Portuguese multidisciplinary recommendations for non-pharmacological and non-surgical interventions in patients with rheumatoid arthritis

Santos EJF[1], Duarte C[2], Ferreira RJ[3], Pinto AM[4], Moreira A[5], Vaz C[6], Branco CA[7], Mateus E[8], Canhão H[9], Campos I[10], Barbosa I[11], Fonseca JE[12], da Silva JC[13], Mourão MH[14], Costa R[15], da Silva JAP[2]

ACTA REUMATOL PORT. 2021;46:40-54

ABSTRACT

Background: Patients with rheumatoid arthritis (RA) report significant levels of disease impact, which are improved, but not fully abrogated by immunosuppressive therapy, even when remission is achieved. This imposes the need for adjuvant interventions targeting the uncontrolled domains of disease impact. Non-pharmacological interventions are widely used for this purpose, but they have not been the object of professional recommendations or guidelines.

Objective: To propose multidisciplinary recommendations to inform clinical care providers regarding the employment of non-pharmacological and non-surgical interventions in the management of patients with RA.

Methods: The EULAR standardized operating procedures for the development of recommendations were followed. First, a systematic literature review was performed. Then, a multidisciplinary Technical Expert Panel (TEP) met to develop and discuss the recommendations and research agenda. For each developed recommendation i) the level of evidence and grade of recommendation were determined, and ii) the level of agreement among TEP members was set. A recommendation was adopted if approved by ≥75% of the TEP members, and the level of agreement was considered high when ≥8. All relevant national societies were included in this construction process to attain their endorsement.

Results: Based on evidence and expert opinion, the TEP developed and agreed on five overarching principles and 12 recommendations for non-pharmacological and non-surgical interventions in patients with RA. The mean level of agreement between the TEP members ranged between 8.5 and 9.9. The recommendations include a broad spectrum of intervention areas, such as exercise, hydrokinesiotherapy, psychological interventions, orthoses, education, general manage-

1. Rheumatology Department - Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal. Abel Salazar Institute of Biomedical Sciences, University of Porto, Porto, Portugal. Health Sciences Research Unit: Nursing (UICISA: E), Nursing School of Coimbra
2. Rheumatology Department - Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal. Coimbra Institute for Clinical and Biomedical Research (iCBR) - Faculty of Medicine, University of Coimbra, Coimbra, Portugal
3. Rheumatology Department - Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal. Health Sciences Research Unit: Nursing (UICISA: E), Nursing School of Coimbra (ESEnfC), Portugal
4. Center for Research in Neuropsychology and Cognitive and Behavioral Intervention (CINEICC), Faculty of Psychology and Educational Sciences, University of Coimbra, Coimbra, Portugal. Psychological Medicine Institute, Faculty of Medicine, University of Coimbra
5. Clínica Manustrata, Portugal;
6. Medicine Department, Rheumatology, Faculdade de Medicina da Universidade do Porto (FMUP); Rheumatology Service, Centro Hospitalar Universitário S. João (CHUSJ) - Porto, Portugal
7. Physical and Rehabilitation Medicine Department-CHEDV-Feira; FMD Porto University, Portuguese Society of Physical and Rehabilitation Medicine (SPMFR)
8. Portuguese League Against Rheumatic Diseases (LPCDR)
9. CHRC, Comprehensive Health Research Center, CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Portugal. CHULC, Rheumatology Unit, Lisboa, Portugal
10. Rehabilitation Center - Rovisco Pais. Portuguese Society of Physical and Rehabilitation Medicine (SPMFR)
11. Unidade Local de Saúde do Alto Minho, Hospital Conde de Bertiandos, Serviço Hospital de Dia, Portugal
12. Serviço de Reumatologia e Doenças Ósseas Metabólicas, Hospital de Santa Maria, CHULN, Centro Académico de Medicina de Lisboa, Portugal. Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa
13. Chefe de Serviço de Reumatologia, Diretor médico da Consulreuma, Portugal
14. Sócia da Associação Nacional de Doentes com Artrite Reumatóide (ANDAR)
15. School of Health Sciences, University of Aveiro (ESSUA), Institute for Research in Biomedicine - University of Aveiro, Portugal

ment of comorbidities, among others; and they set the requirements for their application.

Conclusions: These recommendations are based on the consensus judgment of clinical experts from a wide range of disciplines and patients' representatives from Portugal. Given the evidence for effectiveness, feasibility and safety, non-pharmacological and non-surgical interventions should be an integral part of standard care for people with RA. It is hoped that these recommendations should be widely implemented in clinical practice. The target audience for these recommendations includes all health professionals involved in the care of patients with RA. The target patient population includes adult Portuguese people with RA.

Keywords: Non-pharmacological interventions; Rheumatoid arthritis; Portugal; Recommendations.

BACKGROUND

The management of rheumatoid arthritis (RA) has changed considerably over the past two decades under the influence of new drugs (such as biological agents) and new treatment strategies[1-4]. The current paradigm of RA treatment is epitomized by the Treat-to-Target (T2T) strategy, which establishes that remission is the core therapeutic target and should be achieved as early and as permanently as possible. Remission of the disease, ie complete abrogation of inflammatory activity, provides the best possible conditions to reduce suffering, stop joint damage, prevent disability, and improve quality of life in the long-term[1,2,5,6].

Remission has a markedly positive impact upon patient reported outcomes[2, 5, 7-10]. However, a considerable proportion (14 to 38%) of patients with RA are not in remission only due to a high patient global assessment (PGA) of disease activity and, still report significant levels of disease impact, similar to those described by patients with active disease[11-15]. This so called "PGA--near-remission" status typifies a frequent failure of the treatment strategy aimed at controlling the disease process in achieving the ultimate goal of therapeutic intervention: the enjoyment of life[16]. These patients cannot be improved by additional immunosuppressive therapy, but rather require the introduction of adjunctive interventions targeting the uncontrolled domains of disease impact[17].

The optimal care of patients with RA imposes, therefore, the need for an integrated approach, targeting both the biological remission and the remission of the impact upon patients' lives: the dual-target strategy[17]. This will require both pharmacological and non-pharmacological interventions[18], ideally in the context of a multidisciplinary team[16,19,20]. However, there are currently no recommendations regarding the use of interventions adjunctive to immunosuppressive therapy in RA[21-23]. Besides, it is important to understand how patients perceive remission[24] and how they prioritize treatment outcomes[25], since it may affect nonacceptance or nonadherence to treatment goals and protocols[9], and even to non-pharmacological interventions[26].

The aim of this paper is to propose multidisciplinary recommendations to inform clinical care providers regarding the employment of non-pharmacological and non-surgical interventions in the management of patients with RA.

Its evidence base was essentially provided by a recently performed umbrella review[27] of the effectiveness of such interventions upon the seven main domains of impact of RA identified by patients: pain, functional disability, fatigue, emotional well-being, sleep, coping, and physical well-being[28].

METHODS

To develop these recommendations, a set of rigorous steps were taken, based on the EULAR standardized operating procedures[29].

1st STEP – SYSTEMATIC REVIEW

A systematic literature review (SLR), specifically an umbrella review [30] was conducted by the proponents of this project (EJFS, CD, RJOF and JAPS) following the Joanna Briggs Institute methodology[27]. It aimed at determining the effectiveness of non-pharmacological and non-surgical interventions upon the impact of RA and included studies of adult patients in any context. The search strategy was applied to 13 bibliometric databases and grey literature (CINAHL Plus with Full Text, PubMed, Cochrane Database of Systematic Reviews, Scopus, Embase, PsycINFO, PEDro, Epistemonikos, *JBI Database of Systematic Reviews and Implementation Reports*, the PROSPERO register, Campbell Collaboration Library of Systematic Reviews, RCAAP – Repositório Científico de Acesso Aberto de Portugal; OpenGrey – System for Information on Grey Literature in Europe). It included interventions of any form, duration, frequency and intensity, alone or in combination,

designed to reduce the impact of the disease. The outcomes considered were pain, functional disability, fatigue, emotional well-being, sleep, coping, physical well-being and global impact of disease. Critical appraisal of reports was conducted independently by two reviewers (ES and CD), using the Joanna Briggs Institute critical appraisal checklist for systematic reviews and research syntheses. Data extraction was also performed independently by two reviewers and data was summarized using a tabular format with supporting text (for detailed methodology see Santos EJF *et al.*[27]). The results were organized in a summary of findings using The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) which provides an approach to grading quality of evidence based on risk of bias, heterogeneity, indirectness, imprecision and publication bias[31].

2nd STEP – FOCUSED TECHNICAL EXPERT PANEL (TEP) ON RA

The focused TEP on RA included the proponents, four rheumatologists, two specialist physicians representing the Portuguese Society for Physical Medicine and Rehabilitation (SPMFR), four representative members of the Portuguese Association of Health Professionals in Rheumatology (APPSReuma; one nurse, one physical therapist, one psychologist and one occupational therapist), all with extensive experience in clinical care and research in the field of RA. These health professionals (HPs) were nominated as representatives for this purpose by their respective scientific societies. Rheumatologists were individually invited on the basis of expertise in this field. All involved societies endorsed the final versions of this manuscript. This TEP also incorporated two patients, representing the Portuguese League Against Rheumatic Diseases (LPCDR) and the National Association of Patients with Rheumatoid Arthritis (ANDAR). As requirements, patients had to understand English, had to have more than 10 years of disease duration (RA) and had been treated with at least one biological agent.

TEP members received the results of the SLR and were asked to individually draft overarching principles (background statements to preface recommendations), recommendations, and research agenda points. These proposals were compiled and aggregated into a first draft of statements for consensual evaluation during a plenary meeting, where the final overarching principles, recommendations, and research agenda were consensualized through an iterative process of discussion and rewording. Adoption of each statement required the approval of at least 75% of the TEP members. If majority was not reached, changes were introduced until the agreement of ¾ of the participants was achieved. Additional literature searches were conducted where the evidence provided by the SLR was considered contradictory or insufficient (e.g. hydrotherapy/balneotherapy interventions are general, unspecific, and have contradictory evidence, and more specific and sensitive literature searches were needed for the case of hydrokinesiotherapy).

At last, each TEP member was asked to rate the level of agreement (LoA) with each statement, independently and anonymously on a numeric rating scale (0=totally disagree, 10= totally agree) through an online survey. The mean and SD were calculated. A mean LoA≥ 8 was considered 'high'. A draft version of this paper was circulated and revised by TEP members until consensus was achieved.

3rd STEP – ACCEPTANCE OF RECOMMENDATIONS

The recommendations were sent to all previously involved associations (Sociedade Portuguesa de Reumatologia - SPR, SPMFR, APPSReuma, LPCDR and ANDAR) for public consultation of their members.

They were asked to express any critical views regarding clarity, content or omissions. The final version was improved with these inputs.

4th STEP – ENDORSEMENT BY SCIENTIFIC SOCIETIES

The article incorporating the views of TEP members was sent to the Portuguese Society of Rheumatology (SPR), the Portuguese Society for Physical Medicine and Rehabilitation (SPMFR), the Portuguese Association of Health Professionals in Rheumatology (APPSReuma), the Portuguese League Against Rheumatic Diseases (LPCDR) and the National Association of Patients with Rheumatoid Arthritis (ANDAR) for endorsement.

RESULTS

The TEP agreed on five overarching principles and 12 recommendations for non-pharmacological and non-surgical interventions in the management of RA, based on SLR and expert opinion. High LoA was achieved for all recommendations. Table I summarizes the overarching principles and recommendations with their as-

TABLE I. RECOMMENDATIONS FOR NON-PHARMACOLOGICAL AND NON-SURGICAL INTERVENTIONS IN PEOPLE WITH RHEUMATOID ARTHRITIS

	LoE*	GoR†	LoA (0-10)
Overarching principles			
A. The primary goal of non-pharmacological and non-surgical interventions in RA is to assist patients in maximizing their overall quality and enjoyment of life, through optimized control of the impact of disease, besides and beyond medications and surgery.	-	-	9.9 (0.3)
B. Patients must be given a decisive role in establishing the objectives and the nature of interventions in their particular case, in an informed and shared decision-making process.	-	-	9.7 (0.6)
C. The healthcare team must make sure that the patient has all the information deemed relevant to support his/her participation in self-care and in shared-decision making, including the short and long-term outlook of the disease and of the available scope of treatments and interventions.	-	-	9.8 (0.5)
D. Non-pharmacological and non-surgical interventions demand the involvement of a multiprofessional/ multidisciplinary team, and the adoption of an holistic bio-psycho-social model.	-	-	9.8 (0.5)
E. Non-pharmacological and non-surgical interventions should be selected on the basis of the available evidence and adjusted to the patient's specific clinical features, abilities, preferences and needs.	-	-	9.9 (0.5)
Recommendations			
1. Non-pharmacological and non-surgical interventions should be an integral part of standard care in people with RA and should be considered throughout the course of the disease, whenever they may provide relevant, objective or subjective, benefit to the patient, as adjuvant or as an alternative to symptomatic medication or surgery.	1a	A	9.6 (0.7)
2. Areas of intervention to be considered in this context include, but are not limited to: self-management, pain relief, energy management, joint alignment and support, thermotherapy, exercise, hydrokinesiotherapy, psychological interventions, daily leisure and work activities, education, family involvement, social participation and social care, sleep hygiene and general management of comorbidities.	5	D	9.2 (1.3)
3. Dedicated educational programs and supporting materials should be made available to patients, providing information on the general aspects of the disease and its management, their role in the shared-care process and the specificities of common assessments and interventions.	1a	B	9.8 (0.6)
4. Patients should be regularly inquired for unmet needs, through the use of validated large-scope instruments, and referenced to the most appropriate health professional(s) in the team.	2b	B	9.1 (1.4)
5. The multiprofessional team must try to make interventions as attractive and relevant as possible to patients, as a mean to ensure the best possible adherence and long-term effectiveness.	2b	B	9.8 (0.5)
6. Interventions should be targeted to specific objectives that are relevant to the individual patients, regularly monitored with validated instruments and adapted accordingly.	3	C	9.6 (0.7)
7. All patients should be stimulated to follow a personalized and regular physical exercise program to reduce pain, functional disability, fatigue and global impact of disease.	1a	B	9.7 (0.7)

Continues on the next page

TABLE I. CONTINUATION

	LoE*	GoR†	LoA (0-10)
8. Hydrokinesiotherapy should be considered, to reduce pain and global impact of disease.	2b	B	9.2 (1.0)
9. Orthoses should be considered as a mean to reduce joint pain, functional disability and global impact of disease.	1a	B	9.1 (1.1)
10. Psychosocial interventions should be considered as a mean to reduce pain, functional disability, fatigue and global impact of disease.	1a	B	9.6 (0.9)
11. The prevention and management of comorbidities and adverse effects of all types of interventions should be part of the multiprofessional team goals.	3	C	9.8 (0.5)
12. Commonly used non-pharmacological interventions, without solid experimental evidence support may be considered in individual patients, if and only if: i) there is no reasonable and proven alternative; ii) they have merited consensual approval by qualified health professionals; iii) they are safe and accepted by a duly informed patient.	5	D	8.5 (1.5)

These recommendations should be interpreted in the light of the clarifications provided in the body of the text and by the supporting SLR. *1a: systematic review of RCTs; 1b: individual RCT; 2a: systematic review of cohort studies; 2b: individual cohort study (including low-quality RCT; eg,<80% follow-up); 3a: systematic review of case-control studies; 3b: individual case-control study; 4: case-series (and poor quality cohort and case-control studies); 5: expert opinion without explicit critical appraisal, or based on physiology, bench research or 'first principles'. † A: based on consistent level 1 evidence; B: based on consistent level 2 or 3 evidence or extrapolations from level 1 evidence; C: based on level 4 evidence or extrapolations from level 2 or 3 evidence; D: based on level 5 evidence or on troublingly inconsistent or inconclusive studies of any level. LoE, level of evidence; GoR, grade of recommendation; LoA, level of agreement.

sociated level of evidence, grade of recommendation and LoA. A Portuguese translated version of the recommendations is also provided (Table Ia - annex).

Recommendation 1: Non-pharmacological and non-surgical interventions should be an integral part of standard care in patients with RA and should be considered throughout the course of the disease, whenever they may provide relevant, objective or subjective, benefit to the patient, as adjuvant or as an alternative to symptomatic medication or surgery.

Given the evidence for effectiveness, feasibility and safety, non-pharmacological and non-surgical interventions should be an integral part of the standard of care for patients with RA. Non-pharmacological and non-surgical interventions are effective in reducing pain, functional disability, fatigue and the global impact of RA[21, 27, 32-38], but they are not expected to change the disease process.

Our umbrella review included 8 SLR with a total of 91 RCTs and 9 observational studies (6740 participants) and showed that multicomponent or single exercise/physical activity, orthoses and psychosocial interventions have the highest level of evidence and grade of recommendation[27]. Feasibility of interventions measured by adherence has been reported in 75% of the studies, and generally rated as moderate to high[27, 39]. Non-pharmacological and non-surgical interventions are safe, since no detrimental effects were reported, except for minor joint or muscle pain after exercise[27, 39].

On this basis, non-pharmacological and non-surgical interventions should be considered as adjuvant measures or as an "alternative" to symptomatic medication or surgery, with the exception of disease modifying interventions, and only when relevant benefit to the patient (either objective or subjective) can reasonably be expected[26].

Recommendation 2: Areas of intervention to be considered in this context include, but are not limited to: self-management, pain relief, energy management, joint alignment and support, thermotherapy, exercise, hydrokinesiotherapy, psychological interventions, daily leisure and work activities, education, family involvement, social participation and social care, sleep hygiene and general management of comorbidities.

Non-pharmacological interventions include a diverse set of techniques, strategies and practices described in the literature[21, 27, 32-38, 40-43]. This recommendation aims at widening the health professionals' perspective when

considering all that can be done, beyond medication and surgery, to assist patients with RA in pursuing their personal goals and a better quality of life.

Recommendation 3: Dedicated educational programs and supporting materials should be made available to patients, providing information on the general aspects of the disease and its management, their role in the shared-care process and the specificities of common assessments and interventions.

Patient education is recommended as an integral part of the standard of care[44] and comprises all educational activities provided for patients and their supporters (families and care-providers), including aspects of therapy, health care and health promotion[45]

Several cross-sectional and qualitative studies exploring patients' needs and expectations described a wide range of educational needs, such as knowledge on management of the disease, side effects and risk factors, non-pharmacological treatment, pain control and self-help methods[46-51].

Patient education should be provided by HPs with specific competencies and training and should be tailored to the individual patient's needs, in order to increase and qualify the patients' involvement in shared-care decisions[44, 52, 53].

Special attention should be given to health promotion in general and for specific areas, such as smoking cessation. A recent study confirmed that smoking is a strong risk factor for developing seropositive RA and demonstrated, for the first time, that sustained smoking cessation could delay or even prevent seropositive RA[54]. In addition, RA patients with a history of smoking are more likely to have a poor response to biological medication[55-57]. Therefore, smoking status should be determined and smoking cessation should be encouraged[58]. Patients' organizations may be active partners in the development of educational interventions and/or in the dissemination of educational materials.

Recommendation 4: Patients should be regularly inquired for unmet needs, through the use of validated large-scope instruments, and referenced to the most appropriate health professional(s) in the team.

Despite progress in medication, several unmet needs still have a negative impact on patient's personal experience of RA[59, 60]. In order to minimize this, patients should be regularly inquired for unmet needs, by means of validated large-scope instruments[27]. Currently, in our opinion, the most suitable instrument for this purpose is the Rheumatoid Arthritis Impact of Disease Score (RAID)[28, 61] which was developed with patients and considers seven different domains of impact: pain, functional disability, fatigue, emotional well-being, physical well-being, sleep and coping. RAID has been extensively validated as a combined index of overall impact. The scales it uses to assess individual domains of disease impact are valid, feasible, reliable and sensitive to change in patients with RA[61, 62], also specifically for the Portuguese patients[63]. Using the 7 scores separately (RAID.7i) also offers a feasible tool to analyse impact of disease and to select and monitor individually tailored interventions, targeting the domains of concern.

Multidisciplinary collaborative work seems essential to provide the best service for patients. In our umbrella review, the following HPs were reported to have provided relevant interventions: medical doctors, nurses, physical therapists, psychologists, occupational therapists, counselors, dieticians, and other professionals, namely, yoga teachers[21, 27, 36]. However, as the functions, responsibilities and individual career paths of HPs vary across Europe[64], referral should be carried out to the professional that is best qualified and positioned to deliver the best quality of care[65].

Recommendation 5: The multiprofessional team must try to make interventions as attractive and relevant as possible to patients, as a mean to ensure the best possible adherence and long-term effectiveness.

Low adherence is a prevalent and persistent healthcare problem, also in RA patients[66-68]. Patients need to be motivated to adhere to all proposed interventions and these should be adjusted, individualized and explained, in order to serve that purpose[27]. The multidisciplinary team should consider the different modes of intervention delivery: supervised *vs* not-supervised, individual vs groupal, face to face vs remote, community/home-based vs hospital-centred, and try to adjust to the patients preferences and resources[27]. Increasing adherence to therapy is essential to improve the efficacy of treatments and reduce costs[68]. Patients' organizations should be active stakeholders in promoting adherence, collaborating in the development of interventions and/or disseminating motivation strategies.

Dedicated interventions targeting adherence should be considered in cases where non-adherence is anticipated. These interventions aim to change the patient's behavior by shifting his/her thoughts, feelings, confidence

or motivation to adhere. They can vary widely in content and include techniques and skill-based instructions to enhance patients' sense of self-efficacy, motivation, ownership and problem-solving skills[66, 69].

Recommendation 6: Interventions should be targeted to specific objectives that are relevant to the individual patients, regularly monitored with validated instruments and adapted accordingly.

Non-pharmacological interventions should target well-defined and explicit individual goals, which should be regularly monitored with validated instruments, including patient reported outcomes measures (PROMs). These instruments should have been demonstrated as reliable, transculturally valid and meaningful to patients and HPs[70]. Specifically, physical exercise should be routinely assessed for exercises domains (cardiorespiratory, muscle strength, flexibility and neuromotor) and by performance-based tests[71]. Specific tools have been described for these purposes[39], but we have not evaluated their validity or reliability.

Patients should be instructed on the purpose and interpretation of the measurements, and advised to use them proactively to discuss the treatment plan and results with the multidisciplinary team[72].

Recommendation 7: All patients should be stimulated to follow a personalized and regular physical exercise program to reduce pain, functional disability, fatigue and global impact of disease.

Exercise has been endorsed as a measure to promote health in general[39] but it is ignored by recommendations on the treatment of inflammatory arthritis, with few exceptions[71].

Multicomponent or single exercise/physical activity interventions have a small to moderate beneficial effect for patients with RA in improving pain, functional disability, fatigue and in reducing the global impact of disease[21, 27, 32-34, 41]. The studied interventions comprise resistance, strengthening, aerobic and flexibility exercises. Reported studies are extremely variable, including multicomponent or single modalities and a large array of frequencies (1-5 sessions per week), duration (10 min-4.5 hours per session) and intensity (30-100% of an individual's maximum heart rate)[27]. There is no evidence to support the selection of the best modality or to guide its adaptation to individual needs[21, 27].

Exercise programs should be adapted based on a comprehensive individual assessment and adjusted to the individual patient s abilities, specificities (age, gender, comorbidities, mobility loss…) and preferences[27, 71]. For this reason, the prescription of exercise should be made by a qualified and experienced professional. Professional supervision of the exercise is preferable, but unsupervised exercises can and should be promoted, especially if this is crucial to ensure adherence[27, 39, 71].

To improve acceptance and long-term adherence to physical exercise, group and/or individual maintenance programs should be promoted[33, 67]. The combination of exercise and psychosocial interventions can also provide better overall outcomes[21, 27].

In addition to the exercise programs mentioned above, we found evidence that Tai chi and occupational therapy have also beneficial effects for patients with RA. Particularly, Tai chi has demonstrated benefits on lower extremity range of motion[73], and occupational therapy has been shown to improve functional ability, social participation and quality of life[40].

Recommendation 8: Hydrokinesiotherapy should be considered, to reduce pain and global impact of disease.

Evidence regarding the use of hydrotherapy/ balneotherapy for pain, functional disability and global impact of disease is scarce and contradictory[27, 37, 74]. This is mainly due to the lack of standardization of the interventions administered and most studies have important limitations and low quality[27]. However, it is important to note that some recent evidence supports the benefits of hydrokinesiotherapy and radon-carbon dioxide baths in reducing pain and enhancing quality of life[75-77].

Recommendation 9: Orthoses should be considered as a mean to reduce joint pain, functional disability and global impact of disease.

Orthoses have a moderate beneficial effect in improving pain, functional disability and quality of life in people with RA[27, 38, 78-80].

They include standard orthoses, custom orthoses, silicone orthosis, technical adaptations to over-the-counter shoes, ready or custom-made therapeutic shoes, or a provisional therapy (e.g., felt padding or taping) and has been advocated for patients with abnormal function, joint damage/deformity, or malalignment of the hand, ankle, foot or other joints[27, 38, 42, 78-80]. It seems important that the management of deformity starts in an early stage of the disease, to reduce pain and activity limitations, and to prevent the deteriora-

tion of function[42, 81]. Orthoses should be used throughout the progression of the disease in cases of abnormal function, joint damage/deformity, or malalignment, and even for feet that do not fit in over-the-counter shoes or ready-made therapeutic shoes, not just as a means of preventing deformities[42, 80, 81].
The first multidisciplinary recommendations specific to the management of foot problems in patients with RA have recently been published[80].

Recommendation 10: Psychosocial interventions should be considered as a mean to reduce pain, functional disability, fatigue and global impact of disease.
Psychosocial interventions have a small beneficial effect in improving pain, functional disability and fatigue in patients with RA[21, 27, 36, 82, 83]. Published studies comprise a diverse set of methods and interventions, including expressive writing, cognitive skills training, cognitive behavioral therapy, mindfulness, lifestyle management, self-management, energy conservation, contracting/goal setting, coping, guided imagery and self-instruction, among others[21, 36]. Naturally, this implies consideration of the specific principles and methods of application of each intervention, and that they must be selected and adjusted according to the individual patient's situation[21, 27, 36, 82, 83]. However, the information serving this purpose is scarce.

Recommendation 11: The prevention and management of comorbidities and adverse effects of all types of interventions should be part of the multiprofessional team goals.
It is well known that people with RA have an increased prevalence of numerous comorbidities, such as cardiovascular risk factors, osteoarthritis, depression and osteoporosis, among others[84-87] and this represents a demanding challenge for HPs[88]. Patients with RA and multimorbidity are at risk of insufficient care on both dimensions of their health and present poorer patient-reported outcomes[84].

To achieve better outcomes, we suggest that the management of comorbidities and adverse effects should be recognized by HPs and patients and explicitly included in the program covered by these recommendations. The promotion of healthy lifestyles, with emphasis on smoking cessation, is of paramount importance in this context. These interventions are supported by several recommendations or points to consider[58, 89].

Recommendation 12: Commonly used non-pharmacological interventions, without solid experimental evidence support may be considered in individual patients, if and only if: i) there is no reasonable and proven alternative; ii) they have merited consensual approval by qualified health professionals; iii) they are safe and accepted by a duly informed patient.
There is a diversity of interventions that are commonly used in practice, despite the lack of solid published evidence. Many are supported by a small number of poorly standardized investigations. For example, thermotherapy is commonly used but evidence is limited. Superficial moist heat and cryotherapy can be used but only paraffin wax baths combined with exercises can be recommended for beneficial short-term effects for arthritic hands on the basis of evidence[43]. Evidence for acupuncture is also very limited mainly due to the poor quality and small sample size of studies. However, electroacupuncture may be beneficial to reduce symptomatic knee pain in patients with RA[90]. Low level laser therapy (Classes I, II and III) has been associated with short-term treatment for relief of pain and morning stiffness[91].

Electrical stimulation was shown to have a clinically beneficial effect on grip strength and fatigue resistance for RA patients with muscle atrophy of the hand[92]. Regarding the use of transelectrical nerve stimulation (TENS), a particular type of electrical stimulation that is thought to produce analgesia according to the gate control theory, conflicting effects on pain outcomes were reported in RA[93].

Ultrasound often used by rehabilitation specialists based on expected anti-inflammatory and analgesic properties, have been shown to decrease morning stiffness and reduce the number of painful joints[94].

At last, although there is conflicting evidence when studying specific dietary regimes, it is recognized that nutrition, in general, should not be neglected. In this sense, all patients should be stimulated to follow a personalized, diversified and balanced diet[95, 96].

Using interventions that do not have a robust support in the published literature, ensuring that the scientific and clinical contraindications to their use are recognized, entails a possible risk of non-benefit for both the patient and the health professional, that needs to be acknowledged and accepted by both parties. The lack of evidence precludes that formal recommendations can be made in favor or against the use of these interventions. The decision is left in the hands of the HPs, preferably shared with the multiprofessional team,

TABLE II. RESEARCH AGENDA FOR NON-PHARMACOLOGICAL AND NON-SURGICAL INTERVENTIONS IN PEOPLE WITH RHEUMATOID ARTHRITIS

1. To carry out well-designed RCTs in areas where evidence is scarce, poorly qualified and/or contradictory (e.g. hydrotherapy, physical agents such as electrotherapy and others).
2. To study other relevant outcomes, such as physical and emotional well-being, sleep and coping, in addition to pain, function and fatigue.
3. To evaluate short and long-term effectiveness.
4. To assess the most effective type of exercises, optimal method of delivery, intensity and frequency.
5. To assess which and how different components or interventions should be combined and their interaction effects.
6. To identify disease-specific contraindications.
7. To assess the design of orthosis (material, which joints are supported…).
8. To define the desired content of education.
9. To investigate the optimal design and delivery of psychosocial interventions.
10. To study the feasibility and efficacy of maintenance programs or boost sessions to ensure long-term adherence and maintain therapeutic gains over time.
11. To perform cost-effectiveness studies.
12. To determine the optimal strategies to implement these recommendations in different settings.
13. To identify facilitators and barriers of health professionals towards applying these interventions and recommendations.

but the general rules established in this recommendation should be respected.

Research agenda

A research agenda was developed and is presented in Table II. Additionally, a Portuguese translated version was also provided (Table IIa - annex).

Acceptance of recommendations

We promoted a public consultation of the recommendations among all members of the involved associations. Comments were received from 20 persons, including 6 rheumatologists, 5 nurses, 3 general physicians, 3 physiatrists, 2 nutritionists and 1 patient. All respondents expressed full agreement with the content and clarity of the recommendations and pointed out few omissions and/or suggestions. The final version was improved with these inputs.

DISCUSSION

These are the first multidisciplinary recommendations for non-pharmacological and non-surgical interventions in patients with RA.

Limitations on the evidence base serving these recommendations significantly impact their wording and assertiveness - this must be acknowledged upfront. Besides being limited in number and scope, published studies frequently have low methodological quality, including a poor characterization of the diagnostic criteria, the interventions and conditions of application and/or the outcome measures[18, 27]. For many specific non-pharmacological interventions, evidence is almost totally absent. Additionally, the criteria for classifying the disease have changed over time to encompass earlier disease classifications, and modern treatments and strategies have changed the face of RA and of patients' needs[97, 98]. Despite this, non-pharmacological and non-surgical interventions are widely used and play an important role in the management of RA worldwide, underlining the need for recommendations to guide practice and research, in the best interests of the patient.

The five overarching principles and 12 recommendations represent the consensualized perspective of the TEP members, representing different professional and personal backgrounds, based on the available evidence and on personal experience. A high LoA was reached in all cases.

These recommendations are targeted at all health professionals who care for patients with RA. The publication of the complete SLR, including a detailed description of its methodology and results, provides the in-

terested reader with a full update of the currently available evidence[27]. However, it should be noted that additional searches were conducted where the evidence provided by the SLR was considered contradictory or insufficient. Therefore, it is important to note that the recommendations presented in Table I cannot be correctly interpreted and used without the accompanying text and the supporting SLR.

Efforts to implement these recommendations will be made by dissemination across national societies, online platforms and by presentations in leading international congresses and educational sessions. However, we recognize that due to differences in healthcare systems and particularities of each country, it will be probably necessary to further develop, adapt and evaluate national or regional implementation strategies.

The presented research agenda (Table II) highlights several areas where scientific evidence is lacking and/or scarce.

ACKNOWLEDGMENTS

We wish to thank to Alexandra Cardoso, Ana Filipa Mourão, Andréa Marques, António Courinha, Eduardo Dourado, Fernando Santos, Georgina Pimentel, Guilherme Figueiredo, João Pinheiro, Margarida Cruz, Maria João Andrade, Maria Teresa Sampaio, Pedro Sá, Pedro Silva and Susana Abreu for their critical revision of the recommendations.

AUTHOR CONTRIBUTIONS

ES, CD, RF and JAPS were the proponents of this project. ES and CD conducted the SLR and the additional literature searches that were needed to support the recommendations supervised by JAPS. ES and JAPS organized and chaired the TEP meeting. All authors have equally contributed to the recommendations by participating in the TEP meeting; during discussion and agreement on the recommendations; revising and approving the manuscript for publication.

CONFLICT OF INTEREST STATEMENT

Authors declare no conflicts of interest.

FUNDING

This study had no external funding.

CORRESPONDENCE TO

Eduardo Santos
Serviço de Reumatologia, Centro Hospitalar e
Universitário de Coimbra
Avenida Dr. Bissaya Barreto, 3000-075 Coimbra, Portugal
E-mail: ejf.santos87@gmail.com

REFERENCES

1. Anderson J, Caplan L, Yazdany J, Robbins ML, Neogi T, Michaud K, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012;64:640-647.
2. Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014;73:492-509.
3. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388:2023-2038.
4. Aletaha D, Smolen JS. Diagnosis and Management of Rheumatoid Arthritis: A Review. Jama. 2018;320:1360-1372.
5. Castrejon I, Pincus T. Patient self-report outcomes to guide a treat-to-target strategy in clinical trials and usual clinical care of rheumatoid arthritis. Clin Exp Rheumatol. 2012;30:S50-55.
6. Smolen JS, Aletaha D. The assessment of disease activity in rheumatoid arthritis. Clin Exp Rheumatol. 2010;28:S18-27.
7. Gossec L, Dougados M, Dixon W. Patient-reported outcomes as end points in clinical trials in rheumatoid arthritis. RMD Open. 2015;1:e000019.
8. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol. 2014;67:745--753.
9. Curtis JR, Shan Y, Harrold L, Zhang J, Greenberg JD, Reed GW. Patient perspectives on achieving treat-to-target goals: a critical examination of patient-reported outcomes. Arthritis Care Res (Hoboken). 2013;65:1707-1712.
10. Matcham F, Scott IC, Rayner L, Hotopf M, Kingsley GH, Norton S, et al. The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. Semin Arthritis Rheum. 2014;44:123-130.
11. Studenic P, Smolen JS, Aletaha D. Near misses of ACR/EULAR criteria for remission: effects of patient global assessment in Boolean and index-based definitions. Ann Rheum Dis. 2012;71:1702-1705.
12. Balogh E, Madruga Dias J, Orr C, Mullan R, Harty L, FitzGerald O, et al. Comparison of remission criteria in a tumour necrosis factor inhibitor treated rheumatoid arthritis longitudinal cohort: patient global health is a confounder. Arthritis Res Ther. 2013;15:R221.
13. Ferreira RJO, Duarte C, Ndosi M, de Wit M, Gossec L, da Silva JAP. Suppressing Inflammation in Rheumatoid Arthritis: Does Patient Global Assessment Blur the Target? A Practice-Based Call for a Paradigm Change. Arthritis Care Res (Hoboken). 2018; 70:369-378.
14. Ferreira RJO, Dougados M, Kirwan JR, Duarte C, de Wit M, Soubrier M, et al. Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients. Rheumatology (Oxford). 2017;56:1573-1578.
15. Ferreira RJO, Carvalho PD, Ndosi M, Duarte C, Chopra A, Murphy E, et al. Impact of Patient's Global Assessment on Achieving Remission in Patients With Rheumatoid Arthritis: A Multinational Study Using the METEOR Database. Arthritis Care Res (Hoboken). 2019;71:1317-1325.
16. Santos EJF, Duarte C, Ferreira RJO, Pinto AM, Geenen R, da Silva JAP, et al. Determinants of happiness and quality of life in patients with rheumatoid arthritis: a structural equation modelling approach. Ann Rheum Dis. 2018;77:1118-1124.
17. Ferreira RJO, Ndosi M, de Wit M, Santos EJF, Duarte C, Jacobs JWG, et al. Dual target strategy: a proposal to mitigate the risk of overtreatment and enhance patient satisfaction in rheumatoid arthritis. Annals of the Rheumatic Diseases. 2018.
18. Vliet Vlieland TP, van den Ende CH. Nonpharmacological treatment of rheumatoid arthritis. Curr Opin Rheumatol.

2011;23:259-264.
19. Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Bostrom C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Annals of the Rheumatic Diseases. 2015;74:954-962.
20. Bech B, Primdahl J, van Tubergen A, Voshaar M, Zangi HA, Barbosa L, et al. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Annals of the Rheumatic Diseases. 2020;79:61.
21. Cramp F, Hewlett S, Almeida C, Kirwan JR, Choy EH, Chalder T, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. Cochrane Database Syst Rev. 2013: Cd008322.
22. Cunningham NR, Kashikar-Zuck S. Nonpharmacologic Treatment of Pain in Rheumatic Diseases and Other Musculoskeletal Pain Conditions. Current rheumatology reports. 2013;15:306.
23. Christie A, Jamtvedt G, Dahm KT, Moe RH, Haavardsholm EA, Hagen KB. Effectiveness of nonpharmacological and nonsurgical interventions for patients with rheumatoid arthritis: an overview of systematic reviews. Phys Ther. 2007;87:1697-715.
24. van Tuyl LH, Hewlett S, Sadlonova M, Davis B, Flurey C, Hoogland W, et al. The patient perspective on remission in rheumatoid arthritis: 'You've got limits, but you're back to being you again'. Ann Rheum Dis. 2015;74:1004-1010.
25. Contreras-Yáñez I, Guaracha-Basañez G, Ruiz-Domínguez D, Pascual-Ramos V. Patient's perspective of sustained remission in rheumatoid arthritis. BMC Musculoskeletal Disorders. 2017;18:379.
26. Ritschl V, Lackner A, Boström C, Kundi M, Lehner M, Studenic P, et al. Patient Perspectives from a Qualitative Study Predict Non-Adherence in Rheumatoid Arthritis [abstract]. Arthritis Rheumatol. 2017;69.
27. Santos EJF, Duarte C, Marques A, Cardoso D, Apóstolo J, da Silva JAP, et al. Effectiveness of non-pharmacological and non-surgical interventions for rheumatoid arthritis. JBI Database of Systematic Reviews and Implementation Reports. 2019;17: 1494-14531.
28. Gossec L, Dougados M, Rincheval N, Balanescu A, Boumpas DT, Canadelo S, et al. Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. Ann Rheum Dis. 2009;68:1680-1685.
29. van der Heijde D, Aletaha D, Carmona L, Edwards CJ, Kvien TK, Kouloumas M, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. Ann Rheum Dis. 2015;74:8-13.
30. Aromataris E, Fernandez R, Godfrey C, Holly C, Khalil H, Tungpunkom P. Chapter 10: Umbrella Reviews. In: Aromataris E, Munn Z, editors. Joanna Briggs Institute Reviewer's Manual: The Joanna Briggs Institute; 2017.
31. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Bmj. 2008;336:924-926.
32. Baillet A, Zeboulon N, Gossec L, Combescure C, Bodin LA, Juvin R, et al. Efficacy of cardiorespiratory aerobic exercise in rheumatoid arthritis: meta-analysis of randomized controlled trials. Arthritis Care Res (Hoboken). 2010;62:984-992.
33. Baillet A, Vaillant M, Guinot M, Juvin R, Gaudin P. Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials. Rheumatology (Oxford). 2012;51:519-527.
34. Rongen-van Dartel SA, Repping-Wuts H, Flendrie M, Bleijenberg G, Metsios GS, van den Hout WB, et al. Effect of Aerobic Exercise Training on Fatigue in Rheumatoid Arthritis: A Meta-Analysis. Arthritis Care Res (Hoboken). 2015;67:1054-1062.
35. Al-Qubaeissy KY, Fatoye FA, Goodwin PC, Yohannes AM. The effectiveness of hydrotherapy in the management of rheumatoid arthritis: a systematic review. Musculoskeletal Care. 2013;11:3-18.
36. Knittle K, Maes S, de Gucht V. Psychological interventions for rheumatoid arthritis: examining the role of self-regulation with a systematic review and meta-analysis of randomized controlled trials. Arthritis Care Res (Hoboken). 2010;62:1460-1472.
37. Verhagen AP, Bierma-Zeinstra SM, Boers M, Cardoso JR, Lambeck J, de Bie R, et al. Balneotherapy (or spa therapy) for rheumatoid arthritis. Cochrane Database Syst Rev. 2015:Cd000518.
38. Hennessy K, Woodburn J, Steultjens MP. Custom foot orthoses for rheumatoid arthritis: A systematic review. Arthritis Care Res (Hoboken). 2012;64:311-320.
39. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 10th ed: Wolters Kluwer; 2017.
40. Steultjens EM, Dekker J, Bouter LM, van Schaardenburg D, van Kuyk MA, van den Ende CH. Occupational therapy for rheumatoid arthritis. Cochrane Database Syst Rev. 2004:Cd003114.
41. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, Schoones J, Van den Ende EC. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. Cochrane Database Syst Rev. 2009:Cd006853.
42. Egan M, Brosseau L, Farmer M, Ouimet MA, Rees S, Wells G, et al. Splints/orthoses in the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2003:Cd004018.
43. Robinson V, Brosseau L, Casimiro L, Judd M, Shea B, Wells G, et al. Thermotherapy for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2002:Cd002826.
44. Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Boström C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Annals of the Rheumatic Diseases. 2015;74:954.
45. Albano MG, Giraudet-Le Quintrec JS, Crozet C, d'Ivernois JF. Characteristics and development of therapeutic patient education in rheumatoid arthritis: analysis of the 2003-2008 literature. Joint Bone Spine. 2010;77:405-410.
46. Meesters JJ, Vliet Vlieland TP, Hill J, Ndosi ME. Measuring educational needs among patients with rheumatoid arthritis using the Dutch version of the Educational Needs Assessment Tool (DENAT). Clin Rheumatol. 2009;28:1073-1077.
47. Schildmann J, Grunke M, Kalden JR, Vollmann J. Information and participation in decision-making about treatment: a qualitative study of the perceptions and preferences of patients with rheumatoid arthritis. J Med Ethics. 2008;34:775-779.
48. Brand C, Claydon-Platt K, McColl G, Bucknall T. Meeting the needs of people diagnosed with rheumatoid arthritis: an analysis of patient-reported experience. Journal of Nursing and Healthcare of Chronic Illness. 2010;2:75-83.
49. Dures E, Kitchen K, Almeida C, Ambler N, Cliss A, Hammond A, et al. "They didn't tell us, they made us work it out ourselves": patient perspectives of a cognitive-behavioral program for rheumatoid arthritis fatigue. Arthritis Care Res (Hoboken). 2012;64:494-501.
50. Werner CA, Kaliski KS, Salazar QK, Bustos ML, Rojas RM, Baumert LC, et al. Knowledge about their disease and treatment among patients with rheumatoid arthritis. Rev Med Chil. 2006;134:1500-1506.
51. Riemsma RP, Taal E, Kirwan JR, Rasker JJ. Systematic review of

rheumatoid arthritis patient education. Arthritis Rheum. 2004;51:1045-1059.
52. Leung YY, Tam LS, Lee KW, Leung MH, Kun EW, Li EK. Involvement, satisfaction and unmet health care needs in patients with psoriatic arthritis. Rheumatology (Oxford). 2009;48:53-6.
53. Chewning B, Bylund CL, Shah B, Arora NK, Gueguen JA, Makoul G. Patient preferences for shared decisions: a systematic review. Patient Educ Couns. 2012;86:9-18.
54. Liu X, Tedeschi SK, Barbhaiya M, Leatherwood CL, Speyer CB, Lu B, et al. Impact and Timing of Smoking Cessation on Reducing Risk of Rheumatoid Arthritis Among Women in the Nurses' Health Studies. Arthritis Care Res (Hoboken). 2019;71:914-924.
55. Saevarsdottir S, Wedren S, Seddighzadeh M, Bengtsson C, Wesley A, Lindblad S, et al. Patients with early rheumatoid arthritis who smoke are less likely to respond to treatment with methotrexate and tumor necrosis factor inhibitors: observations from the Epidemiological Investigation of Rheumatoid Arthritis and the Swedish Rheumatology Register cohorts. Arthritis Rheum. 2011;63:26-36.
56. Abhishek A, Butt S, Gadsby K, Zhang W, Deighton CM. Anti-TNF-alpha agents are less effective for the treatment of rheumatoid arthritis in current smokers. J Clin Rheumatol. 2010;16:15--18.
57. Mattey DL, Brownfield A, Dawes PT. Relationship between pack-year history of smoking and response to tumor necrosis factor antagonists in patients with rheumatoid arthritis. J Rheumatol. 2009;36:1180-1187.
58. Roubille C, Richer V, Starnino T, McCourt C, McFarlane A, Fleming P, et al. Evidence-based Recommendations for the Management of Comorbidities in Rheumatoid Arthritis, Psoriasis, and Psoriatic Arthritis: Expert Opinion of the Canadian Dermatology-Rheumatology Comorbidity Initiative. The Journal of Rheumatology. 2015;42:1767.
59. Kaltsonoudis E, Pelechas E, Voulgari PV, Drosos AA. Unmet needs in the treatment of rheumatoid arthritis. An observational study and a real-life experience from a single university center. Semin Arthritis Rheum. 2019;48:597-602.
60. Caporali R, Doria A, Ferraccioli GF, Meroni PL, Zavaglia D, Iannone F. Unmet Needs in the Treatment of RA in the Era of Jaki: IDRA (Italian Delphi Rheumatoid Arthritis) Consensus. BioMed Research International. 2018;2018:10.
61. Gossec L, Paternotte S, Aanerud GJ, Balanescu A, Boumpas DT, Carmona L, et al. Finalisation and validation of the rheumatoid arthritis impact of disease score, a patient-derived composite measure of impact of rheumatoid arthritis: a EULAR initiative. Ann Rheum Dis. 2011;70:935-942.
62. Holten K, Sexton J, Kvien TK, Aga A-B, Haavardsholm EA. Comparative analyses of responsiveness between the Rheumatoid Arthritis Impact of Disease score, other patient-reported outcomes and disease activity measures: secondary analyses from the ARCTIC study. RMD Open. 2018;4:e000754.
63. Ferreira RJO, Gossec L, Duarte C, Nicklin JK, Hewlett S, da Silva JAP, et al. The Portuguese Rheumatoid Arthritis Impact of Disease (RAID) score and its measurement equivalence in three countries: validation study using Rasch Models. Qual Life Res. 2018;27:2909-2921.
64. Stamm T, Hill J. Extended roles of non-physician health professionals and innovative models of care within Europe: results from a web-based survey. Musculoskeletal Care. 2011;9:93-101.
65. Bech B, Primdahl J, van Tubergen A, Voshaar M, Zangi HA, Barbosa L, et al. 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Ann Rheum Dis. 2019.
66. Marengo MF, Suarez-Almazor ME. Improving treatment adherence in patients with rheumatoid arthritis: what are the options? International journal of clinical rheumatology. 2015;10:345--356.
67. Sokka T, Hakkinen A, Kautiainen H, Maillefert JF, Toloza S, Mork Hansen T, et al. Physical inactivity in patients with rheumatoid arthritis: data from twenty-one countries in a cross-sectional, international study. Arthritis Rheum. 2008;59:42-50.
68. van den Bemt BJF, van Lankveld WGJM. How can we improve adherence to therapy by patients with rheumatoid arthritis? Nature Clinical Practice Rheumatology. 2007;3:681.
69. Easthall C, Song F, Bhattacharya D. A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence. BMJ Open. 2013;3.
70. Santos EJF, Duarte C, da Silva JAP, Ferreira RJO. The impact of fatigue in rheumatoid arthritis and the challenges of its assessment. Rheumatology (Oxford). 2019.
71. Rausch Osthoff A-K, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Annals of the Rheumatic Diseases. 2018;77:1251.
72. Ferreira RJO, de Wit M, Henriques M, Pinto AF, Duarte C, Mateus E, et al. 'It can't be zero!' Difficulties in completing patient global assessment in rheumatoid arthritis: a mixed methods study. Rheumatology. 2019.
73. Mudano AS, Tugwell P, Wells GA, Singh JA. Tai Chi for rheumatoid arthritis. Cochrane Database Syst Rev. 2019;9:Cd004849.
74. Santos I, Cantista P, Vasconcelos C. Balneotherapy in rheumatoid arthritis-a systematic review. Int J Biometeorol. 2016;60:1287-1301.
75. Franke A, Reiner L, Resch KL. Long-term benefit of radon spa therapy in the rehabilitation of rheumatoid arthritis: a randomised, double-blinded trial. Rheumatol Int. 2007;27:703-713.
76. Annegret F, Thomas F. Long-term benefits of radon spa therapy in rheumatic diseases: results of the randomised, multi-centre IMuRa trial. Rheumatol Int. 2013;33:2839-2850.
77. Franke A, Reiner L, Pratzel HG, Franke T, Resch KL. Long-term efficacy of radon spa therapy in rheumatoid arthritis--a randomized, sham-controlled study and follow-up. Rheumatology (Oxford). 2000;39:894-902.
78. Clark H, Rome K, Plant M, O'Hare K, Gray J. A critical review of foot orthoses in the rheumatoid arthritic foot. Rheumatology (Oxford). 2006;45:139-145.
79. Farrow SJ, Kingsley GH, Scott DL. Interventions for foot disease in rheumatoid arthritis: a systematic review. Arthritis Rheum. 2005;53:593-602.
80. Tenten-Diepenmaat M, van der Leeden M, Vliet Vlieland TPM, Dekker J, van Schaardenburg D, Drossaers-Bakker W, et al. Multidisciplinary recommendations for diagnosis and treatment of foot problems in people with rheumatoid arthritis. Journal of Foot and Ankle Research. 2018;11:37.
81. Woodburn J, Hennessy K, Steultjens MP, McInnes IB, Turner DE. Looking through the 'window of opportunity': is there a new paradigm of podiatry care on the horizon in early rheumatoid arthritis? J Foot Ankle Res. 2010;3:8.
82. Sharpe L. Psychosocial management of chronic pain in patients with rheumatoid arthritis: challenges and solutions. Journal of pain research. 2016;9:137-146.
83. Astin JA, Beckner W, Soeken K, Hochberg MC, Berman B. Psychological interventions for rheumatoid arthritis: A meta-analysis of randomized controlled trials. Arthritis Care & Research. 2002;47:291-302.

84. Luque Ramos A, Redeker I, Hoffmann F, Callhoff J, Zink A, Albrecht K. Comorbidities in Patients with Rheumatoid Arthritis and Their Association with Patient-reported Outcomes: Results of Claims Data Linked to Questionnaire Survey. The Journal of Rheumatology. 2019:jrheum.180668.
85. Gualtierotti R, Ughi N, Marfia G, Ingegnoli F. Practical Management of Cardiovascular Comorbidities in Rheumatoid Arthritis. Rheumatology and therapy. 2017;4:293-308.
86. Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Annals of the Rheumatic Diseases. 2014;73:62.
87. Dougados M. Comorbidities in rheumatoid arthritis. Current Opinion in Rheumatology. 2016;28:282-288.
88. van Onna M, Boonen A. The challenging interplay between rheumatoid arthritis, ageing and comorbidities. BMC Musculoskeletal Disorders. 2016;17:184.
89. Baillet A, Gossec L, Carmona L, Wit Md, van Eijk-Hustings Y, Bertheussen H, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Annals of the Rheumatic Diseases. 2016;75:965.
90. Casimiro L, Barnsley L, Brosseau L, Milne S, Robinson VA, Tugwell P, et al. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2005:Cd003788.
91. Brosseau L, Robinson V, Wells G, Debie R, Gam A, Harman K, et al. Low level laser therapy (Classes I, II and III) for treating rheumatoid arthritis. Cochrane Database Syst Rev. 2005: Cd002049.
92. Brosseau LU, Pelland LU, Casimiro LY, Robinson VI, Tugwell PE, Wells GE. Electrical stimulation for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2002:Cd003687.
93. Brosseau L, Judd MG, Marchand S, Robinson VA, Tugwell P, Wells G, et al. Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis in the hand. Cochrane Database Syst Rev. 2003:Cd004377.
94. Casimiro L, Brosseau L, Robinson V, Milne S, Judd M, Well G, et al. Therapeutic ultrasound for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2002:Cd003787.
95. Cutolo M, Nikiphorou E. Don't neglect nutrition in rheumatoid arthritis! RMD Open. 2018;4:e000591.
96. Hagen KB, Byfuglien MG, Falzon L, Olsen SU, Smedslund G. Dietary interventions for rheumatoid arthritis. The Cochrane database of systematic reviews. 2009:CD006400-CD.
97. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988;31:315-324.
98. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62:2569-2581.

ANNEX

TABLE Ia. RECOMENDAÇÕES PARA INTERVENCOES NÃO-FARMACOLÓGICAS E NÃO-CIRÚRGICAS EM PESSOAS COM ARTRITE REUMATÓIDE

	NE*	GR†	NC (0-10)
A. O principal objetivo das intervenções não-farmacológicas e não cirúrgicas na AR é ajudar os doentes a maximizar a sua qualidade de vida em geral e a satisfação com a vida, através do controlo otimizado do impacto da doença, além e para além da medicação e da cirurgia.	-	-	9,9 (0,3)
B. Os doentes devem ter um papel decisivo no estabelecimento dos objetivos e da natureza das intervenções no seu caso particular, numa decisão informada e partilhada.	-	-	9,7 (0,6)
C. A equipa de saúde deve certificar-se de que o doente possui toda a informação considerada relevante para apoiar a sua participação no autocuidado e no processo de decisão partilhada, incluindo as perspetivas de curto e longo prazo da doença e do âmbito do tratamento e intervenções disponíveis.	-	-	9,8 (0,5)
D. As intervenções não-farmacológicas e não cirúrgicas exigem o envolvimento de uma equipa multiprofissional/multidisciplinar, e a adoção de um modelo bio-psico-social holístico.	-	-	9,8 (0,5)
E. As intervenções não farmacológicas e não cirúrgicas devem ser selecionadas com base nas evidências disponíveis e ajustadas às características clínicas, capacidades, preferências e necessidades específicas do doente.	-	-	9,9 (0,5)

Continues on the next page

TABLE Ia. CONTINUATION

	NE*	GR†	NC (0-10)
Recomendações			
1. As intervenções não farmacológicas e não cirúrgicas devem ser parte integrante do padrão de cuidados em pessoas com AR e devem ser consideradas ao longo do curso da doença, sempre que possam proporcionar benefícios relevantes, objetivos ou subjetivos ao doente, como adjuvante ou alternativa à medicação ou cirurgia sintomática.	1a	A	9,6 (0,7)
2. As áreas de intervenção a serem consideradas neste contexto incluem, mas não se limitam a: autogestão, alívio da dor, gestão da energia, alinhamento e suporte articular, termoterapia, exercício, hidrocinesioterapia, intervenções psicológicas, atividades diárias, de lazer e trabalho, educação, envolvimento familiar, participação social e cuidados sociais, higiene do sono e gestão geral das comorbilidades.	5	D	9,2 (1,3)
3. Devem ser disponibilizados aos doentes programas educacionais dedicados e materiais de apoio, fornecendo informações sobre os aspetos gerais da doença e a sua gestão, o seu papel no processo de cuidados partilhados e as especificidades das avaliações e intervenções comuns.	1a	B	9,8 (0,6)
4. Os doentes devem ser questionados regularmente sobre necessidades não satisfeitas, através da utilização de instrumentos validados de grande alcance, e referenciados ao(s) profissional(is) de saúde mais adequado(s) da equipa.	2b	B	9,1 (1,4)
5. A equipa multiprofissional deve tentar tornar as intervenções tão atrativas e relevantes quanto possível para os doentes, como forma de assegurar a melhor adesão possível e eficácia a longo prazo.	2b	B	9,8 (0,5)
6. As intervenções devem ser orientadas para objetivos específicos que sejam relevantes para os objetivos individuais do doente, monitorizadas regularmente com instrumentos validados e adaptadas em conformidade.	3	C	9,6 (0,7)
7. Todos os doentes devem ser estimulados a seguir um programa regular de exercício físico personalizado para reduzir a dor, incapacidade funcional, fadiga e impacto global da doença.	1a	B	9,7 (0,7)
Princípios gerais			
8. A hidrocinesioterapia deve ser considerada para reduzir a dor e o impacto global da doença.	2b	B	9,2 (1,0)
9. As ortóteses devem ser consideradas como um meio para reduzir a dor articular, a incapacidade funcional e o impacto global da doença.	1a	B	9,1 (1,1)
10. As intervenções psicossociais devem ser consideradas como um meio de reduzir a dor, a incapacidade funcional, a fadiga e o impacto global da doença.	1a	B	9,6 (0,9)
11. A prevenção e gestão de comorbilidades e efeitos adversos de todos os tipos de intervenções deve fazer parte dos objetivos da equipa multiprofissional.	3	C	9,8 (0,5)
12. Intervenções não farmacológicas comumente utilizadas, sem evidências experimentais sólidas, podem ser consideradas em doentes individuais, se e somente se: i) não houver alternativa razoável e comprovada; ii) tiverem merecido aprovação consensual por profissionais de saúde qualificados; iii) forem seguras e aceites por um doente devidamente informado.	5	D	8,5 (1,5)

Estas recomendações devem ser interpretadas à luz dos esclarecimentos fornecidos no corpo do texto e pelo RSL de apoio.
* 1a: revisão sistemática dos Ensaios Clínicos Aleatorizados e Controlados (ECACs) ; 1b: ECAC individual; 2a: revisão sistemática dos estudos de coorte; 2b: estudo de coorte individual (incluindo ECACs de baixa qualidade; por exemplo,<80% de follow-up); 3a: revisão sistemática dos estudos de caso-controlo; 3b: estudo de caso-controlo individual; 4: série de casos (e estudos de coorte e caso-controlo de baixa qualidade); 5: opinião de especialistas sem avaliação crítica explícita, ou baseada em fisiologia, pesquisa experimental/ "ciência básica" ou "primeiros princípios". † A: baseado em evidência consistente de nível 1; B: baseado em evidência consistente de nível 2 ou 3 ou extrapolações de evidência de nível 1; C: baseado em evidência de nível 4 ou extrapolações de evidência de nível 2 ou 3; D: baseado em evidência de nível 5 ou em estudos inconsistentes ou inconclusivos de qualquer nível. NE, Nível de Evidência; GR, Grau de Recomendação; NC, Nível de Concordância.

TABLE IIa. AGENDA DE INVESTIGAÇÃO PARA INTERVENÇÕES NÃO FARMACOLÓGICAS E NÃO CIRÚRGICAS EM PESSOAS COM ARTRITE REUMATÓIDE.

1. Realizar ensaios clínicos bem desenhados em áreas onde as evidências são escassas, pouco qualificadas e/ou contraditórias (por exemplo, hidroterapia, agentes físicos como eletroterapia e outros).
2. Estudar outros resultados (outcomes) relevantes, tais como o bem-estar físico e emocional, o sono e coping, adicionalmente à dor, função e fadiga.
3. Avaliar a eficácia a curto e longo prazo.
4. Avaliar os tipos de exercícios mais eficazes, método ótimo de realização, intensidade e frequência.
5. Avaliar quais e como diferentes componentes ou intervenções devem ser combinados e os seus efeitos de interação.
6. Identificar as contraindicações específicas da doença.
7. Avaliar o desenho das ortóteses (material, que articulações são suportadas...)
8. Definir o conteúdo desejado para a educação.
9. Investigar a conceção e realização ótima de intervenções psicossociais.
10. Estudar a viabilidade e eficácia de programas de manutenção ou sessões de reforço para assegurar a adesão a longo prazo e manter os ganhos terapêuticos ao longo do tempo.
11. Realizar estudos de custo-eficácia.
12. Determinar as estratégias ótimas para implementar estas recomendações em diferentes contextos.
13. Identificar facilitadores e barreiras dos profissionais de saúde para a aplicação destas intervenções e recomendações.