**2021 EULAR recommendations regarding lifestyle behaviours and work participation to prevent progression of rheumatic and musculoskeletal diseases**

James M. Gwinnutt1, Maud Wieczorek2, Andra Balanescu3,4, Heike A. Bischoff-Ferrari5,6,7, Annelies Boonen8, Giulio Cavalli9,10, Savia de Souza11, Annette de Thurah12, 13, Thomas E. Dorner14, 15, Rikke Helene Moe16, Polina Putrik8,17, Javier Rodríguez-Carrio18,19, Lucía Silva-Fernández20, Tanja Stamm21, 22, Karen Walker-Bone23, Joep Welling24, Mirjana Zlatković-Švenda25,26, Francis Guillemin2,27, Suzanne MM. Verstappen1,23,28

1 Centre for Epidemiology Versus Arthritis, Faculty of Biology, Medicine and Health, The University of Manchester, UK

2 EA 4360 Apemac, Université de Lorraine, Nancy, F-54000, France

3 Internal Medicine and Rheumatology Department, Sf Maria Hospital, Bucharest, Romania

4 Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

5 Department of Aging Medicine and Aging Research, University Hospital Zurich and University of Zurich, Zurich, Switzerland

6 Center on Aging and Mobility, University of Zurich, Zurich, Switzerland

7 University Clinic for Aging Medicine, City Hospital Zurich - Waid, Zurich, Switzerland

8 Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Center and Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, The Netherlands

9 Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Milan, Italy

10 Vita-Salute San Raffaele University, Milan, Italy

11 Centre for Rheumatic Diseases, King's College London, United Kingdom

12 Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

13 Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark

14 Centre for Public Health, Department of Social and Preventive Medicine, Medical University of Vienna, Vienna, Austria

15 Social Insurance Fund for Public Service, Railway and Mining Industries, Sitzenberg-Reidling, Austria

16 National Advisory Unit for Rehabilitation in Rheumatology, Division of Rheumatology and Research, Diakonhjemmet Hospital, Oslo, Norway

17 Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Center, Maastricht, The Netherlands

18 Area of Immunology, Department of Functional Biology, Universidad de Oviedo, Spain

19 Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Asturias, Spain

20 Rheumatology Department. Hospital Universitari Son Espases. Palma de Mallorca, Spain

21 Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Spitalgasse 23, 1090 Vienna, Austria

22 Ludwig Boltzmann Institute for Arthritis and Rehabilitation, Vienna, Austria

23 MRC Versus Arthritis Centre for Musculoskeletal Health and Work, University of Southampton, UK

24 NVLE Dutch Patient Organization for Systemic Autoimmune Diseases, Utrecht, The Netherlands

25 Institute of Rheumatology, University of Belgrade School of Medicine, Belgrade, Serbia

26 University of East Sarajevo Medical Faculty Foča, Republika Srpska, Bosnia and Herzegovina

27 Inserm, CHRU Nancy, Université de Lorraine, CIC-1433 Epidémiologie Clinique, Nancy, F-54000, France

28 NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, UK

Word count: 4592

Key words: diet, exercise, weight, smoking, alcohol, work participation, recommendations

Corresponding author: Suzanne MM Verstappen, Centre for Epidemiology Versus Arthritis, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK. suzanne.verstappen@manchester.ac.uk; 01612755663

**Abstract**

**Objectives:** A EULAR taskforce was convened to review the literature and develop recommendations on lifestyle behaviours for RMDs.

**Methods:** Six lifestyle exposures (exercise, diet, weight, alcohol, smoking, work participation) and seven RMDs (osteoarthritis, rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, systemic lupus erythematosus, systemic sclerosis, gout) were considered. The taskforce included health professionals in rheumatology, geriatricians, epidemiologists, public health experts, people with RMDs and exposure domain experts. Systematic reviews were conducted to gather available evidence, from which recommendations were developed.

**Results:** Five overarching principles and 18 specific recommendations were defined based on available evidence. The overarching principles define the importance of a healthy lifestyle, how lifestyle modifications should be implemented, and their role in relation to medical treatments. Exercise recommendations highlight the safety and benefits of exercise on pain and disability, particularly amongst people with osteoarthritis and axial spondyloarthritis. The diet recommendations emphasise the importance of a healthy, balanced diet for people with RMDs. People with RMDs and health professionals should work together to achieve and maintain a healthy weight. Small amounts of alcohol are unlikely to negatively affect the outcomes of people with RMDs, although people with rheumatoid arthritis and gout may be at risk of flares after moderate alcohol consumption. Smokers should be supported to quit. Work participation may have benefits on RMD outcomes and should be discussed in consultations.

**Conclusions:** These recommendations cover a range of lifestyle behaviours and can guide shared decision making between people with RMDs and health professionals when developing and monitoring treatment plans.

Words: 248

Rheumatic and musculoskeletal diseases (RMDs) comprise a significant proportion of the burden of disability in Europe1 2, which in turn negatively affects the quality of life of those people with RMDs. Whilst some RMDs have efficacious pharmacological treatments that reduce disease activity and hence improve disability (e.g. rheumatoid arthritis [RA]3, gout4), others do not (e.g. osteoarthritis [OA]5). In addition to pharmacological interventions, there are increasing requests from patients, health professionals and policy makers for more information on how changes in lifestyle alongside more effective disease management may prevent progression of RMDs and associated disability and co-morbidities.

The World Health Organisation (WHO) states that all adults should aim for a healthy, balanced diet containing fruits, vegetables, nuts and whole grains, and limited free sugar, fat and salt6; that physical activity is fundamental to health and physical inactivity is a major global health risk7; that obesity leads to negative health consequences but can be prevented8; that tobacco users need to quit9; and that harmful alcohol consumption is a cause of more than 200 disease and injury conditions10. These are clear messages for the general population, but for people with RMDs these aspects of health have not been prioritised in strategies to promote musculoskeletal health. This is in part because available evidence has not been sufficiently collated and synthesised, and in part because there has not been a coherent public health strategy for promoting musculoskeletal health in primary, secondary or tertiary healthcare sectors. Furthermore, there is heterogeneity in information materials on lifestyle factors across countries and often these materials are not evidence-based, are very generic, and may be limited to certain lifestyle domains. Individual socioeconomic factors (including health literacy) may further determine the access to and understanding of information people with RMDs receive, possibly limiting changes in lifestyle behaviour.

Whilst there have recently been recommendations regarding some of these lifestyle factors in RMDs, such as the 2018 European League Against Rheumatism (EULAR) recommendations for physical activity in inflammatory arthritis and OA11, in general there is a lack of consensus regarding which lifestyle modifications can meaningfully modify RMD-specific progression (including both modifiable [e.g. pain, fatigue] and irreversible [e.g. joint damage] outcomes). Nevertheless, people with RMDs frequently ask about this topic, and thus it is a priority. Therefore, a EULAR taskforce (TF) was convened to synthesise the available evidence regarding lifestyle and appropriate behaviour modification in seven common inflammatory and non-inflammatory RMDs with a high socioeconomic burden (OA, RA, axial spondyloarthritis [axSpA], psoriatic arthritis [PsA], systemic lupus erythematosus [SLE], systemic sclerosis [SSc], and gout) and produce evidence-based recommendations on what lifestyle behaviour modifications can contribute to improving disease specific outcomes such as disease activity and disability.

**Methods**

These recommendations were developed following EULAR’s standard operating procedure12. A multidisciplinary TF (N=19) was convened which included health professionals in rheumatology, geriatricians, epidemiologists, public health experts, people with RMDs, two representatives from EMEUNET, and exposure domain experts (e.g. experts on nutrition, exercise, work participation) from 11 different European countries. A steering group managed the TF (convenor: SMMV; methodologist: FG; fellows: JG, MW).

During the first teleconference with the TF in June 2018, the protocol was discussed and the search strategies for the systematic reviews were defined to assess the association between the included exposures (diet, exercise, weight loss, smoking and working) and progression of the RMDs of interest (OA, RA, axSpA, PsA, SLE and SSc). During this meeting, the TF decided to also include gout as one of the RMDs, due to the high prevalence and alleged relation to lifestyle.

A systematic review was then conducted by JG, MW, JRC and GC, aiming to identify systematic reviews and meta-analyses on these RMDs and exposures published between 01/01/2013 and 18/09/2018. A report of this review was written and presented to the TF at a teleconference in January 2019. At this teleconference, it was decided that alcohol should also be included as an exposure. Furthermore, since there were numerous recently-published systematic reviews and meta-analyses on OA and exercise as well as certain dietary exposures, it was decided that a systematic review of original articles did not need to be performed for these exposures in patients with OA13-17.

From March 2019 to May 2019, systematic reviews of original research were conducted, one for each of the six predefined exposures (excluding OA for certain exposures, as mentioned above)18-21. PICOs (Population, Intervention, Comparison, Outcome) were written and search strategies were developed for each review. These strategies were implemented in the PubMed/Medline, EMBASE and CENTRAL databases. Inclusion criteria were: (i) patients with a confirmed RMD of interest, (ii) the study assessed the association between an included exposure and disease progression, and (iii) the study was longitudinal (either experimental or observational). Each review was conducted by two members of the TF (diet: JG & JRC; exercise: JG & GC; weight loss: JG & SMMV; Smoking: MW & Maxime Ransay (public health resident at the University of Lorraine); Alcohol: MW & JG; Work: MW & PP), with oversight from the methodologist (FG). First, titles and abstracts were screened in pairs, with adjudication of any disagreements by a third member of the TF. Subsequently, full manuscripts of abstracts fulfilling the inclusion criteria were then assessed by the lead reviewer, with the second reviewer in each pair applying the inclusion criteria to the full texts of 10% of the included abstracts to assess agreement on the inclusion of full-texts, with good agreement demonstrated. Data were extracted from full manuscripts that met the inclusion and exclusion criteria by the lead reviewer. The quality of each study was assessed using the abbreviated version of the Cochrane Risk of Bias tool22 for randomised controlled trials (RCTs) (assessing random sequence generation, allocation concealment, blinding of participants, blinding of assessors) and the Quality in Prognostic Studies (QUIPS)23 tool for observational studies. The application of the Cochrane Risk of Bias tool was aided by a machine learning algorithm that identifies passages and estimates a grade for each of the categories. This has been demonstrated to speed up the quality assessment process24. A reviewer checked each of the algorithm’s estimates and the passages that the algorithm used to make these estimates, and if there was disagreement the reviewer changed the grade.

In May 2019, a two-day face-to-face meeting was held in which the results of the systematic reviews were presented to the TF. Due to the high volume of information found, results from four out of six exposures were evaluated at this meeting (i.e. diet, work participation, exercise and weight) and preliminary overarching points and recommendations were drafted. The results of the systematic reviews about the remaining two exposures (i.e. smoking and alcohol) were discussed during a teleconference with the entire TF in September 2019. From May 2019 to September 2019, the results of the systematic reviews were written up into reports and distributed to the TF. In October 2019, a second face-to-face meeting was held, in which the final overarching points and recommendations were written and agreed upon by all attending. Those who were unable to attend (N=7) were consulted beforehand to provide feedback on a draft of the recommendations.

In May 2020, a survey containing the overarching points and recommendations, as well as estimates of the strength of evidence supporting each statement (Oxford Centre for Evidence-based Medicine Levels of Evidence)12, was sent by email to all TF members asking them to rate their level of agreement (LoA) for each overarching principle / recommendation on a scale from 0 (totally disagree) to 10 (totally agree). Ideas for future research were also elicited from TF members through this survey.

**Results**

Six systematic reviews were performed for each individual exposure to gather evidence to develop the recommendations. The studies were a combination of RCTs, non-randomised trials and longitudinal observational studies. There was a large variation in the quality of the studies analysed. Many studies of exercise were rated as at low risk of bias, whereas many of the studies on diet were rated as having a high risk of bias (including potential conflicts of interest of study sponsors and incomplete descriptions of the randomisation and blinding processes).

The TF agreed on 5 overarching principles and 18 specific recommendations regarding the individual lifestyle factors (exercise=7; diet=2; weight=2; alcohol=4; smoking=2; working=1) (Table 1). All 19 members of the TF rated their LoA for each overarching principle / recommendation. The mean LoA was >9 for all recommendations indicating high agreement other than one alcohol recommendation, which had a mean LoA of 8.0 (standard deviation: 2.2).

**Overarching Principles (OP)**

**OP 1: Lifestyle improvements complement medical treatment and do not replace it**

For the RMDs assessed, there are efficacious pharmacological and non-pharmacological (e.g. physiotherapy) treatments available25-28. The evidence underpinning the following recommendations are studies that assessed lifestyle modifications alongside medical treatment. Therefore, all lifestyle modifications should be seen as complementary to these medical treatments and not as replacements.

**OP 2: Lifestyle improvements are an essential part of RMD management and add to overall health benefits**

Even where there are few data regarding the effect of lifestyle modifications on RMD-specific outcomes or where the data suggest the effect of lifestyle modifications may be small, making positive lifestyle changes for people with RMDs is important for overall health and wellbeing29-31. Therefore, assessment and encouragement to make positive lifestyle modifications should be an important part of RMD management and education. The benefit of lifestyle modifications may be enhanced if people with RMDs can make positive changes in more than one aspect of their lifestyle.

**OP 3: World Health Organisation recommendations for a healthy lifestyle are also applicable to people with RMDs**

The WHO has provided many useful resources and recommendation reports regarding lifestyle factors for all people (available online)6 8-10, and these resources and recommendations are relevant and useful starting points for individuals with RMDs.

**OP 4: Lifestyle recommendations for each individual with an RMD depend on factors such as age, sex, health condition, pregnancy and comorbidities**

The majority of research studies included in the systematic reviews provide overall estimates of the efficacy of lifestyle modifications, without analysing subgroup variation (often justifiably given the limited power of some studies). Furthermore, some studies excluded whole subgroups of the RMD population (e.g. pregnant women, people over a certain age, people with severe RMDs or comorbidities). These and other factors are likely to influence the effectiveness of lifestyle modification and therefore health professionals need to consider these factors when providing education about changes in lifestyle behaviours.

**OP 5: There should be regular discussions between people with RMDs and health professionals regarding lifestyle factors**

Lifestyle modifications potentially have substantial benefits to overall and RMD-specific health and should be a recurrent and frequent theme in discussions between people with RMDs and health professionals. Furthermore, given the complexity of RMD conditions (e.g. early versus established disease, disease flares) and the potential interactions between lifestyle modifications, current health condition and medical treatment, people with RMDs may need guidance and support from health professionals to implement a combination of healthy lifestyle changes32-34. This guidance and support should stem from a comprehensive management plan known to all health professionals directly involved in the diseases management of people with RMDs.

**Exposure-specific recommendations**

**Exercise 1: Exercise is beneficial for many health outcomes, including but not limited to RMD symptoms and progression**

As stated previously, exercise is beneficial for a multitude of general health outcomes and the WHO and US Department of Health and Human Services have provided general guidelines regarding exercise7 35. These benefits have also been shown for RMD-specific outcomes, such as pain and disability. Health professionals should collaborate with people with RMDs to make shared decisions regarding the type of activity that is appropriate for their ability and condition. EULAR has previously published recommendations for physical activity for people with OA and inflammatory arthritis, and our TF endorses these recommendations11.

**Exercise 2: People with RMDs should exercise because of the benefits on pain, function and quality of life**

There have been many research studies reporting the benefits of exercise on RMD-specific outcomes, with the general consensus being that exercise is beneficial for pain, function, fatigue and health-related quality of life in RMDs14 17 36-41. The evidence is stronger for short-term (6 – 12 months) benefits compared to long-term benefits, although long-term benefits have been demonstrated for the general population on a range of health outcomes and thereby can be extrapolated to people with RMDs42. Exercise may be effective at modifying disease activity in some conditions (e.g. axSpA), although to a smaller extent40 43 44. Furthermore, research has primarily focused on OA, RA and axSpA, with far fewer research studies on SLE, PsA, SSc and gout.

**Exercise 3: People with RMDs should avoid physical inactivity; they should engage in regular exercise according to their abilities**

Sedentary behaviour is associated with many negative health outcomes in the general population45-47. These negative outcomes will also affect people with RMDs. Therefore, health professionals should encourage people with RMDs to avoid a lifestyle characterized by prolonged periods of physical inactivity.

**Exercise 4: People with RMDs should perform both aerobic and strengthening exercises aiming for at least moderate intensity**

In line with previous recommendations11 35, evidence suggests that both aerobic and strengthening exercises are beneficial for people with RMDs, and therefore both should be included when exercising14 17 40 48-50. People with RMDs should aim for at least moderate intensity aerobic exercise (64-76% of maximal heart rate51) for at least 150 minutes per week, and strengthening exercise (50-69% of an individual’s one-repetition maximal effort) twice a week35.

**Exercise 5: People with RMDs should be advised that exercise is safe and that it is never too late to start exercising**

Amongst studies that reported about adverse events from exercise interventions in RMDs, many reported no or very few adverse events related to the interventions52-56. People with RMDs should be reminded that exercise is a safe way to improve their health condition, and that it is never too late to take up exercise, even if people had been less physically active prior to the onset of their condition.

**Exercise 6: Exercise can be performed in different settings, alone or in groups. There is a slight benefit favouring group exercises over exercises performed alone**

People with RMDs should be encouraged to perform the exercise that suits them best, whether that be alone at home or in exercise classes. There is some evidence that supervised exercise providing tutoring and peer-support may be marginally more effective than individual exercise57-60, but this should not discourage individuals from performing home-based exercise if they are unable to travel or unwilling to attend classes, as performing exercise that interests individuals and fits into their schedules is likely to lead to increased adherence.

**Exercise 7: People with osteoarthritis and axial spondyloarthritis should be especially encouraged to exercise as it is particularly beneficial for disease related outcomes**

Whilst exercise is beneficial for all RMDs, people with OA and axSpA should be particularly encouraged to exercise, as the results of studies of exercise in these conditions appear to show strong and consistent effects on reducing pain and improving function (e.g. 14 16 17 40 61 62).

**Diet 1: A healthy, balanced diet is integral to lifestyle improvement for people with RMDs**

It is important that patients with RMDs are educated about the benefits of maintaining a healthy, balanced diet. Imbalances in energy intake and expenditure contribute to obesity increasing the risk of chronic diseases (e.g. cardiovascular disease, type 2 diabetes mellitus) in the general population and also in people with RMDs. Quality of food is also linked to nutrition-related diseases. The WHO recommend that people should eat less high-calorie food, especially high in saturated or trans fats and sugars; eat more fruits, vegetables and legumes, and select foods of plant and marine origin6.

**Diet 2: People with RMDs should be informed that consuming specific food types is unlikely to have large benefits for RMD outcomes**

There have been many studies investigating the clinical efficacy of administering specific food types or components (e.g. nutrients) in people with RMDs. Mostly, these studies have been small scale or pilot studies, resulting in imprecise estimates and therefore reliable conclusions cannot be drawn. For some food components, larger studies have been conducted (e.g. vitamin D for OA63-65; marine oil / omega 3 for RA66 67) which have reported small effect sizes that are unlikely to be clinically meaningful. Whilst a high purine diet is a risk factor for the onset of gout, there is little clinical trial data on the efficacy of lifestyle modifications in people with gout4. However, the 2016 EULAR guidelines on the management of gout recommend people with gout to avoid sugar-sweetened drinks, heavy meals and excessive intake of meat and seafood as well as encouraging low-fat dairy products68 - this TF supports these recommendations. Overall, it is unlikely that consumption of specific food types will have large effects on RMD-specific outcomes.

**Weight 1: People with RMDs should aim for a healthy weight**

As part of a healthy lifestyle, people with RMDs should aim for a healthy weight. Communication of what constitutes a healthy weight for each individual should be based on shared decision-making within a multidisciplinary team and should take into account age, sex, disease state, treatment and comorbidity. When people gain or lose weight, adjustments in medication (e.g. dosage, frequency) or clinical status (e.g. comorbidity occurrence, flare) should be considered.

**Weight 2: People with RMDs who are overweight or obese should work with health professionals to achieve controlled and intentional weight loss through healthy diet and increased physical activity as this may be beneficial for RMD outcomes**

Being overweight / obese is associated with worse RMD specific outcomes69-73, and weight loss can improve-RMD specific outcomes74-76 as well as other health-related outcomes77-79. In adults, a BMI of ≥25kg/m2 is considered overweight and ≥30 kg/m2 is considered obese by the WHO80.

**Alcohol 1: The alcohol consumption of people with RMDs should be discussed together with health professionals, particularly when starting new treatments**

Discussions with people with RMDs about their alcohol consumption should be initiated by health professionals, particularly when starting specific new treatments such as methotrexate. People with RMDs should be aware of the negative health consequences of overconsumption of alcohol81 82, and steps should be taken to curtail unhealthy alcohol usage.

**Alcohol 2: People with RMDs can be reassured that a low level of alcohol consumption is unlikely to negatively impact RMD outcomes except in certain situations**

Whilst there has been relatively few research studies on alcohol and RMDs, those that have been published have shown that, in general, low levels of alcohol consumption are unlikely to have negative impacts on RMD-specific outcomes83-85, except in certain situations such as those with liver disease or who use certain treatments (e.g. methotrexate, leflunomide).

**Alcohol 3: People with rheumatoid arthritis and health professionals should be aware that moderate alcohol consumption is associated with increased risk of rheumatoid arthritis flare and comorbidities**

Several research studies have indicated that moderate alcohol consumption may increase the risk of comorbidities and increase disease activity in people with RA86-88. Health professionals should discuss the risks of alcohol consumption with people with RA.

**Alcohol 4: People with gout and health professionals should be aware that moderate alcohol consumption is associated with increased risk of gout flare**

Several research studies have indicated that alcohol consumption is associated with an increased risk of gout attacks89. Health professionals should discuss the risks of alcohol consumption with people with gout.

**Smoking 1: People with RMDs should be encouraged to stop smoking and be informed that smoking is detrimental to symptoms, function, disease activity, disease progression and occurrence of comorbidities in all RMDs**

Smoking is a well-established risk factor for many negative health outcomes90-92. Research studies of people with RMDs also indicate that smoking has a negative impact on many of their health outcomes, such as disease activity, function, progression and occurrence of comorbidities93-97. People with RMDs who smoke should be made aware that continuing to smoke is likely to lead to worse symptom burden as well as increased risk of serious comorbidity, such as cardiovascular disease as outlined by a 2016 EULAR TF on cardiovascular disease risk management98. These people should be offered support to quit and progress towards quitting should be monitored by health professionals.

**Smoking 2: People with rheumatoid arthritis and health professionals should be aware that smoking may affect disease modifying anti-rheumatic drug treatment response**

There is some evidence that smoking may limit response to DMARDs in RA99-101. Therefore, health professionals should make people with RA who smoke aware of this effect and support smokers towards quitting.

**Work 1: Work participation may have beneficial effects on health outcomes of people with RMDs and therefore should receive attention within healthcare consultations**

There have been several studies about work participation in people with RMDs, including studies of interventions aiming to keep people in work102. Whilst there are some inconsistencies between these studies, perhaps due to power and different outcome assessments, many indicated that work was probably not detrimental (although there is evidence that physically demanding jobs are associated with increased radiographic progression in axSpA103 104) and in some cases beneficial for people with RMDs in terms of RMD outcomes105-107. Given this, and the benefits of work on quality of life seen in the general population108, work should receive increased attention in healthcare consultations with people with RMDs, and specialised health professionals should be involved. Moreover, institutions in the health and social sector, employers and patient organisations should offer support regarding work participation.

**Research agenda**

The amount of research performed regarding lifestyle exposures and outcomes varied between the RMDs covered by this TF. The majority of the research had been performed in RA and OA, and to a lesser extent in axSpA. However, there is limited evidence on lifestyle exposures and progression of disease outcomes for populations with SLE, PsA, SSc and gout. Good quality research is needed for all the lifestyle exposures included in this TF for SLE, PsA, SSc and gout (Table 2). Furthermore, many of the studies investigating diet were of low quality, being non-randomised trials or very-small scale pilot studies. Given that the effect of singular dietary exposures is likely to be small, large well-designed trials with long follow-up are necessary.

A vast majority of studies included in the reviews of this TF investigated each lifestyle exposure individually. More research is needed to understand the synergistic effect of multiple lifestyle interventions given how intrinsically linked many of these lifestyle factors are, such as diet, exercise and weight (Table 2).

The accumulation of multiple unhealthy lifestyle behaviours is also likely deleterious, and this accumulation may be influenced by people’s personal and environmental context. For instance, people with lower socioeconomic status are more likely to eat poorly109 110, exercise less111 112, be obese113 114, smoke more115 and experience more adverse outcomes from alcohol116. They are also more likely to be employed in physically demanding jobs117. There are also disease-specific barriers to making lifestyle changes118. The influence these have on the association between lifestyle and RMD progression is not clear and a greater understanding of this may lead to improved targeting of lifestyle advice and interventions (Table 2).

**Evaluation and dissemination**

We will aim to evaluate these recommendations by conducting an online survey across several European countries, collecting data on the feasibility, acceptability and transparency of the recommendations. To disseminate these recommendations, we will develop information materials about healthy living and the impact of lifestyle on RMD progression in collaboration with patients and patient organisations. Summaries of evidence will also be written and distributed to health professionals and stakeholder organisations (WHO, EULAR, National Institute for Health and Care Excellence [NICE]).

|  |
| --- |
| *Table 1 – Overarching principles and exposure specific recommendations regarding lifestyle factors for people with RMDs* |
| Overarching Principles | **Level of evidence §** | **Grade of recommendation §** | **Level of agreement, mean (SD) [% who rated ≥7]** |
| 1. Lifestyle improvements complement medical treatment and do not replace it | 5 | D | 9.4 (1.2) [94.7] |
| 2. Lifestyle improvements are an essential part of RMD management and add to overall health benefits | 5 | D | 9.9 (0.5) [100] |
| 3. World Health Organisation recommendations for a healthy lifestyle are also applicable to people with RMDs | 5 | D | 9.3 (1.3) [94.7] |
| 4. Lifestyle recommendations for each individual with an RMD depend on factors such as age, sex, health condition, pregnancy and comorbidities | 5 | D | 9.5 (1.1) [94.7] |
| 5. There should be regular discussions between people with RMDs and health professionals regarding lifestyle factors | 5 | D | 9.7 (0.7) [100] |
| Exercise |  |  |  |
| 1. Exercise is beneficial for many health outcomes, including but not limited to RMD symptoms and progression | 1a | A | 9.9 (0.3) [100] |
| 2. People with RMDS should exercise because of the benefits on pain, function and quality of life | 1a | A | 9.7 (0.7) [100] |
| 3. People with RMDs should avoid physical inactivity; they should engage in regular exercise according to their abilities | 5 | D | 9.9 (0.5) [100] |
| 4. People with RMDs should perform both aerobic and strengthening exercises aiming for at least moderate intensity | 1a | A | 9.5 (0.8) [100] |
| 5. People with RMDs should be advised that exercise is safe and that it is never too late to start exercising | 1a | A | 9.9 (0.3) [100] |
| 6. Exercise can be performed in different settings, alone or in groups. There is a slight benefit favouring group exercises over exercises performed alone | 1a | A | 9.3 (1.4) [94.7] |
| 7. People with osteoarthritis and axial spondyloarthritis should be especially encouraged to exercise as it is particularly beneficial for disease related outcomes | 1a | A | 9.5 (0.8) [100] |
| Diet |  |  |  |
| 1. A healthy, balanced diet is integral to lifestyle improvement for people with RMDs | 5 | D | 9.5 (1.0) [100] |
| 2. People with RMDs should be informed that consuming specific food types is unlikely to have large benefits for RMD outcomes | 1a | A | 9.7 (0.8) [100] |
| Weight |  |  |  |
| 1. People with RMDs should aim for a healthy weight | 5 | D | 9.7 (0.7) [100] |
| 2. People with RMDs who are overweight or obese should work with health professionals to achieve controlled and intentional weight loss through healthy diet and increased physical activity as this may be beneficial for RMD outcomes | 2a | B | 9.5 (1.6) [94.7] |
| Alcohol |  |  |  |
| 1. The alcohol consumption of people with RMDs should be discussed together with health professionals, particularly when starting new treatments | 5 | D | 9.5 (1.0) [100] |
| 2. People with RMDs can be reassured that a low level of alcohol consumption is unlikely to negatively impact RMD outcomes except in certain situations | 2a | B | 8.0 (2.2) [73.7] |
| 3. People with rheumatoid arthritis and health professionals should be aware that moderate alcohol consumption is associated with increased risk of rheumatoid arthritis flare and comorbidities | 2a | B | 9.1 (1.6) [89.5] |
| 4. People with gout and health professionals should be aware that moderate alcohol consumption is associated with increased risk of gout flare | 2a | B | 9.6 (0.7) [100] |
| Smoking |  |  |  |
| 1. People with RMDs should be encouraged to stop smoking and be informed that smoking is detrimental to symptoms, function, disease activity, disease progression and occurrence of comorbidities in all RMDs | 2a | B | 9.9 (0.2) [100] |
| 2. People with rheumatoid arthritis and health professionals should be aware that smoking may affect disease modifying anti-rheumatic drug treatment response | 2a | B | 9.8 (0.7) [100] |
| Work |  |  |  |
| 1. Work participation may have beneficial effects on health outcomes of people with RMDs and therefore should receive attention within healthcare consultations | 2a | B | 9.8 (0.5) [100] |
| *RMD = rheumatic and musculoskeletal disease (here referring to: osteoarthritis, rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, systemic lupus erythematosus, systemic sclerosis and gout), SD = standard deviation. § Level of evidence defined by the EULAR SOP: 1a: systematic review with homogeneity of RCTs, 2a: Systematic review with homogeneity of cohort studies, 5: expert opinion; Grade of recommendation: A: consistent level 1 studies, B:* *consistent level 2 or 3 studies or extrapolations from level 1 studies, D: level 5 evidence or troublingly inconsistent or inconclusive studies of any level* |

|  |
| --- |
| *Table 2 – Research agenda* |
| Item | **Research area** |
| 1. | To address the large imbalance in the available evidence across the diseases within the scope of these recommendations, more high quality studies are needed on SLE, PsA, SSc and gout for all the lifestyle exposures included in this TF. Larger, high quality studies are needed for all RMDs on certain lifestyle exposures (such as diet, where effect sizes are likely to be small) |
| 2. | To understand the synergistic effect of multiple lifestyle improvements on disease progression. |
| 3. | To gain a greater understanding of the effect of socioeconomic deprivation on the associations between lifestyle factors and the outcomes assessed in this TF. |
| PsA = psoriatic arthritis, RMDs = rheumatic and musculoskeletal diseases, SLE = systemic lupus erythematosus, SSc = systemic sclerosis, TF = taskforce |

**Discussion**

This TF agreed on five overarching principles and 18 specific recommendations covering a range of important lifestyle factors and work participation for seven common RMDs. These recommendations are consistent with and build upon previous WHO, US government and EULAR recommendations6 7 11 35 80. These recommendations represent the consensus views of a wide spectrum of health professionals, scientists and people with RMDs and, due to the wide geographic representation of the TF members, should be appropriate for all individuals with RMDs across Europe. These recommendations are based on a broad review of the literature and thus, for the most part, are evidence-based. The level of agreement was high across the recommendations, indicating the broad acceptability of this recommendation set. While the evidence-base was primarily on individual lifestyle factors only, the TF acknowledge the potential benefit of several lifestyle changes in combination for people with RMDs.

Defining recommendations based on evidence is the first step towards improving the lifestyles, and ultimately the disease outcomes, of people with RMDs. The next step is to disseminate these recommendations as widely as possible across Europe. This will be done in the form of manuscripts, presentations, and bespoke leaflets translated into languages from across the continent.

Once these recommendations have been disseminated, people with RMDs themselves will be encouraged to implement these recommendations, with support from health professionals and/or family and friends. First, patients with RMDs may require education on the benefits of making lifestyle behaviour changes. Then theory-driven behaviour change interventions are required to aid people with RMDs to implement these recommendations119. System level changes are also needed – the ability to make lifestyle changes should be affordable and available to all.

Limitations of these recommendations include the breath of the scope of the project; including six exposures across seven RMDs necessitated a series of large systematic reviews. Consequently, findings from more than 700 papers were included. Whilst this surely represents a significant proportion of the research on these exposures, there is the possibility that some studies were missed. Furthermore, there is likely some publication bias in the selected papers, particularly for certain exposures. For many dietary exposures, only one small-scale study with a large effect size was found, indicating potential selective reporting. Furthermore, for some dietary exposures, there were concerns regarding conflicts of interest, with overlap between companies producing the dietary exposures and sponsoring the studies. For some exposures, the main evidence base was derived from observational studies, given that it would be unethical to test these exposures within interventional studies (e.g. smoking, alcohol). Appropriate caution was used when assessing these observational studies (due to the difficulties inferring causation from observational data) whilst devising the recommendations. Lastly, there was a large disparity in the amount of evidence published between the included RMDs. Whilst we have tried to be general in the majority of the recommendations, and believe that each recommendation is relevant for all the included RMDs, necessarily some recommendations will be supported by greater or lesser amounts of evidence depending on the RMD.

The research agenda highlighted the lack of high-quality, homogenous studies for certain exposures (e.g. diet) and the imbalance in the amount of studies across the included RMDs. Also, greater understanding is needed regarding how various lifestyle factors interact to produce positive or negative outcomes in RMDs, as research to date has primarily focused on each lifestyle exposure in isolation. The delivery of future lifestyle interventions as packages aiming to influence all aspects of lifestyle should be evaluated, given the interrelatedness of these exposures. Lastly, the influence of personal and environmental context, such as socioeconomic deprivation, on the associations between lifestyle exposures, work participation and outcomes requires more research, given the potentially large influence this has on exposure to negative lifestyle factors.

In conclusion, we have developed an extensive set of recommendations that can serve as a foundation for discussion and shared decision-making regarding positive modifications to the lifestyles of people with RMDs, with the ultimate goal being improvements in symptoms, quality of life and long-term outcomes.

**Acknowledgements:** The Taskforce would like to thank the library teams at the University of Lorraine and the University of Manchester, especially Mary Ingram at the Centre for Epidemiology Versus Arthritis, for their help with the literature reviews. Thanks to Maxime Ransay for help with the systematic review on smoking. Thanks also to the administrative team of the Division of Musculoskeletal and Dermatological Science at the University of Manchester for their help with organising the face-to-face meetings. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. SV and JG are supported by Versus Arthritis (grant numbers 20385, 20380) and the NIHR Manchester Biomedical Research Centre. JRC is supported by the Juan de la Cierva (IJCI-2017-32070) and Sara Borrell (CD19/00120) programs.

**Contributors:** JG, MW, FG and SMMV contributed equally. SMMV conceived the idea and submitted the project with a contribution from FG to the EULAR executive committee. JG and MW were the research fellows on the project who carried out the systematic literature reviews, with the help of PP, Maxime Ransay and EMEUNET members GC and JRC. These reviews were overseen by FG (methodologist) and SMMV (convenor). SMMV organised and chaired the telephone and face-to-face meetings. All authors contributed to the drafting of recommendations at the telephone and face-to-face meetings and helped to revise the recommendations manuscript.

**Funding:** The taskforce would like to thank EULAR for providing financial support for this project

**Competing interests:** None declared

**References**

1. March L, Smith EU, Hoy DG, et al. Burden of disability due to musculoskeletal (MSK) disorders. *Best Pract Res Clin Rheumatol* 2014;28(3):353-66. doi: S1521-6942(14)00082-5 [pii];10.1016/j.berh.2014.08.002 [doi]

2. Sebbag E, Felten R, Sagez F, et al. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization Burden of Diseases Database. *Ann Rheum Dis* 2019;78(6):844-48. doi: 10.1136/annrheumdis-2019-215142 [published Online First: 2019/04/17]

3. Smolen JS, Aletaha D, Barton A, et al. Rheumatoid arthritis. *Nat Rev Dis Primers* 2018;4:18001. doi: nrdp20181 [pii];10.1038/nrdp.2018.1 [doi]

4. Dalbeth N, Choi HK, Joosten LAB, et al. Gout. *Nat Rev Dis Primers* 2019;5(1):69-69. doi: 10.1038/s41572-019-0115-y

5. Martel-Pelletier J, Barr AJ, Cicuttini FM, et al. Osteoarthritis. *Nat Rev Dis Primers* 2016;2:16072. doi: nrdp201672 [pii];10.1038/nrdp.2016.72 [doi]

6. World Health Organisation. Diet, nutrition and the prevention of chronic diseases. Report of the joint WHO/FAO expert consultation. WHO Technical Report Series. World Health Organisation, 2018.

7. World Health Organisation. Global recommendations on physical activity for health, 2010.

8. World Health Organisation. Obesity and overweight factsheet 2018 [Available from: <https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight> accessed 28/01/2020.

9. World Health Organisation. WHO Report on the Global Tobacco Epidemic, 2019, 2019.

10. World Health Organisation. Alcohol fact sheet 2018 [Available from: <https://www.who.int/news-room/fact-sheets/detail/alcohol> accessed 28/01/2020.

11. Rausch Osthoff AK, Niedermann K, Braun J, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis* 2018;77(9):1251-60. doi: annrheumdis-2018-213585 [pii];10.1136/annrheumdis-2018-213585 [doi]

12. van der Heijde D, Aletaha D, Carmona L, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. *Ann Rheum Dis* 2015;74(1):8-13. doi: annrheumdis-2014-206350 [pii];10.1136/annrheumdis-2014-206350 [doi]

13. Liu X, Machado GC, Eyles JP, et al. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. *Br J Sports Med* 2018;52(3):167-75. doi: bjsports-2016-097333 [pii];10.1136/bjsports-2016-097333 [doi]

14. Juhl C, Christensen R, Roos EM, et al. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol* 2014;66(3):622-36. doi: 10.1002/art.38290 [doi]

15. Hurley M, Dickson K, Hallett R, et al. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev* 2018;4:CD010842. doi: 10.1002/14651858.CD010842.pub2 [doi]

16. Corbett MS, Rice SJ, Madurasinghe V, et al. Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis. *Osteoarthritis Cartilage* 2013;21(9):1290-98. doi: S1063-4584(13)00800-5 [pii];10.1016/j.joca.2013.05.007 [doi]

17. Uthman OA, van der Windt DA, Jordan JL, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *BMJ* 2013;347:f5555. doi: 10.1136/bmj.f5555 [doi]

18. Gwinnutt JM, Wieczorek M, Rodríguez-Carrio J, et al. Effects of diet on the outcomes of rheumatic and musculoskeletal diseases (RMDs): systematic review and meta-analyses informing the 2021 EULAR recommendations for lifestyle improvements in people with RMDs. *RMD Open* 2022;(Under Review)

19. Gwinnutt JM, Wieczorek M, Cavalli G, et al. Effects of physical exercise and body weight on disease-specific outcomes of people with rheumatic and musculoskeletal diseases (RMDs): systematic reviews and meta-analyses informing the 2021 EULAR recommendations for lifestyle improvements in people with RMDs. *RMD Open* 2022;(Under review)

20. Wieczorek M, Gwinnutt JM, Ransay M, et al. Smoking, alcohol consumption and disease-specific outcomes in rheumatic and musculoskeletal diseases (RMDs): systematic reviews informing the 2021 EULAR recommendations for lifestyle improvements in people with RMDs. *RMD Open* 2022;(Under review)

21. Wieczorek M, Verstappen SMM, Putrik P, et al. Association of vocational interventions and work-related factors with disease-specific outcomes in individuals with rheumatic and musculoskeletal diseases (RMDs): A Systematic Literature Review informing the 2021 EULAR recommendations for lifestyle improvements in people with RMDs. *(in preperation)* 2022

22. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj* 2011;343:d5928. doi: 10.1136/bmj.d5928 [published Online First: 2011/10/20]

23. Hayden JA, van der Windt DA, Cartwright JL, et al. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013;158(4):280-86. doi: 1650776 [pii];10.7326/0003-4819-158-4-201302190-00009 [doi]

24. Soboczenski F, Trikalinos TA, Kuiper J, et al. Machine learning to help researchers evaluate biases in clinical trials: a prospective, randomized user study. *BMC Med Inform Decis Mak* 2019;19(1):96. doi: 10.1186/s12911-019-0814-z [doi];10.1186/s12911-019-0814-z [pii]

25. Singh JA, Christensen R, Wells GA, et al. Biologics for rheumatoid arthritis: an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2009(4):CD007848. doi: 10.1002/14651858.CD007848.pub2 [doi]

26. Coates LC, Cawkwell LS, Ng NWF, et al. Real life experience confirms sustained response to long-term biologics and switching in ankylosing spondylitis. *Rheumatology (Oxford, England)* 2008;47(6):897-900. doi: 10.1093/rheumatology/ken094 [published Online First: 2008/04/10]

27. Lord PAC, Farragher TM, Lunt M, et al. Predictors of response to anti-TNF therapy in ankylosing spondylitis: results from the British Society for Rheumatology Biologics Register. *Rheumatology* 2009;49(3):563-70. doi: 10.1093/rheumatology/kep422

28. Walsh NE, Pearson J, Healey EL. Physiotherapy management of lower limb osteoarthritis. *British Medical Bulletin* 2017;122(1):151-61. doi: 10.1093/bmb/ldx012

29. Akbaraly TN, Ferrie JE, Berr C, et al. Alternative Healthy Eating Index and mortality over 18 y of follow-up: results from the Whitehall II cohort. *The American Journal of Clinical Nutrition* 2011;94(1):247-53. doi: 10.3945/ajcn.111.013128

30. Shivappa N, Hebert JR, Kivimaki M, et al. Alternative Healthy Eating Index 2010, Dietary Inflammatory Index and risk of mortality: results from the Whitehall II cohort study and meta-analysis of previous Dietary Inflammatory Index and mortality studies. *Br J Nutr* 2017;118(3):210-21. doi: 10.1017/S0007114517001908

31. Ford ES, Bergmann MM, Boeing H, et al. Healthy lifestyle behaviors and all-cause mortality among adults in the United States. *Prev Med* 2012;55(1):23-27. doi: 10.1016/j.ypmed.2012.04.016 [published Online First: 2012/04/29]

32. Carson KV, Verbiest MEA, Crone MR, et al. Training health professionals in smoking cessation. *Cochrane Database of Systematic Reviews* 2012(5) doi: 10.1002/14651858.CD000214.pub2

33. Veldhuijzen van Zanten JJCS, Rouse PC, Hale ED, et al. Perceived Barriers, Facilitators and Benefits for Regular Physical Activity and Exercise in Patients with Rheumatoid Arthritis: A Review of the Literature. *Sports Med* 2015;45(10):1401-12. doi: 10.1007/s40279-015-0363-2

34. Walker RE, Kusch J, Fink JT, et al. Facilitating Factors and Barriers to Weight Management in Women: Physician Perspectives. *J Patient Cent Res Rev* 2018;5(1):18-27. doi: 10.17294/2330-0698.1495

35. Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. *Jama* 2018;320(19):2020-28. doi: 10.1001/jama.2018.14854 [published Online First: 2018/11/13]

36. Bartholdy C, Juhl C, Christensen R, et al. The role of muscle strengthening in exercise therapy for knee osteoarthritis: A systematic review and meta-regression analysis of randomized trials. *Semin Arthritis Rheum* 2017;47(1):9-21. doi: S0049-0172(16)30172-X [pii];10.1016/j.semarthrit.2017.03.007 [doi]

37. Baillet A, Vaillant M, Guinot M, et al. Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials. *Rheumatology (Oxford)* 2012;51(3):519-27. doi: ker330 [pii];10.1093/rheumatology/ker330 [doi]

38. Baillet A, Zeboulon N, Gossec L, et al. Efficacy of cardiorespiratory aerobic exercise in rheumatoid arthritis: meta-analysis of randomized controlled trials. *Arthritis Care Res (Hoboken )* 2010;62(7):984-92. doi: 10.1002/acr.20146 [doi]

39. Millner JR, Barron JS, Beinke KM, et al. Exercise for ankylosing spondylitis: An evidence-based consensus statement. *Semin Arthritis Rheum* 2016;45(4):411-27. doi: S0049-0172(15)00201-2 [pii];10.1016/j.semarthrit.2015.08.003 [doi]

40. Pecourneau V, Degboe Y, Barnetche T, et al. Effectiveness of Exercise Programs in Ankylosing Spondylitis: A Meta-Analysis of Randomized Controlled Trials. *Arch Phys Med Rehabil* 2018;99(2):383-89. doi: S0003-9993(17)31019-5 [pii];10.1016/j.apmr.2017.07.015 [doi]

41. Cramp F, Hewlett S, Almeida C, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. *Cochrane Database Syst Rev* 2013(8):CD008322. doi: 10.1002/14651858.CD008322.pub2 [doi]

42. Reiner M, Niermann C, Jekauc D, et al. Long-term health benefits of physical activity--a systematic review of longitudinal studies. *BMC Public Health* 2013;13:813-13. doi: 10.1186/1471-2458-13-813

43. Liang H, Zhang H, Ji H, et al. Effects of home-based exercise intervention on health-related quality of life for patients with ankylosing spondylitis: a meta-analysis. *Clin Rheumatol* 2015;34(10):1737-44. doi: 10.1007/s10067-015-2913-2 [doi];10.1007/s10067-015-2913-2 [pii]

44. Martins NA, Furtado GE, Campos MJ, et al. Exercise and ankylosing spondylitis with New York modified criteria: a systematic review of controlled trials with meta-analysis. *Acta Reumatol Port* 2014;39(4):298-308. doi: AR140056 [pii]

45. Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia* 2012;55(11):2895-905. doi: 10.1007/s00125-012-2677-z [published Online First: 2012/08/14]

46. Ekelund U, Tarp J, Steene-Johannessen J, et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ (Clinical research ed)* 2019;366:l4570-l70. doi: 10.1136/bmj.l4570

47. Kerr J, Anderson C, Lippman SM. Physical activity, sedentary behaviour, diet, and cancer: an update and emerging new evidence. *Lancet Oncol* 2017;18(8):e457-e71. doi: 10.1016/S1470-2045(17)30411-4 [published Online First: 2017/07/26]

48. Rausch Osthoff AK, Juhl CB, Knittle K, et al. Effects of exercise and physical activity promotion: meta-analysis informing the 2018 EULAR recommendations for physical activity in people with rheumatoid arthritis, spondyloarthritis and hip/knee osteoarthritis. *RMD Open* 2018;4(2):e000713. doi: 10.1136/rmdopen-2018-000713 [doi];rmdopen-2018-000713 [pii]

49. Rongen-van Dartel SA, Repping-Wuts H, Flendrie M, et al. Effect of Aerobic Exercise Training on Fatigue in Rheumatoid Arthritis: A Meta-Analysis. *Arthritis Care Res (Hoboken )* 2015;67(8):1054-62. doi: 10.1002/acr.22561 [doi]

50. Williams MA, Srikesavan C, Heine PJ, et al. Exercise for rheumatoid arthritis of the hand. *Cochrane Database Syst Rev* 2018;7:CD003832. doi: 10.1002/14651858.CD003832.pub3 [doi]

51. Centers for Disease Control and Prevention. Target Heart Rate and Estimated Maximum Heart Rate 2020 [Available from: <https://www.cdc.gov/physicalactivity/basics/measuring/heartrate.htm> accessed 07/01/2021.

52. Lamb SE, Williamson EM, Heine PJ, et al. Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial. *Lancet* 2015;385(9966):421-29. doi: S0140-6736(14)60998-3 [pii];10.1016/S0140-6736(14)60998-3 [doi]

53. Katz P, Margaretten M, Gregorich S, et al. Physical Activity to Reduce Fatigue in Rheumatoid Arthritis: A Randomized Controlled Trial. *Arthritis Care Res (Hoboken )* 2018;70(1):1-10. doi: 10.1002/acr.23230 [doi]

54. Baillet A, Payraud E, Niderprim VA, et al. A dynamic exercise programme to improve patients' disability in rheumatoid arthritis: a prospective randomized controlled trial. *Rheumatology (Oxford)* 2009;48(4):410-15. doi: ken511 [pii];10.1093/rheumatology/ken511 [doi]

55. Pinto AL, Oliveira NC, Gualano B, et al. Efficacy and safety of concurrent training in systemic sclerosis. *J Strength Cond Res* 2011;25(5):1423-28. doi: 10.1519/JSC.0b013e3181d6858b [doi]

56. Roger-Silva D, Natour J, Moreira E, et al. A resistance exercise program improves functional capacity of patients with psoriatic arthritis: a randomized controlled trial. *Clin Rheumatol* 2018;37(2):389-95. doi: 10.1007/s10067-017-3917-x [doi];10.1007/s10067-017-3917-x [pii]

57. Seneca T, Hauge EM, Maribo T. Comparable effect of partly supervised and self-administered exercise programme in early rheumatoid arthritis--a randomised, controlled trial. *Dan Med J* 2015;62(8):A5127. doi: A5127 [pii]

58. Anwer S, Alghadir A, Brismee JM. Effect of Home Exercise Program in Patients With Knee Osteoarthritis: A Systematic Review and Meta-analysis. *J Geriatr Phys Ther* 2016;39(1):38-48. doi: 10.1519/JPT.0000000000000045 [doi]

59. Aydin T, Taspinar O, Sariyildiz MA, et al. Evaluation of the effectiveness of home based or hospital based calisthenic exercises in patients with ankylosing spondylitis. *J Back Musculoskelet Rehabil* 2016;29(4):723-30. doi: BMR677 [pii];10.3233/BMR-160677 [doi]

60. Analay Y, Ozcan E, Karan A, et al. The effectiveness of intensive group exercise on patients with ankylosing spondylitis. *Clin Rehabil* 2003;17(6):631-36. doi: 10.1191/0269215503cr658oa [doi]

61. Sveaas SH, Bilberg A, Berg IJ, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axSpA): a multicentre randomised trial of 100 patients. *Br J Sports Med* 2019 doi: bjsports-2018-099943 [pii];10.1136/bjsports-2018-099943 [doi]

62. Tanaka R, Ozawa J, Kito N, et al. Efficacy of strengthening or aerobic exercise on pain relief in people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil* 2013;27(12):1059-71. doi: 0269215513488898 [pii];10.1177/0269215513488898 [doi]

63. Arden NK, Cro S, Sheard S, et al. The effect of vitamin D supplementation on knee osteoarthritis, the VIDEO study: a randomised controlled trial. *Osteoarthritis Cartilage* 2016;24(11):1858-66. doi: S1063-4584(16)30109-1 [pii];10.1016/j.joca.2016.05.020 [doi]

64. Bischoff-Ferrari HA, Orav EJ, Egli A, et al. Recovery after unilateral knee replacement due to severe osteoarthritis and progression in the contralateral knee: a randomised clinical trial comparing daily 2000 IU versus 800 IU vitamin D. *RMD Open* 2018;4(2):e000678. doi: 10.1136/rmdopen-2018-000678 [doi];rmdopen-2018-000678 [pii]

65. Jin X, Jones G, Cicuttini F, et al. Effect of Vitamin D Supplementation on Tibial Cartilage Volume and Knee Pain Among Patients With Symptomatic Knee Osteoarthritis: A Randomized Clinical Trial. *JAMA* 2016;315(10):1005-13. doi: 2499277 [pii];10.1001/jama.2016.1961 [doi]

66. Senftleber NK, Nielsen SM, Andersen JR, et al. Marine Oil Supplements for Arthritis Pain: A Systematic Review and Meta-Analysis of Randomized Trials. *Nutrients* 2017;9(1) doi: nu9010042 [pii];10.3390/nu9010042 [doi]

67. Gioxari A, Kaliora AC, Marantidou F, et al. Intake of omega-3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A systematic review and meta-analysis. *Nutrition* 2018;45:114-24. doi: S0899-9007(17)30134-X [pii];10.1016/j.nut.2017.06.023 [doi]

68. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis* 2017;76(1):29-42. doi: 10.1136/annrheumdis-2016-209707 [published Online First: 2016/07/28]

69. Liu Y, Hazlewood GS, Kaplan GG, et al. Impact of Obesity on Remission and Disease Activity in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. *Arthritis Care Res (Hoboken )* 2017;69(2):157-65. doi: 10.1002/acr.22932 [doi]

70. Nikiphorou E, Norton S, Young A, et al. The association of obesity with disease activity, functional ability and quality of life in early rheumatoid arthritis: data from the Early Rheumatoid Arthritis Study/Early Rheumatoid Arthritis Network UK prospective cohorts. *Rheumatology (Oxford)* 2018 doi: 4953791 [pii];10.1093/rheumatology/key066 [doi]

71. Katz P, Yazdany J, Julian L, et al. Impact of obesity on functioning among women with systemic lupus erythematosus. *Arthritis Care Res (Hoboken )* 2011;63(10):1357-64. doi: 10.1002/acr.20526 [doi]

72. Ottaviani S, Allanore Y, Tubach F, et al. Body mass index influences the response to infliximab in ankylosing spondylitis. *Arthritis Res Ther* 2012;14(3):R115. doi: ar3841 [pii];10.1186/ar3841 [doi]

73. Nguyen UD, Zhang Y, Louie-Gao Q, et al. Obesity Paradox in Recurrent Attacks of Gout in Observational Studies: Clarification and Remedy. *Arthritis Care Res (Hoboken )* 2017;69(4):561-66. doi: 10.1002/acr.22954 [doi]

74. Di Minno MN, Peluso R, Iervolino S, et al. Weight loss and achievement of minimal disease activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor alpha blockers. *Ann Rheum Dis* 2014;73(6):1157-62. doi: annrheumdis-2012-202812 [pii];10.1136/annrheumdis-2012-202812 [doi]

75. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013;310(12):1263-73. doi: 1741824 [pii];10.1001/jama.2013.277669 [doi]

76. Somers TJ, Blumenthal JA, Guilak F, et al. Pain coping skills training and lifestyle behavioral weight management in patients with knee osteoarthritis: a randomized controlled study. *Pain* 2012;153(6):1199-209. doi: S0304-3959(12)00118-2 [pii];10.1016/j.pain.2012.02.023 [doi]

77. Riaz H, Khan MS, Siddiqi TJ, et al. Association Between Obesity and Cardiovascular Outcomes: A Systematic Review and Meta-analysis of Mendelian Randomization Studies. *JAMA Netw Open* 2018;1(7):e183788-e88. doi: 10.1001/jamanetworkopen.2018.3788

78. Abdullah A, Peeters A, de Courten M, et al. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. *Diabetes Res Clin Pract* 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012 [published Online First: 2010/05/20]

79. Flegal KM, Kit BK, Orpana H, et al. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA* 2013;309(1):71-82. doi: 10.1001/jama.2012.113905

80. World Health Organisation. Obesity: Preventing and Managing the Global Epidemic. WHO Technical Report Series. Geneva, 2000.

81. Hart CL, Morrison DS, Batty GD, et al. Effect of body mass index and alcohol consumption on liver disease: analysis of data from two prospective cohort studies. *BMJ (Clinical research ed)* 2010;340:c1240-c40. doi: 10.1136/bmj.c1240

82. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer* 2015;112(3):580-93. doi: 10.1038/bjc.2014.579 [published Online First: 2014/11/25]

83. Bird P, Nicholls D, Barrett R, et al. Longitudinal study of clinical prognostic factors in patients with early rheumatoid arthritis: the PREDICT study. *Int J Rheum Dis* 2017;20(4):460-68. doi: 10.1111/1756-185X.13036 [doi]

84. Davis MLR, Michaud K, Sayles H, et al. Associations of alcohol use with radiographic disease progression in African Americans with recent-onset rheumatoid arthritis. *The Journal of rheumatology* 2013;40(9):1498-504. doi: 10.3899/jrheum.121325 [published Online First: 2013/06/15]

85. Nissen MJ, Gabay C, Scherer A, et al. The effect of alcohol on radiographic progression in rheumatoid arthritis. *Arthritis and rheumatism* 2010;62(5):1265-72. doi: 10.1002/art.27388

86. Humphreys JH, Warner A, Costello R, et al. Quantifying the hepatotoxic risk of alcohol consumption in patients with rheumatoid arthritis taking methotrexate. *Annals of the rheumatic diseases* 2017;76(9):1509-14. doi: 10.1136/annrheumdis-2016-210629 [published Online First: 2017/03/23]

87. Doran MF, Crowson CS, Pond GR, et al. Predictors of infection in rheumatoid arthritis. *Arthritis and rheumatism* 2002;46(9):2294-300. doi: 10.1002/art.10529

88. Lu B, Rho YH, Cui J, et al. Associations of smoking and alcohol consumption with disease activity and functional status in rheumatoid arthritis. *The Journal of rheumatology* 2014;41(1):24-30. doi: 10.3899/jrheum.130074 [published Online First: 2013/12/01]

89. Neogi T, Chen C, Niu J, et al. Alcohol quantity and type on risk of recurrent gout attacks: an internet-based case-crossover study. *Am J Med* 2014;127(4):311-18. doi: 10.1016/j.amjmed.2013.12.019 [published Online First: 2014/01/17]

90. Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: a meta-analysis. *Int J Cancer* 2008;122(1):155-64. doi: 10.1002/ijc.23033

91. Huxley RR, Woodward M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. *Lancet (London, England)* 2011;378(9799):1297-305. doi: 10.1016/S0140-6736(11)60781-2 [published Online First: 2011/08/10]

92. Willi C, Bodenmann P, Ghali WA, et al. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2007;298(22):2654-64. doi: 10.1001/jama.298.22.2654

93. de Rooij M, van der Leeden M, Heymans MW, et al. Prognosis of Pain and Physical Functioning in Patients With Knee Osteoarthritis: A Systematic Review and Meta-Analysis. *Arthritis Care Res (Hoboken )* 2016;68(4):481-92. doi: 10.1002/acr.22693 [doi]

94. Baghdadi LR, Woodman RJ, Shanahan EM, et al. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. *PLoS One* 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952 [doi];PONE-D-14-43366 [pii]

95. Rodriguez Huerta MD, Trujillo-Martin MM, Rua-Figueroa I, et al. Healthy lifestyle habits for patients with systemic lupus erythematosus: A systemic review. *Semin Arthritis Rheum* 2016;45(4):463-70. doi: S0049-0172(15)00232-2 [pii];10.1016/j.semarthrit.2015.09.003 [doi]

96. Villaverde-Garcia V, Cobo-Ibanez T, Candelas-Rodriguez G, et al. The effect of smoking on clinical and structural damage in patients with axial spondyloarthritis: A systematic literature review. *Semin Arthritis Rheum* 2017;46(5):569-83. doi: S0049-0172(16)30146-9 [pii];10.1016/j.semarthrit.2016.11.004 [doi]

97. Tillett W, Jadon D, Shaddick G, et al. Smoking and delay to diagnosis are associated with poorer functional outcome in psoriatic arthritis. *Annals of the rheumatic diseases* 2013;72(8):1358-61. doi: 10.1136/annrheumdis-2012-202608 [published Online First: 2013/01/03]

98. Agca R, Heslinga SC, Rollefstad S, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. *Ann Rheum Dis* 2017;76(1):17-28. doi: 10.1136/annrheumdis-2016-209775 [published Online First: 2016/10/05]

99. Daien CI, Hua C, Combe B, et al. Non-pharmacological and pharmacological interventions in patients with early arthritis: a systematic literature review informing the 2016 update of EULAR recommendations for the management of early arthritis. *RMD Open* 2017;3(1):e000404. doi: 10.1136/rmdopen-2016-000404 [doi];rmdopen-2016-000404 [pii]

100. Söderlin MK, Petersson IF, Bergman S, et al. Smoking at onset of rheumatoid arthritis (RA) and its effect on disease activity and functional status: experiences from BARFOT, a long-term observational study on early RA. *Scand J Rheumatol* 2011;40(4):249-55. doi: 10.3109/03009742.2010.541495 [published Online First: 2011/02/22]

101. Levitsky A, Brismar K, Hafstrom I, et al. Obesity is a strong predictor of worse clinical outcomes and treatment responses in early rheumatoid arthritis: results from the SWEFOT trial. *RMD Open* 2017;3(2):e000458. doi: 10.1136/rmdopen-2017-000458 [doi];rmdopen-2017-000458 [pii]

102. Hoving JL, Lacaille D, Urquhart DM, et al. Non-pharmacological interventions for preventing job loss in workers with inflammatory arthritis. *Cochrane Database Syst Rev* 2014(11):CD010208. doi: 10.1002/14651858.CD010208.pub2 [doi]

103. Ramiro S, Landewe R, van TA, et al. Lifestyle factors may modify the effect of disease activity on radiographic progression in patients with ankylosing spondylitis: a longitudinal analysis. *RMD Open* 2015;1(1):e000153. doi: 10.1136/rmdopen-2015-000153 [doi];rmdopen-2015-000153 [pii]

104. Nikiphorou E, Ramiro S, Sepriano A, et al. Do smoking and socioeconomic factors influence imaging outcomes in axial spondyloarthritis? Five-year data from the DESIR cohort. *Arthritis Rheumatol* 2020 doi: 10.1002/art.41408 [published Online First: 2020/06/21]

105. Green DJ, Lewis M, Mansell G, et al. Clinical course and prognostic factors across different musculoskeletal pain sites: A secondary analysis of individual patient data from randomised clinical trials. *Eur J Pain* 2018;22(6):1057-70. doi: 10.1002/ejp.1190 [published Online First: 2018/02/22]

106. Chopp-Hurley JN, Brenneman EC, Wiebenga EG, et al. Randomized Controlled Trial Investigating the Role of Exercise in the Workplace to Improve Work Ability, Performance, and Patient-Reported Symptoms Among Older Workers With Osteoarthritis. *J Occup Environ Med* 2017;59(6):550-56. doi: 10.1097/JOM.0000000000001020

107. Zhou W, Chandran V, Cook R, et al. The association between occupational-related mechanical stress and radiographic damage in psoriatic arthritis. *Semin Arthritis Rheum* 2019;48(4):638-43. doi: 10.1016/j.semarthrit.2018.06.001 [published Online First: 2018/06/19]

108. Black C. Working for a Healthier Tomorrow. Norwich, 2008.

109. Hiza HA, Casavale KO, Guenther PM, et al. Diet quality of Americans differs by age, sex, race/ethnicity, income, and education level. *Journal of the Academy of Nutrition and Dietetics* 2013;113(2):297-306. doi: 10.1016/j.jand.2012.08.011 [published Online First: 2012/11/22]

110. Backholer K, Spencer E, Gearon E, et al. The association between socio-economic position and diet quality in Australian adults. *Public Health Nutr* 2016;19(3):477-85. doi: 10.1017/s1368980015001470 [published Online First: 2015/05/21]

111. Shuval K, Li Q, Gabriel KP, et al. Income, physical activity, sedentary behavior, and the 'weekend warrior' among U.S. adults. *Prev Med* 2017;103:91-97. doi: 10.1016/j.ypmed.2017.07.033 [published Online First: 2017/08/15]

112. O'Donoghue G, Kennedy A, Puggina A, et al. Socio-economic determinants of physical activity across the life course: A "DEterminants of DIet and Physical ACtivity" (DEDIPAC) umbrella literature review. *PLoS One* 2018;13(1):e0190737. doi: 10.1371/journal.pone.0190737 [published Online First: 2018/01/20]

113. Newton S, Braithwaite D, Akinyemiju TF. Socio-economic status over the life course and obesity: Systematic review and meta-analysis. *PLoS One* 2017;12(5):e0177151. doi: 10.1371/journal.pone.0177151 [published Online First: 2017/05/17]

114. Cohen AK, Rai M, Rehkopf DH, et al. Educational attainment and obesity: a systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2013;14(12):989-1005. doi: 10.1111/obr.12062 [published Online First: 2013/07/31]

115. Hiscock R, Bauld L, Amos A, et al. Socioeconomic status and smoking: a review. *Annals of the New York Academy of Sciences* 2012;1248:107-23. doi: 10.1111/j.1749-6632.2011.06202.x [published Online First: 2011/11/19]

116. Collins SE. Associations Between Socioeconomic Factors and Alcohol Outcomes. *Alcohol research : current reviews* 2016;38(1):83-94. [published Online First: 2016/05/10]

117. Warren JR, Hoonakker P, Carayon P, et al. Job characteristics as mediators in SES-health relationships. *Social science & medicine (1982)* 2004;59(7):1367-78. doi: 10.1016/j.socscimed.2004.01.035 [published Online First: 2004/07/13]

118. Gwinnutt JM, Verstappen SM, Humphreys JH. The impact of lifestyle behaviours, physical activity and smoking on morbidity and mortality in patients with rheumatoid arthritis. *Best practice & research Clinical rheumatology* 2020:101562. doi: 10.1016/j.berh.2020.101562 [published Online First: 2020/07/11]

119. Knittle K, De Gucht V, Maes S. Lifestyle- and behaviour-change interventions in musculoskeletal conditions. *Best practice & research Clinical rheumatology* 2012;26(3):293-304. doi: 10.1016/j.berh.2012.05.002 [published Online First: 2012/08/08]