednisolone. It is unclear whether the improvement comes from a direct action of these interventions on fatigue or indirectly through reduction in inflammation or disease activity.

The SLRs conducted to inform these recommendations highlighted existing gaps in the literature, which, together with key discussion points raised during the taskforce meetings, resulted in our proposed research agenda (Box 1).

DISCUSSION

Existing EULAR recommendations include self-management advice in routine clinical care and the role of health professionals such as nurses to support self-management skills to increase the sense of control, self-efficacy and empowerment of people with I-RMDs.[57,58] Patient education recommendations highlight the importance of an approach tailored to individual needs, including activity regulation, physical activity and behaviour change.[59] These recommendations can potentially help people with I-RMDs cope with the impact of symptoms. In this EULAR taskforce, we developed four OAPs and four recommendations for managing fatigue in people with I-RMDs. The OAPs are based on theoretical reasons, clinical experience and models of patient-centred healthcare, while the recommendations incorporate the evidence from two SLRs. The low number of recommendations reflects the limited evidence available at the time.

Historically, the scientific uncertainty about the pathogenesis of fatigue and the absence of a curative treatment has led to a reluctance to discuss fatigue in clinical practice. These OAPs and recommendations are intended to address this. They are premised on understanding fatigue as multifactorial and the need to communicate this to people with I-RMDs and to help them reflect on potential underlying drivers. Related to this, is the understanding that fatigue is a long-term challenge for many people with I-RMDs, so access to support should be reviewed regularly. The taskforce recognises that some healthcare systems, insurers and providers might challenge ongoing access to support provision. However, the consensus is to recommend optimal care.

Regular assessment of fatigue severity, impact and coping strategies should be part of usual care and used to facilitate discussions between people with I-RMDs and health professionals. These discussions require knowledge, and the taskforce understands that health professionals may need to acquire skills, for example, how to explore individual fatigue drivers and coping strategies. Assessment of fatigue raises the issue of measurement.[49] In 2007, the OMERACT group agreed that fatigue should be measured in RA clinical trials whenever possible,[60] but there are no recommendations about which instruments to use in research and clinical practice across I-RMDs. Addressing this complex issue is beyond the scope of this taskforce. However, we have included a list of which instruments were used (Box 2) in the two SLRs. [35,36]

Assessment of fatigue and identifying people with I-RMDs who are being negatively impacted should lead to shared decision-making about the offer and uptake of management options. Although shared decision-making has been part of patient-centred models of rheumatology healthcare in recent

years, it is not easy to undertake. Recent research has suggested the need for education and training that equips and empowers health professionals to apply shared decision-making, plus the need for a commitment of time, resources and financial support for national, regional and organisational initiatives to make it a reality.[61] However, the taskforce agreed that shared decision-making should be an important feature because there is clinical experience that people actively involved in health management decisions are more satisfied with their care and more adherent to treatment recommendations. It has been proposed that health professionals can promote shared decision-making by communicating respect for the opinions and values of the person with an I-RMD, providing adequate information on management options, and assisting them in weighing the benefits and risks of those options, including how they might be incorporated into their daily lives.[62]

The SLR evidence for non-pharmacological interventions for fatigue mainly concerned structured, time-limited physical activity and psychoeducational interventions. However, the taskforce reflected that there could be other non-pharmacological interventions for which there is currently insufficient evidence but which might be helpful at the level of an individual with an I-RMD due to the factors implicated in their fatigue, e.g., cognitive behavioural therapy for insomnia or weight management for obesity.[63,64] Structured and time-limited interventions are typically more therapeutically intensive than the provision of informational materials such as booklets and self-help guides. In a stepped model of care (whereby the most effective yet least resource-intensive treatment is delivered to patients first, only 'stepping up' to intensive interventions as clinically required), health professionals can consider including these less therapeutically intensive interventions as part of the management options that they offer to people with I-RMDs.

The SLR found that pharmacological interventions aimed at reducing disease activity are also efficacious and safe for managing fatigue in people with I-RMDs, particularly biologics. The evidence was robust and applicable to many I-RMDs. In virtually all RCTs, fatigue was assessed as a secondary outcome, with the primary outcome being disease-specific treatment response measures. These results suggest that control of inflammatory activity, the primary indication for treatment, co-adjuvants the reduction of fatigue levels. [35] Safety results of pharmacological interventions were reassuring and in line with known safety profiles and summaries of product characteristics of the respective drug. It should be noted that although the taskforce intended to review the safety of non-pharmacological interventions for fatigue, safety outcomes were often underreported, but there was no indication that they were not safe.

In conclusion, EULAR recommendations have been developed to manage fatigue in people with I-RMDs. Central to these are regular assessment of fatigue and shared decision-making about the best management options at that time. Dissemination will focus on promoting these

recommendations to people with I-RMDs and their networks, health professionals and other stakeholders involved in the provision of healthcare services, including patient organisations.

Box 1. Research agenda

1. The development of recommendations for instruments to measure fatigue across I-RMDs. This should include summaries of what individual instruments capture and their psychometric properties, plus identification of any missing domains. Ultimately, it would be helpful to standardise fatigue measurement in research and clinical practice (i.e., define a gold-standard).
2. Understanding of the mechanisms of fatigue interventions, including the efficacy of single modalities or components in non-pharmacological interventions such as sleep hygiene training, physical activity, pacing, cognitive-behavioural management, or weight reduction in case of obesity, plus predictors of improvement and long-term adherence.
3. Understanding the efficacy and safety of interventions in specific I-RMDs where evidence is still scarce, for example, systemic sclerosis, idiopathic inflammatory myopathies, and giant cell arteritis.
4. Understanding tailoring and implementation of fatigue support in different contexts, including what works, for whom and under what circumstances. This research should be pragmatic and wide-ranging and involve investigation of modes of delivery, content and structure designed to address varying levels of therapeutic intensity, health literacy, cultural appropriateness and inclusivity.
5. Related to the point above, there is a need for innovative trial designs that can provide insight into tailored intervention effects at the individual level as well as the group level.

Box 2. List of instruments to measure fatigue*

1. Functional Assessment of Chronic Illness Therapy (FACIT)
2. FACIT-F (Functional Assessment of Chronic Illness Therapy Fatigue Subscale)
3. Fatigue Severity Scale (FSS)
4. Fatigue Self-Efficacy Scale (FSES)
5. Multidimensional Assessment of Fatigue (MAF)
6. Global Fatigue Index (GBI)
7. Fatigue Impact Scale (FIS)
8. EULAR Primary Sjogren's Syndrome Patient-Reported Index (ESSPRI) score-fatigue scale
9. Multidimensional Fatigue Inventory (MFI)
10. MAC Fatigue Scale
11. Profile of Mood States (POMS) Fatigue Scale
12. VAS-fatigue (VAS-F)
13. Vitality scale Short Form 36 (SF-36)
14. Fatigue scale of the Checklist Individual Strength (CIS)
15. Bristol Rheumatoid Arthritis Fatigue- Multi- Dimensional Questionnaire (BRAFF-MDQ)
16. Bristol RA Fatigue effect numerical Rating scale (BRAFF-NRS)
17. Multidimensional Fatigue Inventory (MFI-20)
18. PROMIS (Patient-Reported Outcome Measurement Information System) Fatigue Short Form
19. 20-item Checklist of Individual Strengths (CIS-20)
20. Rheumatoid Arthritis Impact of Disease questionnaire (RAID-F)
21. Bath Ankylosing Spondylitis Disease Activity Index-Fatigue (BASDAI-F)
22. Fatigue - Profile of Fatigue questionnaire (ProF)
23. Chalder Fatigue Scale (CFS)
24. Fatigue - Numerical Rating Scales (NRS)
25. Fatigue Assessment Scale (FAS)
26. Health Assessment Questionnaire (HAQ) fatigue domain

*This list is based on the instruments used to measure fatigue in the two systematic reviews undertaken to inform these recommendations.

Table 1: EULAR overarching principles and recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal diseases (I-RMDs)

Overarching principles	LoA		Mean (SD)	% with score ≥8
	Mean (SD)	% with score ≥8		
1. Health professionals should be aware that fatigue encompasses multiple and mutually interacting biological, psychological and social factors.			9.9 (0.3)	100
2. In people with I-RMDs, fatigue should be monitored, and management options should be offered as part of their clinical care.			9.6 (1.0)	96
3. Management of fatigue should be a shared decision between the person with an I-RMD and health and well-being professionals.			9.7 (0.7)	100
4. Management of fatigue should be based on the needs and preferences of people with I-RMDs, as well as their clinical disease activity, comorbidities and other individual psychosocial and/or contextual factors.			9.9 (0.3)	100
Recommendations	LoE	GoR	Mean (SD)	% with score ≥8
1. Health professionals should incorporate regular assessment of fatigue severity, impact and coping strategies into clinical consultations.	5	D	9.5 (1.3)	91
2. As part of their clinical care, people with I-RMDs and fatigue should be offered access to tailored physical activity interventions and encouraged to engage in long-term physical activity.	1a	A	9.6 (1.0)	96
3. As part of their clinical care, people with I-RMDs and fatigue should be offered access to structured and tailored psychoeducational interventions.	1a	A	9.5 (1.2)	96
4. The presence or worsening of fatigue should trigger evaluation of inflammatory disease activity status and consideration of immunomodulatory treatment initiation or change, if clinically indicated.	1a	A	9.4 (1.2)	82

EULAR, European Alliance of Associations of Rheumatology; LoA, Level of Agreement; LoE, Level of Evidence (1 to 5; 1=high quality RCT, and 5=expert opinion), GoR, Grade of Recommendation (A to D; A=consistent level 1 studies, and D=level 5 evidence); SD, standard deviation.

Competing interests

ED none.

BF none.

ES none.

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TU none.

CF none.

CH has received speaker fees from AbbVie.

CEA none.

DC none.

EE none.

FEL none.

IB none.

JP none.

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MU none.

MvL none.

MR none.

PB none.

RA none.

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VR none.

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All authors are members of the EULAR's taskforce for the development of 2023 EULAR Recommendations for the management of fatigue in people with inflammatory rheumatic diseases. ES and BF were the fellows. ED was the convenor. PMM was the methodologist. All authors have contributed to the work, read, and finally approved the manuscript for submission.

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None or not applicable.

Data sharing statement

Data sharing not applicable as no datasets generated and/or analysed for this study. All data relevant to the study are included in the article.

References

- [1] Ifesemen OS, McWilliams DF, Norton S, Kiely PDW, Young A, Walsh DA. Fatigue in early rheumatoid arthritis: data from the Early Rheumatoid Arthritis Network. *Rheumatology* 2021. <https://doi.org/10.1093/rheumatology/keab947>.
- [2] Dures E, Cramp F, Hackett K, Primdahl J. Fatigue in inflammatory arthritis. *Best Pract Res Clin Rheumatol* 2020;34. <https://doi.org/10.1016/j.berh.2020.101526>.
- [3] Basu N, Yang X, Luben RN, Whibley D, Macfarlane GJ, Wareham NJ, et al. Fatigue is associated with excess mortality in the general population: Results from the EPIC-Norfolk study. *BMC Med* 2016;14. <https://doi.org/10.1186/s12916-016-0662-y>.
- [4] van Hoogmoed D, Fransen J, Bleijenberg G, van Riel P. Physical and psychosocial correlates of severe fatigue in rheumatoid arthritis n.d. <https://doi.org/10.1093/rheumatology/keq043>.
- [5] Hewlett S, Zoe`cockshott ZZ, Byron M, Kitchen K, Tipler S, Pope D, et al. Patients' Perceptions of Fatigue in Rheumatoid Arthritis: Overwhelming, Uncontrollable, Ignored 2005. <https://doi.org/10.1002/art.21450>.
- [6] Seifert O, Baerwald C. Impact of fatigue on rheumatic diseases. *Best Pract Res Clin Rheumatol* 2019;33:101435. <https://doi.org/10.1016/J.BERH.2019.101435>.
- [7] Primdahl J, Hegelund A, Lorenzen AG, Loeppenthin K, Dures E, Esbensen BA. The Experience of people with rheumatoid arthritis living with fatigue: a qualitative metasynthesis. *BMJ Open* 2019;9:24338. <https://doi.org/10.1136/bmjopen-2018-024338>.
- [8] Overman CL, Kool MB, da Silva JAP, Geenen R. The prevalence of severe fatigue in rheumatic diseases: an international study n.d. <https://doi.org/10.1007/s10067-015-3035-6>.
- [9] Gossec L, Walsh JA, Michaud K, Holdsworth E, Peterson S, Meakin S, et al. Effect of Fatigue on Health-Related Quality of Life and Work Productivity in Psoriatic Arthritis: Findings From a Real-World Survey. *J Rheumatol* 2022;49:1221–8. <https://doi.org/10.3899/jrheum.211288>.
- [10] Dar WR, Mir IA, Siddiq S, Nadeem M, Singh G. The Assessment of Fatigue in Rheumatoid Arthritis Patients and Its Impact on Their Quality of Life. *Clin Pract* 2022;12:591–8. <https://doi.org/10.3390/clinpract12040062>.
- [11] Macfarlane GJ, Shim J, Jones GT, Walker-Bone K, Pathan E, Dean LE, et al. Identifying Persons with Axial Spondyloarthritis At Risk of Poor Work Outcome: Results from the British Society for Rheumatology Biologics Register. *J Rheumatol* 2018;46:145–52. <https://doi.org/10.3899/jrheum.180477>.
- [12] Michaud K, Messer J, Choi HK, Wolfe F. Direct Medical Costs and Their Predictors in Patients With Rheumatoid Arthritis A Three-Year Study of 7,527 Patients. *Arthritis Rheum* 2003;48:2750–62. <https://doi.org/10.1002/art.11439>.
- [13] Galloway J, Edwards J, Bhagat S, Parker B, Tan AL, Maxwell J, et al. Direct healthcare resource utilisation, health-related quality of life, and work productivity in patients with moderate rheumatoid arthritis: an observational study. *BMC Musculoskelet Disord* 2021;22. <https://doi.org/10.1186/s12891-021-04110-1>.
- [14] Druce KL, Bhattacharya Y, Jones GT, Macfarlane GJ, Basu N. Concise report Most patients who reach disease remission following anti-TNF therapy continue to report fatigue: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis n.d. <https://doi.org/10.1093/rheumatology/kew241>.
- [15] Choy EH, Dures E. Fatigue in rheumatoid arthritis. *Rheumatology (United Kingdom)* 2019;58. <https://doi.org/10.1093/rheumatology/kez314>.

- [16] Pilgaard T, Hagelund L, Elkjaer S, Id S, Holm Jensen H, Esbensen BA. Severity of fatigue in people with rheumatoid arthritis, psoriatic arthritis and spondyloarthritis – Results of a cross-sectional study 2019. <https://doi.org/10.1371/journal.pone.0218831>.
- [17] Druce KL, Jones GT, MacFarlane GJ, Verstappen SMM, Basu N. The longitudinal course of fatigue in rheumatoid arthritis: Results from the norfolk arthritis register. *Journal of Rheumatology* 2015;42:2059–65. <https://doi.org/10.3899/jrheum.141498>.
- [18] Steunebrink LMM, Oude Voshaar MAH, Taal E, Vonkeman HE, Zijlstra TR, van de Laar MAFJ. Determinants of Perceived Health Nonimprovement in Early Rheumatoid Arthritis Patients With Favorable Treatment Outcomes. *Arthritis Care Res (Hoboken)* 2018;70:510–5. <https://doi.org/10.1002/acr.23305>.
- [19] Roodenrijs NMT, de Hair MJH, van der Goes MC, Jacobs JWG, Welsing PMJ, van der Heijde D, et al. Characteristics of difficult-to-treat rheumatoid arthritis: results of an international survey. *Ann Rheum Dis* 2018;77:1705–9. <https://doi.org/10.1136/annrheumdis-2018-213687>.
- [20] Dures E, Hewlett S, Lord J, Bowen C, McHugh N, Tillett W. Important Treatment Outcomes for Patients with Psoriatic Arthritis: A Multisite Qualitative Study. *Patient* 2017;10. <https://doi.org/10.1007/s40271-017-0221-4>.
- [21] Garrido-Cumbrera Ottfrid Hillmann Raj Mahapatra David Trigos Petra Zajc Luisa Weiss Galya Bostynets Laure Gossec Laura Coates MC. Improving the Management of Psoriatic Arthritis and Axial Spondyloarthritis: Roundtable Discussions with Healthcare Professionals and Patients. *Rheumatol Ther n.d.*;4. <https://doi.org/10.1007/s40744-017-0066-2>.
- [22] Mistry J, Sharif M, Prideaux A, Smith C, Sumbwanyambe M, Sibley M, et al. Concise Report Use of rheumatoid arthritis impact of disease (RAID) in routine care; identification of DAS28 remission and unmet patient-reported outcomes n.d. <https://doi.org/10.1093/rap/rkaa013>.
- [23] Feldthusen C, Björk M, Forsblad-d'Elia H, Mannerkorpi K, University of Gothenburg Centre for Person-Centred Care (GPCC). Perception, consequences, communication, and strategies for handling fatigue in persons with rheumatoid arthritis of working age--a focus group study. *Clin Rheumatol* 2013;32:557–66. <https://doi.org/10.1007/s10067-012-2133-y>.
- [24] Repping-Wuts H, Repping T, van Riel P, van Achterberg T. Communication: Observational Study Fatigue communication at the out-patient clinic of Rheumatology n.d. <https://doi.org/10.1016/j.pec.2008.11.011>.
- [25] Davies K, Ng W-F. Autonomic Nervous System Dysfunction in Primary Sjögren's Syndrome. *Front Immunol* 2021;12:702505. <https://doi.org/10.3389/fimmu.2021.702505>.
- [26] Davies K, Dures E, Ng W-F. Fatigue in inflammatory rheumatic diseases: current knowledge and areas for future research. *Nat Rev Rheumatol* 2021;17:651–64. <https://doi.org/10.1038/s41584-021-00692-1>.
- [27] Hewlett S, Chalder T, Choy E, Cramp F, Davis B, Dures E, et al. Fatigue in rheumatoid arthritis: time for a conceptual model. *Rheumatology (Oxford)* 2011;50. <https://doi.org/10.1093/rheumatology/keq282>.
- [28] Druce KL, Basu N. Predictors of fatigue in rheumatoid arthritis. *Rheumatology (Oxford)* 2019;58:v29–34. <https://doi.org/10.1093/rheumatology/kez346>.
- [29] Treharne GJ, Lyons AC, Hale ED, Goodchild CE, Booth DA, Kitas GD. Predictors of fatigue over 1 year among people with rheumatoid arthritis. *Psychol Health Med* 2008;13:494–504. <https://doi.org/10.1080/13548500701796931>.

- [30] Nikolaus S, Bode C, Taal E, van de Laar MAFJ. Fatigue and Factors Related to Fatigue in Rheumatoid Arthritis: A Systematic Review 2013. <https://doi.org/10.1002/acr.21949>.
- [31] Geenen R, Dures E. A biopsychosocial network model of fatigue in rheumatoid arthritis: A systematic review. *Rheumatology (United Kingdom)* 2019;58. <https://doi.org/10.1093/rheumatology/kez403>.
- [32] van der Heijde D, Aletaha D, Carmona L, Edwards CJ, Kvien TK, Kouloumas M, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. *Ann Rheum Dis* 2015;74:8–13. <https://doi.org/10.1136/annrheumdis-2014-206350>.
- [33] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *The BMJ* 2021;372. <https://doi.org/10.1136/bmj.n71>.
- [34] Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0 (updated July 2019): Cochrane; 2019. Available from: www.training.cochrane.org/handbook.
- [35] Farisogullari B, Santos E, Dures E, Machado PM. Efficacy of pharmacological interventions: a systematic review informing the 2023 EULAR recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal diseases. *RMD Open* 2023 (In Press).
- [36] Santos E, Farisogullari B, Dures E, Machado PM. Efficacy of non-pharmacological interventions: a systematic review informing the 2023 EULAR recommendations for the management of fatigue in people with inflammatory rheumatic and musculoskeletal diseases. *RMD Open* 2023;9:e003350. doi: 10.1136/rmdopen-2023-003350
- [37] Oxford Centre for Evidence-Based Medicine. *Levels of Evidence* (updated in 2012) 2009. Available from: <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009>
- [38] Berry A, Bridgewater S, Abbott B, Adams J, Dures E. Acceptability of a brief fatigue intervention for inflammatory arthritis: a qualitative process evaluation. *Rheumatol Adv Pract* 2022;6. <https://doi.org/10.1093/rap/rkac064>.
- [39] Dures E, Kitchen K, Almeida C, Ambler N, Cliss A, Hammond A, et al. “They didn’t tell us, they made us work it out ourselves”: Patient perspectives of a cognitive-behavioral program for rheumatoid arthritis fatigue. *Arthritis Care Res (Hoboken)* 2012;64. <https://doi.org/10.1002/acr.21562>.
- [40] Dean LE, Macfarlane GJ, Jones GT. Five Potentially Modifiable Factors Predict Poor Quality of Life in Ankylosing Spondylitis: Results from the Scotland Registry for Ankylosing Spondylitis. *J Rheumatol* 2018;45:62–9. <https://doi.org/10.3899/jrheum.160411>.
- [41] Druce KL, Jones GT, Macfarlane GJ, Basu N. Determining Pathways to Improvements in Fatigue in Rheumatoid Arthritis: Results From the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. *Arthritis & Rheumatology* 2015;67:2303–10. <https://doi.org/10.1002/art.39238>.
- [42] Matcham F, Davies R, Hotopf M, Hyrich KL, Norton S, Steer S, et al. The relationship between depression and biologic treatment response in rheumatoid arthritis: An analysis of the British Society for Rheumatology Biologics Register. *Rheumatology (United Kingdom)* 2018;57:835–43. <https://doi.org/10.1093/rheumatology/kex528>.

- [43] Dures E, Fraser I, Almeida C, Peterson A, Caesley J, Pollock J, et al. Patients' Perspectives on the Psychological Impact of Inflammatory Arthritis and Meeting the Associated Support Needs: Open-Ended Responses in a Multi-Centre Survey. *Musculoskeletal Care* 2017;15. <https://doi.org/10.1002/msc.1159>.
- [44] Dures E, Hewlett S, Ambler N, Jenkins R, Clarke J, Gooberman-Hill R. Rheumatology clinicians' experiences of brief training and implementation of skills to support patient self-management. *BMC Musculoskelet Disord* 2014;15. <https://doi.org/10.1186/1471-2474-15-108>.
- [45] Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: A model for clinical practice. *J Gen Intern Med* 2012;27:1361–7. <https://doi.org/10.1007/s11606-012-2077-6>.
- [46] Ferreira RJO, Santos E, de Wit M, Marques A, Barbieri-Figueiredo M do C, Marques A, et al. Shared decision-making in people with chronic disease: Integrating the biological, social and lived experiences is a key responsibility of nurses. *Musculoskeletal Care* 2020;18:84–91. <https://doi.org/10.1002/msc.1443>.
- [47] Silva CFR, Duarte C, Ferreira RJO, Santos E, da Silva JAP. Depression, disability and sleep disturbance are the main explanatory factors of fatigue in rheumatoid arthritis: a path analysis model. *Clin Exp Rheumatol* 2020;38:314–21. <https://doi.org/10.55563/clinexprheumatol/hkhbad>.
- [48] Pollard LC, Choy EH, Gonzalez J, Scott DL. Fatigue in rheumatoid arthritis reflects pain, not disease activity. *Rheumatology* 2006;45:885–9. <https://doi.org/10.1093/rheumatology/kei021>.
- [49] Santos E, Duarte C, da Silva JAP, Ferreira RJO. The impact of fatigue in rheumatoid arthritis and the challenges of its assessment. *Rheumatology (Oxford)* 2019;58:v3–9. <https://doi.org/10.1093/rheumatology/kez351>.
- [50] Sanderson TC, Hewlett SE, Flurey C, Dures E, Richards P, Kirwan JR. The impact triad (severity, importance, self-management) as a method of enhancing measurement of personal life impact of rheumatic diseases. *Journal of Rheumatology* 2011;38. <https://doi.org/10.3899/jrheum.100700>.
- [51] Kirwan JR, Fries JF, Hewlett SE, Osborne RH, Newman S, Ciciriello S, et al. Patient perspective workshop: Moving towards OMERACT guidelines for choosing or developing instruments to measure patient-reported outcomes. *Journal of Rheumatology* 2011;38. <https://doi.org/10.3899/jrheum.110391>.
- [52] Rausch Osthoff A-K, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis* 2018;77:1251–60. <https://doi.org/10.1136/annrheumdis-2018-213585>.
- [53] Tiffreau V, Rannou F, Kopciuch F, Hachulla E, Mouthon L, Thoumie P, et al. Postrehabilitation Functional Improvements in Patients With Inflammatory Myopathies: The Results of a Randomized Controlled Trial. *Arch Phys Med Rehabil* 2017;98:227–34. <https://doi.org/10.1016/j.apmr.2016.09.125>.
- [54] Durcan L, Wilson F, Cunnane G. The Effect of Exercise on Sleep and Fatigue in Rheumatoid Arthritis: A Randomized Controlled Study. *J Rheumatol* 2014;41:1966–73. <https://doi.org/10.3899/jrheum.131282>.
- [55] Ambrosino P, Iannuzzi GL, Formisano R, Spedicato GA, D'Abrosca V, di Gioia L, et al. Exergaming as an Additional Tool in Rehabilitation of Young Patients with Rheumatoid

Arthritis: A Pilot Randomized Controlled Trial. *Games Health J* 2020;9:368–75. <https://doi.org/10.1089/g4h.2019.0167>.

- [56] Durmus D, Alayli G, Cil E, Canturk F. Effects of a home-based exercise program on quality of life, fatigue, and depression in patients with ankylosing spondylitis. *Rheumatol Int* 2009;29:673–7. <https://doi.org/10.1007/s00296-008-0756-8>.
- [57] Nikiphorou E, Santos E, Marques A, Böhm P, Bijlsma J, Daien C, et al. 2021 EULAR recommendations for the implementation of self-management strategies in patients with inflammatory arthritis. *Ann Rheum Dis* 2021. <https://doi.org/10.1136/annrheumdis-2021-220249>.
- [58] Bech B, Primdahl J, van Tubergen A, Voshaar M, Zangi HA, Barbosa L, et al. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Ann Rheum Dis* 2020;79:61–8. <https://doi.org/10.1136/annrheumdis-2019-215458>.
- [59] Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Boström C, et al. EULAR recommendations for patient education for people with inflammatory arthritis 2014. <https://doi.org/10.1136/annrheumdis-2014-206807>.
- [60] Kirwan JR, Minnock P, Adebajo A, Bresnihan B, Choy E, de Wit M, et al. Patient perspective: fatigue as a recommended patient centered outcome measure in rheumatoid arthritis. *J Rheumatol* 2007;34:1174–7.
- [61] Mathijssen E, van den Bemt B, Wielsma S, van den Hoogen F, Vriezekolk J. Exploring healthcare professionals' knowledge, attitudes and experiences of shared decision making in rheumatology. *RMD Open* 2020;6. <https://doi.org/10.1136/rmdopen-2019-001121>.
- [62] Fraenkel L, McGraw S. What are the essential elements to enable patient participation in medical decision making? *J Gen Intern Med* 2007;22:614–9. <https://doi.org/10.1007/s11606-007-0149-9>.
- [63] Mccrae CS, Williams J, Roditi D, Anderson R, Mundt JM, Miller MB, et al. Cognitive behavioral treatments for insomnia and pain in adults with comorbid chronic insomnia and fibromyalgia: clinical outcomes from the SPIN randomized controlled trial. *Sleep* 2019;42. <https://doi.org/10.1093/sleep/zsy234>.
- [64] Nikiphorou E, Fragoulis GE. Inflammation, obesity and rheumatic disease: common mechanistic links. A narrative review. *Ther Adv Musculoskelet Dis* 2018;10:157–67. <https://doi.org/10.1177/1759720X18783894>.