EULAR recommendations for the non-pharmacological management of systemic lupus erythematosus and systemic sclerosis

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Abstract

Objective: To develop evidence-based recommendations for the non-pharmacological management of systemic lupus erythematosus (SLE) and systemic sclerosis (SSc).

Methods: A task force (TF) comprising 7 rheumatologists, 15 other healthcare professionals, and 3 patients was established. Following a systematic literature review performed to inform the recommendations, statements were formulated, discussed during online meetings, and graded based on risk of bias assessment, level of evidence (LoE), and strength of recommendation (SoR; scale A–D, A comprising consistent LoE 1 studies, D comprising LoE 4 or inconsistent studies), following the EULAR standard operating procedure. Level of agreement (LoA; scale 0–10, 0 denoting complete disagreement, 10 denoting complete agreement) was determined for each statement through online voting.

Results: Four overarching principles and twelve recommendations were developed. These concerned common and disease-specific aspects of non-pharmacological management. SoR ranged from A to D. The mean LoA with the overarching principles and recommendations ranged from 8.4 to 9.7. Briefly, non-pharmacological management of SLE and SSc should be tailored, person-centred, and participatory. It is not intended to preclude but rather complement pharmacotherapy. Patients should be offered education and support for physical exercise, smoking cessation, and avoidance of cold exposure. Photoprotection and psychosocial interventions are important for SLE patients, while mouth and hand exercises are important in SSc.

Conclusions: The recommendations will guide healthcare professionals and patients toward a holistic and personalised management of SLE and SSc. Research and educational agendas were developed to address needs toward a higher evidence level, enhancement of clinician-patient communication, and improved outcomes.

Key messages

What is already known about this subject?

- Non-pharmacological management of systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) is helpful but unstandardised and often underused in current clinical practice.

What does this study add?

- We developed recommendations to provide guidance for non-pharmacological management of people living with SLE and SSc.
- In this work, we present evidence to support common and disease-specific non-pharmacological interventions for SLE and SSc.
- We generated a research agenda as well as an educational agenda to support non-pharmacological management of people with SLE and SSc.

How might this impact on clinical practice?

- These recommendations will provide guidance on non-pharmacological interventions in the management of SLE and SSc in clinical practice, and promote their use alongside pharmacotherapy to improve the overall quality of care.

Introduction

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease that predominantly affects women and is characterised by multisystem involvement.[1] SLE can affect all organs or tissues, including the skin, joints, kidneys, central and peripheral nervous system, lungs, heart, white blood cells, and platelets.[1, 2] Despite advances in pharmacotherapy during the last decades, patients with SLE still experience poor health-related quality of life (HRQoL).[3] Systemic sclerosis (SSc), also known as scleroderma, is another rheumatic autoimmune disease that is characterised by vasculopathy and fibrosis of the skin and visceral organs.[4] SSc is coupled with a high morbidity burden and has a major impact on patients' HRQoL.[4] New therapies hold promise regarding prevention or even improvement of skin and lung fibrosis, as well as disease manifestations such as renal crisis, pulmonary arterial hypertension (PAH), digital ulcerations, and gastro-oesophageal reflux, yet premature death remains a concern, pointing to the urgent need for further optimisation of the disease management.[4]

Non-pharmacological management and self-management strategies are progressively substantiated through growing evidence.[5] While a substantial use of non-pharmacological interventions is generally seen, the usage, content, delivery methods, and access to such interventions are not always optimised, or even suitable. Importantly, no standardised European Alliance of Associations for Rheumatology (EULAR)-endorsed guidance has been developed for the non-pharmacological management of people with SLE and SSc. The absence of proper guidance hinders the widespread adoption of non-pharmacological interventions, representing a missed opportunity to enhance patient care to its fullest potential.

Hence, a EULAR task force convened to develop recommendations for the non-pharmacological management of SLE and SSc. Successful implementation of the recommendations is likely to result in improved quality of care for people with SLE and SSc across Europe and worldwide.

Methods

Steering committee and task force

Following the EULAR standard operating procedure (SOP) for the development of EULAR-endorsed recommendations,[6] the convener (CB; physiotherapist) formed the steering committee and task force. The steering committee included the convener, a methodologist (TS; outcomes researcher, health scientist, occupational therapist), a deputy methodologist (CG; rheumatologist), and a post-doctoral fellow within rheumatology who also was an Emerging EULAR network (EMEUNET)

representative and rheumatologist (IP; rheumatologist). In addition to the steering committee members, the task force comprised five rheumatologists (one representing EMEUNET), four nurses, two physiotherapists, two occupational therapists, two psychologists, one exercise psychologist, one dietician, one podiatrist, and three patient research partners. All healthcare professionals in the task force were experienced in managing patients with SLE and/or SSc. Many had also participated in clinical trials, observational studies, outcome research, and research deriving from quality registries. All task force members declared potential conflicts of interest prior to commencement of the task and updated those before submitting the manuscript.

Target audience

In compliance with the 2014 update of EULAR SOP for the development of EULAR-endorsed recommendations,[6] the main target audience of the recommendations presented herein is healthcare providers (health professionals in rheumatology and physicians), as well as people living with SLE or SSc. Nevertheless, the recommendations and the accompanying research and educational agenda derived by the task force also highlight important unmet needs, thus targeting policy makers and health insurance companies.

Definitions

Upon proposals by the steering committee, the task force agreed on definitions and uniform nomenclature concerning non-pharmacological management and its goals, as well as the patient population for a subsequent systematic literature review (SLR). These were discussed and amended until consensus during the first task force meeting, which was held remotely in December 2020.

The task force defined non-pharmacological management as all management that is not classified as pharmacological by the Directive 2001/83/EC of the European Parliament and the Council of the European Union (November 6, 2001) on the Community code relating to medicinal products for human use i.e., any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting, or modifying physiological functions by exerting a pharmacological, immunological, or metabolic action, or to making a medical diagnosis.[7, 8] In addition, non-registered pharmaceuticals under current investigation e.g., in clinical trials, were not considered non-pharmacological management. However, the task force included dietary substitutes, pre- and probiotics, and faecal microbiota transplants as non-pharmacological interventions, unless they are pharmaceuticals licensed by drug regulatory authorities.

Non-pharmacological management of connective tissue diseases (CTDs) may be invasive and non-invasive, and includes but is not limited to patient education,[9] self-management,[10] physical exercise,[11] lifestyle or behaviour interventions (e.g., photoprotection or smoking cessation),[12, 13] psychological counselling,[14] cognitive behavioural therapy,[15] relaxation or yoga,[16, 17] dietary, nutritional or microbiome interventions,[18, 19] stretching,[20] massage,[21] hand and foot interventions, assistive technology and devices,[22] mouth exercise therapy,[23] dental health and hygiene,[24] modalities such as paraffin baths,[25] shockwave therapy,[26] acupuncture[27] and transcutaneous electrical nerve stimulation (TENS),[28] hydrotherapy, and manual lymph drainage.[29] Furthermore, it may include skin and wound care, ulcer management (e.g., debridement),[30] minor surgical procedures such as calcinosis removal, and detection and management of malnutrition.[31]

Non-pharmacological management can be provided as a single intervention or a combination of several non-pharmacological interventions, and alone or adjunct to pharmaceutical treatment.[20, 32] Non-pharmacological management should not substitute pharmaceutical treatment when the latter is required.[33, 34]

The goals of non-pharmacological management of CTDs include but are not limited to optimisation of body function and structures, increased activities and participation,[11] as well as implementation of favourable environmental and personal factors as defined by the International Classification of Functioning nomenclature.[35] In this context, environmental factors include working and living conditions, health promotion services, access to insurance and treatments, housing and transportation, and social support. Personal factors include well-being, social integration, expectations, capacity to act, and lifestyle e.g., physical and intellectual activity, eating and drinking habits, and smoking.

To mention some examples, non-pharmacological management in CTDs aims for amelioration of disease symptoms,[36] improvement of HRQoL,[37] as well as prevention of disease progression, organ damage accrual,[38] co-morbidities (e.g., cardiovascular disease), and adverse events.[36] Additional aims include contribution to increased patient knowledge of the disease through structured patient education[9] and optimisation of psychosocial functioning[15] e.g., distress abatement, increased coping ability, alleviation of maladaptive illness perceptions and fear for disease progression, increased adherence to treatment, optimised care use, and improvement of work capacity.

While several aspects of non-pharmacological management may be generic or apply to more than one CTD, this task force focused on two CTDs i.e., SLE and SSc, and particularly adult patients. This decision was made to ensure feasibility and facilitate in-depth analysis within the given scope.

Research questions and systematic literature review

The task force formulated nine research questions to be addressed during the SLRs and should steer the development of the recommendation statements. Those comprised (i) what non-pharmacological management should aim for, (ii) which non-pharmacological interventions have been used, (iii) which non-pharmacological interventions have been shown to be efficacious, (iv) which instruments have been used to assess the outcome of non-pharmacological management, (v) when the outcome of non-pharmacological management should be assessed, (vi) within which health-related domains or organ systems non-pharmacological management should be assessed, (vii) SLE and SSc patients' needs, expectations, and preferences with regard to non-pharmacological management, (viii) the educational needs for healthcare providers and patients regarding non-pharmacological management, and (ix) identification of facilitators and barriers for the use of non-pharmacological management of SLE and SSc.

Subsequently, one SLR was performed about SLE and one about SSc, by the fellow (IP) and colleagues, under the supervision of the methodologists (TS, CG), in compliance with the 2014 update of the EULAR SOP.[6] The search strategies were designed in collaboration with an expert librarian from the Karolinska Institutet, Stockholm, Sweden. The MEDLINE, EMBASE, Web of Science and CINAHL databases were searched for content published between January 2000 and June 2021. For each SLR, a two-block search was conducted including the diagnosis of interest and a list of non-pharmacological management strategies. Case series of less than five individuals were excluded, as were articles in languages other than English, Spanish, or Swedish. Due to the diverse nature of the research questions, we did not exclude articles based on study design. Two independent reviewers screened the identified titles and abstracts for final selection. Disagreements between reviewers were discussed until consensus; the discussions were guided by the fellow (IP) and the convener (CB). All selected papers underwent risk of bias (RoB) assessment and were deemed robust, intermediate, or weak, using the Joanna Briggs Institute critical appraisal (CA) checklists.[39] The detailed process and results of the SLR are reported elsewhere.

Formulation of overarching principles and recommendation statements

Based on the results from the SLR and mainly driven by the overall CA, but also expert opinion, overarching principles and recommendation statements were proposed by the steering committee and were presented and discussed with the task force members at four consecutive online meetings in May and June 2022. In these meetings, 23, 20, 17, and 16 of 25 task force members participated, respectively.

Upon discussion and amendment of the overarching principles and recommendation statements, a voting process was applied for each statement. In the first round of this voting process, a majority of at least 75% was required to adopt the respective statement. If this was not reached, the statement was discussed and amended further. Subsequently, a second voting round was applied, where a majority of at least 66% was required for adoption of the rephrased statement. If this was not reached, the statement was discussed and amended further to next be subjected to a third voting round. In this third round, a majority of at least 50% was required for adoption of the rephrased statement. If this was not reached, the statement was discarded.

The voting process was supported by preformulated motivational texts summarising results of the SLR, including the result of the RoB and level of evidence (LoE) assessment, the latter based on the 2011 Oxford Centre for Evidence-Based Medicine LoE 2 system.[40] After the meetings, final LoE and strength of recommendation (SoR; scale A–D, with A comprising consistent LoE 1 studies and D comprising LoE 4 or inconsistent studies) assessment was performed following the 2011 Oxford Centre for Evidence-Based Medicine LoE 2 system[40] and the EULAR SOP.[6] The agreed upon overarching principles and recommendation statements were distributed to all task force members through the Research Electronic Data Capture (REDCap) system. Level of agreement (LoA) with each statement was scored in a pseudonymous manner on a scale from 0 (compete disagreement) to 10 (complete agreement). Results from the LoA scoring are presented in Table 1 as mean, standard deviation, and range.

Additionally, the task force proposed a research agenda based on identified needs (Table 2), as well as an educational agenda for providers of non-pharmacological management of people with SLE and SSc (Table 3).

Results

Twelve recommendations for the non-pharmacological management of people with SLE and SSc were developed based on evidence and expert opinion within the task force, emanating the derivation of four overarching principles, as detailed in Table 1. The recommendations were grouped into five generic recommendation statements applicable to people with SLE and people with SSc, four recommendation statements applicable to people with SLE, and three recommendation statements applicable to people with SSc. Examples of studies supporting each statement are provided.

Table 1. Recommendations for the non-pharmacological management of SLE and SSc

	LoE	SoR	LoA		
			Mean	SD	Range
Overarching principles					
1. Non-pharmacological management of SLE and SSc should be tailored to patients' needs, expectations, and preferences, and be based on a shared-decision making.	NA	NA	9.7	0.8	7–10
2. Non-pharmacological management of SLE and SSc may comprise one or more interventions.	NA	NA	9.7	0.5	8–10
3. Non-pharmacological management of SLE and SSc may be provided alone or as an adjunct to pharmaceutical treatment.	NA	NA	9.4	1.1	6–10
4. Non-pharmacological management of SLE and SSc should not substitute for pharmaceutical treatment when the latter is required.	NA	NA	9.6	0.8	7–10
Recommendations for the non-pharmacological management of SLE and SSc					
1. Non-pharmacological management should be directed toward improving health-related quality of life in people with SLE (LoE: 1–3) and SSc (LoE: 2–4).	1–4	C	9.4	1.1	6–10
2. People with SLE and SSc should be offered patient education and self-management support (LoE: 2–4).	2–4	C	9.7	0.7	7–10
3. In people with SLE (LoE: 3) and SSc (LoE: 4), smoking habits should be assessed, and cessation strategies should be implemented.	3–4	B/C	9.4	1.1	6–10
4. In people with SLE (LoE: 5) and SSc (LoE: 4), avoidance of cold exposure should be considered for the prevention of Raynaud's phenomenon. In people with SSc, this is of particular importance for the mitigation of severe Raynaud's phenomenon (LoE: 4).	4–5	C/D	9.4	0.9	7–10
5. Physical exercise should be considered for people with SLE (LoE: 1–3) and SSc (LoE: 2–4).	1–4	C	9.6	0.7	8–10
Recommendations for the non-pharmacological management of SLE					
1. In people with SLE, patient education and self-management support should be considered for improving physical exercise outcomes (LoE: 2) and HRQoL (LoE: 2–4), and could be considered for enhancing self-efficacy (LoE: 3).	2–4	C	9.4	0.9	8–10
2. In people with SLE, photoprotection should be advised for the prevention of flares (LoE: 4).	4	C	9.2	1.0	7–10
3. In people with SLE, psychosocial interventions should be considered for improving health-related quality of life (LoE: 1–2), anxiety (LoE: 1), and depressive symptoms (LoE: 1).	1–2	B	9.2	1.2	6–10
4. In people with SLE, aerobic exercise should be considered for increasing aerobic capacity (LoE: 1), and for reducing fatigue (LoE: 1–3) and depressive symptoms (LoE: 3).	1–3	B	9.2	1.4	4–10
Recommendations for the non-pharmacological management of SSc					
1. In people with SSc, patient education and self-management support should be considered for improving hand function (LoE: 2–4), mouth-related outcomes (LoE: 2), HRQoL (LoE: 2–4), and ability to perform daily activities (LoE: 2–3).	2–4	C	9.4	0.9	7–10
2. In people with SSc, orofacial, hand, and aerobic and resistance exercise should be considered for improving microstomia (LoE: 2–4), hand function (LoE: 2–4), and physical capacity (LoE: 2–4), respectively.	2–4	C	9.3	0.9	7–10
3. In people with SSc and puffy hands, manual lymph drainage could be considered for improving hand function (LoE: 2).	2	B	8.4	1.9	3–10

Table legends:
LoE was assessed using the 2011 Oxford Centre for Evidence-Based Medicine LoE 2 system. LoA with each statement was scored in a pseudonymous manner on a scale from 0 (compete disagreement) to 10 (complete agreement). SoR ranges from A to D, with A comprising consistent LoE 1 studies and D comprising LoE 4 or inconsistent studies.
LoE levels
LoE 1: Systematic reviews or meta-analyses of randomised controlled trials with consistent results.
LoE 2: Well-conducted randomised controlled trials.
LoE 3: Non-randomised controlled trials, cohort studies, case-control studies, or systematic reviews of these types of studies.
LoE 4: Case series, case reports, or studies with poor methodological quality.
LoE 5: Expert opinion or consensus statements.
Abbreviations
LoA: level of agreement; LoE: level of evidence; SD: standard deviation; SLE: systemic lupus erythematosus; SoR: strength of recommendation; SSc: systemic sclerosis.

Recommendations for the non-pharmacological management of SLE and SSc

1. Non-pharmacological management should be directed toward improving health-related quality of life in people with SLE (LoE: 1–3) **and SSc** (LoE: 2–4)**.**

Physical exercise[41] and psychological interventions[42] were found in meta-analyses of RCTs (two and three RCTs, respectively)[41, 42] (LoE: 1) to improve HRQoL in patients with SLE. Furthermore, non-pharmacological management in the form of physical exercise was proven efficacious in improving fatigue in patients with SLE based on two meta-analyses, one of an RCT and a quasi-experimental study (LoE: 3) and one of two RCTs and one quasi-experimental study (LoE: 1)[43, 44], and psychological interventions were found to improve anxiety in patients with SLE based on a meta-analysis of three RCTs[45] (LoE: 1); these studies were assessed as robust in RoB assessment.

In patients with SSc, improvements in HRQoL were noted after occupational therapy provided for improving upper extremity function in a quasi-experimental study[46] (LoE: 4). RCTs encompassing patients with SSc assessed as intermediate in critical appraisal found rehabilitative treatment of the hands[47] (LoE: 2) and home-based aerobic exercise[48] (LoE: 2) to improve HRQoL.

2. People with SLE and SSc should be offered patient education and self-management support (LoE: 2–4)**.**

RCTs assessed as intermediate in RoB assessment employed patient education as a part of physical exercise programmes. The addition of patient education was efficacious in improving aerobic capacity in an RCT of SLE[49] (LoE: 2) and mouth opening as compared with the same physical exercise programme (mouth stretching) in an RCT of SSc[50] (LoE: 2). Qualitative assessments of multidisciplinary patient education programmes[51] (LoE: 4) and group education on disease management[52] (LoE: 4) found these strategies to be beneficial for patients with SLE in terms of improving HRQoL[51] (LoE: 4), as well as for implementing favourable lifestyle changes[52] (LoE: 4); these studies were assessed as robust.

In patients with SSc, internet-based self-management programmes could improve self-efficacy and fatigue[53] (LoE: 4), and patient education as a complement to occupational therapy improved functional abilities over a longer term (i.e., 24 weeks)[54] (LoE: 3); these two quasi-experimental studies were deemed robust.

3. In people with SLE (LoE: 3) **and SSc** (LoE: 4)**, smoking habits should be assessed, and cessation strategies should be implemented.**

In the general population, tobacco smoking is an established risk factor for cardiovascular disease, cancer, osteoporosis, and chronic obstructive pulmonary disease, among other conditions that constitute relevant comorbidities for patients with SLE and SSc.[1, 4] A meta-analysis of 9 case-control studies found that current smokers had an approximately 50% increased risk for SLE compared with non-smokers (OR: 1.49; 95% CI: 1.06–2.08; p=0.02)[55] (LoE: 3; CA: robust). Moreover, among patients with SLE, smoking has been associated with reduced treatment efficacy. A meta-analysis of 10 observational studies found smoking to be negatively associated with the response of cutaneous SLE to antimalarial therapy (OR: 0.53; 95% CI: 0.31–0.93; p=0.002),[55] while prospective cohort studies have reported reduced overall belimumab efficacy in smokers compared with non-smokers in a Swedish[56] (LoE: 3; CA: robust) and an Italian SLE population[57] (LoE: 3; CA: robust), as well as reduced belimumab efficacy in mucocutaneous disease activity[58] (LoE: 3; CA: robust).

In the SSc population, a cross-sectional study of 101 patients found that current smokers were more likely to require intravenous vasodilators (OR: 3.8; 95% CI: 1.1–12.9) and digital debridement (OR: 4.5; 95% CI: 1.1–18.3) for digital vascular disease compared with non-smokers[59] (LoE: 4; CA: robust). Similarly, in a cohort study using the European Scleroderma Trials and Research (EUSTAR) database, heavy smokers (>25 pack-years) had an increased risk for digital ulcers (OR: 1.6; 95% CI: 1.1–2.3) compared with non-smokers, although no differences were observed in skin fibrosis or gastrointestinal symptoms across different smoking status groups[60] (LoE: 4; CA: robust). In the Canadian Scleroderma Research Group cohort, smoking was found to have a negative impact on vascular, gastrointestinal, and respiratory outcomes, while cessation was associated with reduced severity of Raynaud's phenomenon[61] (LoE: 4; CA: robust).

Despite the lack of interventional studies specifically assessing the efficacy of smoking cessation strategies in the SLR performed to inform the recommendations, it was consensual among the task force members that smoking cessation should be encouraged and facilitated in smokers with SLE and SSc based on the above evidence and expert opinion. Nevertheless, cost-effectiveness aspects should be accounted

for, and there should be awareness that literature is inconsistent regarding the effect of smoking on vascular outcomes.[62]

4. In people with SLE (LoE: 5) **and SSc** (LoE: 4)**, avoidance of cold exposure should be considered for the prevention of Raynaud's phenomenon. In people with SSc, this is of particular importance for the mitigation of severe Raynaud's phenomenon** (LoE: 4)**.**

Raynaud's phenomenon constitutes one of the most frequent and troublesome manifestations of SSc.[63] Albeit less frequent, Raynaud's phenomenon also impacts negatively on SLE patients' hand function and performance of daily activities.[64] Cold exposure and sudden temperature changes trigger episodes of Raynaud's phenomenon acknowledged by healthcare providers and patients. In a qualitative study, patients with SSc identified cold as the main exacerbating factor for Raynaud's phenomenon[65] (LoE: 4; CA: robust). In a cross-sectional study, SSc patients reported more frequent and longer Raynaud's phenomenon exacerbations during winter compared with summer[66] (LoE: 4; CA: intermediate). Consistently, cold challenge induces delayed reperfusion as evidenced by imaging techniques in people suffering from Raynaud´s phenomenon[67] (LoE: 4; CA: robust). Lastly, the task force argued that practical advice to people with SSc suffering from Raynaud's phenomenon may include the use of gloves and heating devices for the hands, avoidance of direct contact with cold surfaces, and a thorough drying of the skin, as recommended by the Arthritis Research and Collaboration Hub study group.[5] A recent RCT corroborated that gloves decrease the burden of Raynaud's phenomenon, but silver fibre gloves yielded no difference compared with conventional ones[68] (LoE: 2; CA: robust).

5. Physical exercise should be considered for people with SLE (LoE: 1–3) **and SSc** (LoE: 2–4)**.**

For both diseases, exercise and promotion of physical activity were among the most studied intervention strategies and were found to improve patient outcomes in several studies. Physical exercise was found to be a viable management strategy in improving fatigue in adult patients with SLE based on two meta-analyses, one of one RCT and one quasi-experimental study (LoE: 3) and one of two RCTs and one quasi-experimental study (LoE: 1)[43, 44], and in improving aerobic capacity, based on one meta-analysis of seven RCTs[43] (LoE: 1); both studies were deemed as robust in overall critical appraisal. In adult patients with SSc, an RCT found improvements in mouth opening after application of an oral exercise programme[23] (LoE: 2; CA: intermediate). Physiotherapy was found to improve functional impairment in a quasi-experimental study[69] (LoE: 4; CA: robust).

The task force felt that it is important to underline that the patient's health status, cardiorespiratory status in particular, potential risks, or medical contraindications should always be

considered before commencing physical exercise programmes, and such programmes should be provided or suggested based on risk and benefit ponderation. Moreover, it is important that physical exercise programmes are tailored to each individual patient, based not only on the risk/benefit ratio but also the patient's individual needs, expectations, and preferences.

Recommendations for the non-pharmacological management of SLE

1. In people with SLE, patient education and self-management support should be considered for improving physical exercise outcomes (LoE: 2) **and HRQoL** (LoE: 2–4)**, and could be considered for enhancing self-efficacy** (LoE: 3)**.**

An RCT employed patient education and self-management support as parts of a supervised aerobic exercise programme and found the intervention to be efficacious in improving aerobic capacity and mental health as compared with usual care in an RCT of SLE[49] (LoE: 2; CA: intermediate). Furthermore, an RCT that investigated web-based patient education and counselling[14] (LoE: 3; CA: weak) and a quasi-experimental study that examined an educational programme for enhancing self-management in patients with SLE[70] (LoE: 3; CA: intermediate) found these interventions to be efficacious in improving self-efficacy. A pilot RCT that investigated an internet-based coping skills training programme in patients with SLE revealed benefit in HRQoL[71] (LoE: 3; CA: weak), as did a qualitative study of multidisciplinary patient education[51] (LoE: 4; CA: robust).

2. In people with SLE, photoprotection should be advised for the prevention of flares (LoE: 4)**.**

Ultraviolet (UV) radiation is a well-acknowledged triggering factor of cutaneous and systemic lupus flares.[72, 73] Quasi-experimental studies have shown that broad-spectrum sunscreens prevent cutaneous lesions upon photo-provocation (LoE: 4; CA: robust[74] and LoE: 4; CA: weak[75]). Based on this evidence and expert opinion within the task force, people with SLE should avoid direct sun exposure, especially during days with high UV index, use physical barriers such as hats, sunglasses, and long-sleeved shirts and pants, and use broad-spectrum sunscreen; assessment of the need for vitamin D supplements should be done when indicated.[1, 72]

3. In people with SLE, psychosocial interventions should be considered for improving health-related quality of life (LoE: 1–2)**, anxiety** (LoE: 1)**, and depressive symptoms** (LoE: 1)**.**

In systematic literature reviews with meta-analyses that were assessed as robust in overall critical appraisal, psychological interventions in the form of cognitive behavioural therapy (CBT), group therapy, and psychoeducational programmes were shown to be an efficacious management strategy for improving

HRQoL in adults with SLE based on a meta-analysis of two RCTs[41] (LoE: 2) and a meta-analysis of three RCTs[42] (LoE: 1). Counselling, CBT, and supported psychotherapy improved anxiety based on a meta-analysis of three RCTs[45] (LoE: 1). CBT and psychoeducational self-management support ameliorated depressive symptoms based on a meta-analysis of three RCTs[42] (LoE: 1). Counselling and psychoeducational programmes were led by different healthcare providers, including social workers, psychologists, and nurses, whereas psychotherapeutic interventions were delivered by certified psychotherapists. Which healthcare providers deliver different psychoeducational programmes may differ considerably across countries, depending on local legislation, as well as access to and use of resources.

4. In people with SLE, aerobic exercise should be considered for increasing aerobic capacity (LoE: 1)**, and for reducing fatigue** (LoE: 1–3) **and depressive symptoms** (LoE: 3)**.**

A systematic literature review with meta-analyses from 2017 found that aerobic exercise increased aerobic capacity in patients with SLE (based on a meta-analysis of two RCTs and three quasi-experimental studies; LoE: 1), while decreasing fatigue (based on a meta-analysis of one RCT and one quasi-experimental study; LoE: 3), and depressive symptoms (based on a meta-analysis of two RCTs and one quasi-experimental study; LoE: 3),[43] and was assessed as robust in critical appraisal. Another meta-analysis of two RCTs and one quasi-experimental study assessed as robust in critical appraisal found that aerobic physical exercise was effective in managing fatigue in patients with SLE[44] (LoE: 1). Moreover, aerobic exercise improved functional performance as assessed using the six-minute walk distance (6MWD) test in an RCT deemed as intermediate in critical appraisal[76] (LoE: 2).

Recommendations for the non-pharmacological management of SSc

1. In people with SSc, patient education and self-management support should be considered for improving hand function (LoE: 2–4)**, mouth-related outcomes** (LoE: 2)**, HRQoL** (LoE: 2–4)**, and ability to perform daily activities** (LoE: 2–3)**.**

An RCT found self-administered hand exercises effective in improving hand mobility[77] (LoE: 2; CA: intermediate). Another RCT demonstrated the efficacy of face-to-face training in improving the outcomes of orofacial exercise[50] (LoE: 2; CA: intermediate). An RCT assessed as intermediate in critical appraisal found that home-based exercise comprising aerobic exercise on a stationary bike, muscular endurance training of the upper limb, and stretching exercises for the hands, following a physiotherapist-supported educational programme, was effective in improving SSc patients' HRQoL and functional ability[48] (LoE: 2). Individualised rehabilitation programmes were found to improve hand mobility and

HRQoL[78] (LoE: 3) while psychoeducational group programmes ameliorated feelings of helplessness[79] (LoE: 4) in quasi-experimental studies of patients with SSc assessed as robust in overall critical appraisal. Another robust in critical appraisal quasi-experimental study found patient education as a complement to occupational therapy to improve functional abilities as assessed with the Health Assessment Questionnaire (HAQ) and the Evaluation of Daily Activity Questionnaire (EDAQ)[54] (LoE: 3). A home-based self-management programme for hand exercise was found to improve hand function in a quasi-experimental study[80] that was also deemed as robust in critical appraisal (LoE: 4).

2. In people with SSc, orofacial, hand, and aerobic and resistance exercise should be considered for improving microstomia (LoE: 2–4)**, hand function** (LoE: 2–4)**, and physical capacity** (LoE: 2–4)**, respectively.**

Microstomia and hand function emerged as major targets of non-pharmacological management, especially in studies evaluating physical exercise. RCTs assessed as intermediate in critical appraisal found mouth exercise to be efficacious in improving microstomia[23] (LoE: 2) and hand exercise in improving hand function[77] (LoE: 2), while body exercise increased the 6MWD[48] (LoE: 2). The favourable effects of rehabilitation programmes were discussed. Quasi-experimental studies assessed as robust in critical appraisal found that rehabilitative exercise programmes were efficacious in improving hand function and HRQoL e.g., programmes comprising warm-up and cool-down exercises, training of motor functions, and respiratory exercises[78] (LoE: 3), mouth stretching and oral augmentation exercises ameliorated microstomia[81] (LoE: 4), thermal modalities (e.g., baths), tissue mobilisation, and hand mobility exercises improved hand function[46] (LoE: 4), and combined resistance and aerobic exercise enhanced aerobic capacity[82] (LoE: 4) in patients with SSc.

3. In people with SSc and puffy hands, manual lymph drainage could be considered for improving hand function (LoE: 2)**.**

One RCT examined the effect of five weekly sessions of manual lymph drainage (MLD) compared with usual care in SSc patients with oedematous hands and found that MLD improved hand function measured using the Hand Mobility in Scleroderma index (HAMIS) and SSc patients' perception of upper extremity function assessed using visual analogue scales[83] (LoE: 2; CA: robust). The improvements in these outcomes were maintained up to nine weeks after treatment discontinuation. Improvements were also noted in HAQ and 36-item Short Form health survey (SF-36) scores at the end of treatment, although these improvements were not fully sustained at the 9-week follow-up. The findings from this study and expert opinion within the task force supported the endorsement of this recommendation statement.

Research agenda

Table 2 details the research agenda proposed by the task force. This was based on areas of limited or weak evidence, as well as identified needs. The overarching principles should be applied when addressing the proposed research topics.

In brief, while the SLR identified several RCTs dealing with the non-pharmacological management of SLE and SSc, design details were not always clearly indicated, especially the blinding strategies, which limited their level of evidence. Identification of patients' needs is essential, and strategies for identification of such needs should be implemented e.g., as suggested by the James Lind Alliance Priority Setting Partnerships.[84, 85] The majority of interventional studies had a limited follow-up time of 4–12 weeks, seldom longer. Hence, studies assessing outcomes of non-pharmacological management over a longer term are needed.

While the efficacy of diverse psychological interventions was investigated in several studies encompassing people with SLE, it has yet to be explored within SSc. Dietary therapy was not thoroughly explored in either of the two diseases. Adherence to a Mediterranean diet was associated with a lower cardiovascular risk, lower disease activity levels, and protection against organ damage in a cross-sectional study of SLE assessed as robust in critical appraisal[36] (LoE: 3), but no conclusions regarding causality can be drawn from this study.

Moreover, recommendations about wound management could not be derived based on current evidence, indicating a need for further studies within this area, which is particularly important for patients with SSc. Lastly, further identification of barriers for the implementation of non-pharmacological management of SLE and SSc, as well as means to alleviate those barriers, is warranted.

Table 2. Research agenda

1. RCTs of non-pharmacological management of people with SLE and SSc with blinding strategies detailed in the study protocols are encouraged.
2. Identification of patients' needs for non-pharmacological management is essential, and strategies for identification of such needs should be implemented.
3. Studies assessing outcomes of non-pharmacological management over a longer term are needed.
4. Investigation of the efficacy of psychosocial interventions in patients with SSc is required.
5. Investigation of the efficacy of skin and wound management strategies is required, particularly for people with SSc.
6. Investigation of the efficacy of different dietary programmes is encouraged.
7. Further identification of barriers for the implementation of non-pharmacological management of SLE and SSc, as well as means to alleviate those barriers, is warranted.

Abbreviations:*SLE: systemic lupus erythematosus; SSc: systemic sclerosis.*

Educational agenda for providers of non-pharmacological management of SLE and SSc

Table 3 details the educational agenda proposed by the task force for providers of non-pharmacological management of people with SLE and SSc. The purpose of this agenda is to enhance the healthcare professionals' skills and competencies as well as the confidence needed for providing these services.

Table 3. Educational agenda for providers of non-pharmacological management of SLE and SSc

1. Regular training for providers of non-pharmacological management of SLE and SSc is advised to ensure the best possible quality of services and patient outcomes.
2. Increased awareness and education on how to facilitate and evaluate patient education and self-management for people with SLE and SSc should be reinforced among healthcare professionals.
3. Educational programmes within EULAR and EMEUNET dedicated to the non-pharmacological management of people with SLE and SSc are advocated, both for healthcare providers and patients. This could be done in collaboration with the EULAR School of Rheumatology.

Abbreviations: *EULAR: European Alliance of Associations for Rheumatology; EMEUNET: Emerging EULAR network; SLE: systemic lupus erythematosus; SSc: systemic sclerosis.*

Discussion

Increasing awareness of the importance of non-pharmacological management and self-management strategies for people living with SLE and SSc necessitated the development of overarching principles and recommendations by a group of experts, to be used as a guide in the identification of needs, implementation, and evaluation of non-pharmacological management. Hence, a multidisciplinary EULAR task force convened and formulated the overarching principles and recommendations presented herein following standard operating procedures.[6] A systematic literature review preceded to inform the recommendations. Along with recommendations regarding lifestyle behaviours[86] as well as recommendations for physical activity,[87] patient education,[88] and implementation of self-management strategies in inflammatory arthritis[89], the statements presented herein intend to not only guide non-pharmacological management, but also increase awareness of the importance of patient involvement in the management of their disease, encourage interprofessional and multidisciplinary teams to tackle clinical challenges and prompt orchestrated research for addressing remaining important questions that form a research agenda, as determined by the task force.

The heterogeneity in study design and conduct limited the level of evidence and strength of recommendation in several instances. Data in the literature were scarce even for well-established non-pharmacological strategies such as photoprotection for patients with SLE, which is not surprising considering the known contribution of sun exposure to disease precipitation, imposing ethical limitations for the conduct of RCTs on such interventions. The same could be argued for the contribution of assistive

devices to enhancing mobility or improving accessibility, which is rather self-evident. Nonetheless, the rarity of SLE and SSc necessitate global collaborative efforts in the design of studies, especially investigator-initiated endeavours that deserve better funding.

Moderate to strong evidence existed in the literature for the benefits of physical activity and exercise for SLE and SSc patients, including documented benefits regarding HRQoL, fatigue, and cardiovascular burden.[33, 90-103] Despite sparse evidence regarding smoking cessation for improving disease activity and treatment outcomes and avoidance of cold exposure for the prevention of Raynaud's phenomenon, the task force agreed on the crucial importance of these two recommendations. The task force also agreed that cost-effectiveness aspects should be accounted for; to illustrate why, proper modelling of the effect of smoking has been shown to be essential in studies of vascular outcomes within rheumatic diseases, SSc in particular, resulting in rather insipid evidence.[62]

It is important to underscore that concomitant conditions such as fibromyalgia or other syndromes causing chronic pain, as well as established irreversible organ damage, pose challenges when evaluating the effectiveness of non-pharmacological management. Together with the complexity of SLE and SSc in terms of heterogeneity of disease manifestations, the multidimensionality of non-pharmacological interventions and sparsity of high-quality data and RCTs, especially RCTs meeting their predetermined endpoints, is not unexpected. These factors also form incentives for large-scale collaborative efforts to determine patient needs and priorities, identify barriers and means for overcoming them, and investigate the efficacy of psychosocial interventions, different dietary schemes, and skin and wound management. Also, efforts should be applied in educating healthcare professionals and patients on the potentiality of different non-pharmacological strategies, which in turn is expected to facilitate person-centredness in non-pharmacological management, accounting for the heterogeneity of SLE and SSc. While implementation of the recommendations will be conducted at various phases according to Loza et al.,[104] a first step will be a survey-based investigation of SLE and SSc patients' and healthcare professionals' perception of whether the recommendations and overarching principles align with current management praxis across different countries, as well as their views on facilitators and barriers they foresee for their implementation. This will provide an important mapping of the current practice patterns and highlight needs for the implementation. Further steps will include determination of implementation strategies at a centre, national, or international level such as educational activities designed for patients and for healthcare professionals, and evaluation of the implementation.

In summary, results from a systematic literature review, risk of bias assessment, and expert opinion within the task force resulted in the formulation of overarching principles and a comprehensive

set of recommendations for the non-pharmacological management of people living with SLE and SSc. The overarching principles and recommendations presented herein promote holistic and multidisciplinary approaches in SLE and SSc patient management, patient involvement in their care, and individually tailored strategies toward optimised outcomes. Despite a sparsity in high-quality evidence, the recommendations presented herein may be seen as a useful guide for healthcare providers and patients with SLE and SSc when setting up individual disease management strategies, with non-pharmacological constituents as integral components. Last but not least, the task force developed a research agenda to guide future endeavours in the field.

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Contributors

IP wrote the first draft of the manuscript with help and guidance from CG, TS, and CB. All authors participated in the work of the task force, including the formulation of the overarching principles and recommendation statements, as well as read and approved the final manuscript. The convenor (CB) is responsible for the overall content as guarantor, controlled the decision to publish, and accepts full responsibility for the finished work and conduct of the project.

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Patient and public involvement

Patient research partners were involved in the design, conduct, reporting, and dissemination plans of this research. Further details are found in the Methods section.

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