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Review

Guidelines on the management of fibromyalgia syndrome – A systematic review

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ABSTRACT

We compared the methodology and the recommendations of evidence-based guidelines for the management of fibromyalgia syndrome (FMS) to give an orientation within the continuously growing number of reviews on the therapy of FMS. Systematic searches up to April 2008 of the US-American National Guideline Clearing House, the Scottish Intercollegiate Guidelines Network, the Association of the Scientific Medical Societies in Germany (AWMF) and Medline were conducted. Three evidence-based guidelines for the management of FMS published by professional organizations were identified: The American Pain Society (APS) (2005), the European League Against Rheumatism (EULAR) (2007), and the AWMF (2008). The steering committees and panels of APS and AWMF were comprised of multiple disciplines engaged in the management of FMS and included patients, whereas the task force of EULAR only consisted of physicians, predominantly rheumatologists. APS and AWMF ascribed the highest level of evidence to systematic reviews and meta-analyses, whereas EULAR credited the highest level of evidence to randomised controlled studies. Both APS and AWMF assigned the highest level of recommendation to aerobic exercise, cognitive-behavioral therapy, amitriptyline, and multicomponent treatment. In contrast, EULAR assigned the highest level of recommendation to a set of to pharmacological treatment. Although there was some consistency in the recommendations regarding pharmacological treatments among the three guidelines, the APS and AWMF guidelines assigned higher ratings to CBT and multicomponent treatments. The inconsistencies across guidelines are likely attributable to the criteria used for study inclusion, weighting systems, and composition of the panels.

1. Introduction

According to the criteria of the American College of Rheumatology (ACR), fibromyalgia syndrome (FMS) is defined as chronic widespread pain and tenderness in at least eleven of 18 defined tender points (Wolfe et al., 1990). Population based estimates of the prevalence of FMS range from 0.5% to 5.8% (Croft, 2002; Gran, 2003). FMS is frequently associated with fatigue, sleep disorder, other functional somatic syndromes, mental and physical disorders, as well as disability and diminished quality of life (Henningsen et al., 2003; van Houdenhove and Luyten, 2006). FMS patients incur high direct medical costs (Boonen et al., 2005; Penrod et al., 2004; White et al., 1999) and consume significant indirect costs (e.g. sick-leave, disability pension) (Wolfe et al., 1997; Henriksson et al., 2005). Effective treatment options are therefore needed for both medical and economic reasons (Robinson and Jones, 2006).

Despite increased knowledge about FMS, there is currently no cure. The absence of any definitive treatment has resulted in a variety of pharmacological and non-pharmacological treatments being prescribed and used by patients diagnosed with FMS (Bennett et al., 2007; Müller et al., 2000). The results of various treatments have been modest and inconsistent. The large number of patients diagnosed with FMS and the conflicting data on treatment effectiveness has led to the development of a number of attempts to create evidence-based guidelines designed to provide patients and physicians guidance in selecting among the alternatives.

Although guidelines covering the same diagnosis and relevant clinical trials would be expected to come to comparable conclusions, this is not always the case. A number of factors may contribute to inconsistencies. To date there have been no systematic attempts to compare recommendations from available guidelines for the treatment of patients with FMS. The aim of the current review is to compare the recommendations of the existing evidence-based guidelines that have been published to identify consistencies

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but also to examine the presence and basis for any contradictory conclusions.

2. Methods

2.1. Search strategy

A systematic search of the US Agency for Healthcare Research and Quality (AHRQ)'s American National Guideline Clearing House (NGC) (www.guideline.gov), the Scottish Intercollegiate Guidelines Network (SGN) (www.sign.ac.uk/guidelines/index.html), and the Association of the Scientific Medical Societies in Germany (AWMF) (www.uni-duesseldorf.de/WWW/AWMF/ll/index.html) was conducted from October 2006 through April 2008, using the key words "Fibromyalgia" and "Fibromyalgia Syndrome". Medline was also searched up to April 2008 with the search terms "Guideline "(Publication Type) AND "Fibromyalgia" (Mesh). A manual search of the guideline bibliographies was undertaken to verify that all published guidelines were identified.

2.2. Inclusion criteria

To be included in our analysis, the guidelines had to meet the following criteria:

1. The guideline was commissioned by a scientific organisation.
2. The guideline focused on FMS according to ACR criteria (Wolfe et al., 1990).
3. A systematic search strategy was outlined.
4. Recognized criteria of classification evidence and recommendations were used.
5. The formal process for establishing recommendations (Delphi exercise, panel conference) was outlined.
6. Guidelines mixing FMS with other diagnoses, such as chronic fatigue syndrome, Myalgic Encephalomyelitis or somatoform disorders were excluded.

2.3. Analysis of the guidelines

Inclusion criteria and the composition of the steering committees and panels, search strategies, the classification of evidence and recommendations, the procedures for establishing recommendations, and the recommendations given by the guidelines that met inclusion criteria were assessed by two independent reviewers (WH, KT). The intraclass correlations were used to assess agreement between reviewers. All discrepancies were rechecked and consensus achieved by discussion.

3. Results

3.1. Guideline selection

The literature search yielded 46 citations (17 in NGC, three in SIGN, 23 in Medline, and three in AWMF). Three of these met our inclusion criteria – the guidelines of the American Pain Society (APS) (Burckhardt et al., 2005), the European League Against Rheumatism (EULAR) (Carville et al., 2008), and the Association of the Scientific Medical Societies in Germany (AWMF) (Klement et al., 2008). The reasons for excluding the other 43 references were: (1) Not guidelines, but reviews ($n = 11$); (2) guidelines on diseases other than FMS ($n = 14$); (3) duplications ($n = 5$); (4) mixing FMS with other diagnoses ($n = 11$); (5) no criteria for establishing level of evidence outlined ($i = 1$); and (6) not commissioned by a scientific society ($n = 1$). The interrater-reliability of this assessment was good (ICC = 0.89; $p < 0.001$).

3.2. Organisations asked for the development of the guidelines

The development of the US-American guideline was initiated and conducted by the American Pain Society. APS is a multidisciplinary organization committed to improvement of management of pain that is supported by member dues and corporate support (www.ampainsoc.org).

The EULAR-recommendations were developed by the European League Against Rheumatism. EULAR aims to promote, stimulate and support the research, prevention, treatment and rehabilitation of rheumatic diseases. EULAR is a pan-European organisation with 44 scientific member societies, 31 national social leagues, and four allied health professionals associations. Thirty-one corporate members support EULAR financially with their membership fees (www.eular.org).

The German guideline was initiated and coordinated by the German Interdisciplinary Association of Pain Therapy (DIVS). The DIVS, an umbrella organisation of 18 scientific societies, is dedicated to the improvement of interdisciplinary pain therapy. The DIVS is financed only by the membership fees of their scientific member societies (www.divs.info). The methodological development of the guideline was supported by the Association of the Scientific Medical Societies, the umbrella organisation of 152 scientific medical societies in Germany (www.awmf.org).

3.3. Composition of the working groups and sources of funding for the guidelines

Details of the working group (i.e. panel, steering committee) that were responsible for the developed the guidelines are outlined in Table 1. The APS panel consisted of a set of medical, allied health professionals, and psychological experts and a patient advocate with two panel members (a rheumatologist and a nurse) serving as co-chairs. Multiple health care disciplines engaged in the management of FMS were represented within the panel (see Table 1). Panel members wee selected because of scientific and/or clinical expertise (Burckhardt et al., 2005). The EULAR Committee was comprised 19 experts from 11 European countries, largely rheumatologists. There were no chairs designated. Details regarding the criteria by which experts were selected were not provided (Carville et al., 2008). The steering committee of AWMF consisted of 15 experts from 10 different scientific societies and two patients representing the two largest German FMS self-help organisations. All health professionals engaged in the management of FMS were represented within the steering committee and in the eight work groups. The two chairs of the steering committee had been deputized by two German umbrella organizations, the DIVS and the AWMF. The chair of the DIVS was responsible for the coordination of the search and the analysis of the literature. The chair of the AWMF was responsible for the consensus procedures to establish the recommendations. Both chairs were not permitted to vote on the recommendations. Two members from different medical and psychological societies were included in each work group. All members of the steering committee and the work groups had been nominated by the board of directors of the scientific societies engaged in the guideline. Members of the steering committee were selected because of scientific and clinical FMS expertises, members of the work group were selected because of scientific and/or clinical expertise. Furthermore, gender, hierarchical position within the medical system, and experience were equally distributed attributes amongst members of the work groups (Bernardy et al., 2008).

The development of the APS guidelines was supported by a program fund contributed to by 14 pharmaceutical companies. The EULAR guidelines were supported by EULAR itself; however, EULAR has 31 corporate members from the pharmaceutical industry. The

Table 1
Comparison of the composition of the guideline groups and the funding of the three guidelines.

	American pain society	European league against rheumatism	Association of the scientific medical societies in Germany
Nomination of members of the guideline group	Selected by panel chairs and the members of the Board of Directors	Not specified	Nominated by German scientific socities or self-help organisations
Number of members in steering committee	13	19	15
Clinical expertise of members of steering committee			
Rheumatology/Internal medicine	2	12	2
Pain therapy	1	1	1
Orthopedics/Rehabilitation	2	2	2
Neurology	1	0	1
Pediatrics	2	0	1
Family medicine	0	0	1
Pharmacology	1	0	0
Psychiatry	1	0	1
Psychological Pain Therapy	1	0	1
Psychosomatic Medicine	0	0	1
Self-help organisations	0	0	2
Others	2	4	2
Competing interests of members of steering committee	7	9	1
Sources of financial support	Membership dues, pharmaceutical companies	EULAR (pharmaceutical companies corporate members)	Scientific medical and psychological societies; self-help organisations

AWMF guidelines were financed by membership fees of the scientific societies, one self-help organization, and a grant provided by a private founder to another self-help organization. Support provided by pharmaceutical companies was not accepted. A set consisting of 7/13 members of the consensus panel of APS, 9/13 of EULAR and 1/15 of AWMF declared potential competing interests such as reimbursements for attending medical conferences, fees for speaking, being a consultant or member of an advisory board, or research grants.

4. Methodologies

Details of the methodologies used for establishing the three guidelines included in this synthesis are presented in Tables 2 and 3. The primary data bases used for the three guidelines were the same: Medline, Embase or Scopus, PsychINFO, CINHAL, Web of Sciences, Science Citation Indices, Cochrane Database of Systematic Reviews.

EULAR only included "trials" in the search strategy, whereas AWMF also included "systematic reviews" and "guidelines". Only studies with reported pain and physical function as outcome parameters were included in EULAR. Furthermore, studies deemed to be of low methodological quality were excluded by EULAR, even though the criteria for its assessment were not described. Neither the APS nor AWMF excluded studies due to low methodological quality. Thus, if randomized control trials (RCTs) were not available for frequently used therapies, APS and AWMF considered non-controlled studies. Although the search conducted by APS ended 1.5 years before the search conducted by EULAR, the number of references cited that helped to establish the recommendations was higher within the APS guideline as a result of their less stringent inclusion criteria.

APS and AWMF did not metaanalyse the outcomes of the studies reviewed. EULAR calculated the between-group difference from the mean change between the pre- and post-treatment values in the outcome measures pain and physical function. Where possible, an effect size for the "best" treatments in each category was calculated (averaged if there was more than 1 trial).

There were differences among all guidelines concerning the categorization of evidence and recommendations. EULAR used a categorizing system of evidence that was not used for evidence-based guidelines before. AWMF applied the Oxford-criteria (Oxford Centre for Evidence Based Medicine, 1995). APS used criteria of the Agency for Health Care Policy and Research, at the US Department of Health and Human Services, Public Health Service (Carr et al., 1992; Jacox et al., 1994). EULAR used the grading of recommendations suggested by (Shekelle and coworkers (1999). The grading of recommendations is based on a categorizing of evidence which is similar to the Oxford-criteria. AWMF used the grading of recommendations of the German National Disease Management Guidelines Programme (Association of the Scientific Medical Societies in Germany, 2001). The strength of recommendations given by the German National Disease Management Guidelines Programme was not always in accordance with the level of evidence available. An upgrading or down-grading was possible with the steering committee taking into consideration the consistency of study results, clinical relevance of outcome measures and effect sizes, benefit-risk-ratio, ethical obligations, patients' preferences, and practicability (to give patients and physicians an orientation within the continuously growing number of studies on the therapy of FMS).

The APS guideline was developed by a panel of 12 experts, one patient representative, and one project staff. Initial drafts of the guideline underwent two examinations conducted by 50 peer reviewers. No details were given regarding the degree of the consent, attempts were however made to address issues raised by the reviewers (Burckhardt et al., 2005). The EULAR guidelines did not specify who compiled the recommendations and they did not describe whether there guideline was submitted to any experts for review prior to publication. A consensus regarding the recommendations was reached by discussion at a final committee meeting and by email. A Deplhi exercise was used for recommendations where the systematic review only yielded limited evidence (Carville et al., 2008). The recommendations of AWMF were established through a stepwise consensus process involving the speakers and the members of the work groups, comprising four Delphi exercises conducted by electronic mail and one on-line vote to prepare the recommendations for the consensus conferences. The final recommendations were discussed and voted for at two conferences. Standardized, formal procedures to reach a consensus on recommendations were used. Each scientific society participating in the guideline process had one vote and the two patient organisations

Table 2
Comparison of the methodology of the three guidelines.

	American pain society	European league against rheumatism	Association of the scientific medical societies in Germany
Data bases	Medline, embase, PsychINFO, CINHAL, web of sciences, science citation indices, cochrane database of systematic reviews	Medline, embase, PsychINFO, CINHAL, web of sciences, science citation indices, cochrane central register of controlles trials, cochrane database of systematic reviews	Medline, scopus, PsychINFO, cochrane central register of controlles trials, cochrane database of systematic reviews
Search terms	Description of searched data bases	"Fibromyalgia", "treatment and management", "trial"	"Fibromyalgia", "fibromyalgia syndrome", "Guideline", "Meta-Analysis", "Systematic review", "randomized controlled trial", "clinical trial"
Dates of search strategy	Until April 2004	Until December 2005	Until December 2006
Sources of evicence	Systematic reviews, meta-analyses, clinical trials	Clinical trials	Systematic reviews, meta-analyses, clinical trials
Number of studies and systematic reviews cited for recommendations pharmacological therapy	60	39	81
Physical therapy and exercise	40	37	88
Education and psychotherapy	16	4	45
Complementary and alternative treatment	27	3	52
Multicomponent treatment	12	10	22
Children and adolescents	10	0	10
Sources of recommendations	Systematic reviews, meta-analyses, clinical trials, panel consensus	Controlled clinical trials, Delphi exercice	Systematic reviews, meta-analyses, clinical trials,formal panel consensus
Classification of evidence	Agency for Health Care Policy and Research criteria	No literature indicated	Oxford-criteria
Classification of recommendations	No literature indicated	Shekelle et al. (1999)	German national guidelines

had one combined vote. The degree of consensus that was reached at the two conferences was included in the guideline (strong consensus: >95% of the participants consented; consensus: 75–95% of the participants consented; Majority: 50–75% of the participants consented). A minority statement and an explanatory statement were possible. The guideline was reviewed and approved by the board of directors and the guideline committees of the societies involved in the project (Bernardy et al., 2008).

Table 3
Comparison of the categorisation of evidence and recommendations of the three guidelines.

	American pain society	European league against rheumatism	Association of the scientific medical societies in Germany
Evidence level I	Meta-analysis of multiple well-designed controlled studies	Randomised controlled double-blind trials	Ia – SR (with homogenity) of RCTs Ib-Individual RCT (with narrow Confidence Interval) IC-All or none
Evidence level II	Well-designed experimental studies	Randomised, blinded crossover trials	IIa-SR (with homogenity*) of cohort studies IIb-Individual cohort study (including low quality RCT; e.g. <80% follow-up) IIc-"Outcomes" Research; Ecological studies
Evidence level III	Well-designed quasi-experimental studies, such as nonrandomised controlled studies, single-group pre-post, cohort, time series, or matched controlled studies	Randomised single blind trials	IIIa-SR (with homogenity) of case-control studies IIIB-Individual Case-Control Study
Evidence level IV	Well-designed nonexperimental studies, such as comparative and correlational descriptive and case studies	Randomised open trials/non-randomised single blind	Case-series (and poor quality cohort and case-control studies)
Evidence level V	Case reports and clinical examples	Non-randomised open trials	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"
Recommendation Strength A	Evidence level I or consistent findings from multiple studies of level II,II or IV	Directly based on evidence level I*	Based on evidence level I**
Recommendation Strength B	Evidence of level II,II or IV with generally consistent findings	Directly based on evidence level II or extrapolated recommendation evidence level I*	Based on evidence level II**
Recommendation Strength C	Evidence of level II,II or IV with inconsistent findings	Directly based on evidence level III orextrapolated recommendation from evidence levels I,II or III*	Based on evidence levels III, IV and V**
Recommendation Strength D	Evidence level V or little/no evidence	Directly based on evidence level IV or extrapolated recommendation from evidence level I,II or III*	
Panel consensus	Expert opinion		

Abbreviations: RCT = randomised controlled trial; SR = Systematic review or meta-analysis.
* The levels of evidence underlying these recommendations differ between the literature (19) and the levels of evidence defined by EULAR.
** An up- or down-grading is possible by taking into consideration the following factors: consistency of study results, clinical relevance of outcome measures and effect sizes, benefit-risk-ratio, ethical obligations, patients' preferences and practicability.

4.1. Level of evidence and strength of recommendations

The interrater-reliability of all three guidelines regarding the levels of recommendations was very small (ICC = 0.63, $p = 0.04$), the agreement for APS and AWMF was excellent (ICC = 0.89, $p < 0.001$). Whereas the interrater-reliability of strengths of recommendations was not given (ICC = 0.26, ns), APS and AWMF showed a high agreement (ICC = 0.63, $p = 0.02$).

The primary recommendations of the three guidelines are outlined in Table 4.

APS and AWMF gave the highest level of recommendation to (1) aerobic exercise, (2) cognitive-behavioral therapy (CBT), (3) amitriptyline, and (4) multicomponent therapy. The APS guideline and AWMF guideline were completed prior to the approval of pregabalin and duloxetine for the treatment of FMS by the United States Food and Drug Administration. EULAR gave the highest level of recommendation to a set of pharmacological treatments (i.e. tramadol, amitriptyline, fluoxetine, duloxetine, milnacipran, moclobemide, pirlindol, tropisetron, pramiprexole, and pregabalin), a recommendation strength B to aerobic exercise and a recommendation strength of only D to CBT. EULAR did not give any recommendations for cyclobenzaprine, multicomponent treatment, patient education, hypnotherapy, biofeedback, or other complementary and alternative medicine approaches (CAM), such as acupuncture or homeopathy. Whereas EULAR gave a D recommendation for CBT, APS and AWMF decided an A recommendation. Whereas EULAR and AWMF did not recommend strong opioids (expert opinion), APS recommended the strength C. APS and AWMF provided the same strength of recommendation (B) to tramadol, balneotherapy, hypnotherapy, biofeedback, massage therapy, pregabalin, fluoxetine, and duloxetine. Whereas APS recommended patient education as single intervention (B), acupuncture (C) and trigger point injections (C), AWMF did not recommend patient education as single intervention (A), acupuncture (A) [a minority report recommended acupuncture with strength B], and trigger point injections (C). All three guidelines recommend against the use of NSAID's (as single intervention) or corticosteroids.

In contrast to EULAR, APS and AWMF suggested a stepwise approach to the management of FMS and stressed the importance of patients' self-management in long-term therapy. Furthermore, APS and AWMF provided separate recommendations for the management of FMS in children and adults. APS recommended CBT, aerobic exercise, and physical therapy without giving levels of evidence or grades of recommendation. APS recommended that antidepressants for pain therapy should be used with extreme caution, extensive parenteral education and psychiatric consultation. AWMF recommended CBT (B), multicomponent therapy (C), exercise and physical therapy. The guideline acknowledged that any kind of pharmacological therapy (analgesics, antidepressants) should only be used with extreme caution and by physicians with extensive experiences with the use of these drugs in children and adolescents (Michels et al., 2008).

5. Discussion

We detected a number of similarities between APS and AWMF regarding the recommendations for "first line" therapies (aerobic exercise, CBT, amitriptyline, and multicomponent treatment), as opposed to the recommendations of EULAR, which only favored pharmacologcial treatments including amitriptyline, tramadol, fluoxetine, duloxetine, milnacipran, moclobemide, pirlindol, tropisetron, pramiprexole, and pregabalin.

There are several explanations for the striking differences, especially between the APS and AWMF guidelines on the one hand and the EULAR guidelines on the other. Specifically, the grading system used by APS and AWMF ascribed the highest level of evidence to systematic reviews and meta-analyses of RCTs, whereas EULAR did not take these sources of evidence into consideration. All the clearing houses that established guidelines and were used for this review (USA, Great Britain, Germany) ascribe the highest level of evidence to systematic reviews and meta-analyses of RCTs. EULAR argued against using meta-analyses because of the poor quality of the studies included (e.g. exercise). Yet a recently published Cochrane review of the efficacy of exercise for treating FMS described a 'gold standard' of evidence to the beneficial effects of supervised aerobic exercise training on physical capacity and FMS symptoms (Busch et al., 2007).

Although the search strategies of all thee guidelines were comparable, EULAR did not include studies on multicomponent

Table 4
Comparison of the recommendations of the three guidelines (according to the APS guideline order of scientific evidence).

	American Pain Society		European League Against Rheumatism Level of Evidence		Association of the Scientific Medical Societies in Germany	
	Level of Evidence	Strength of recommendation	Level of Evidence	Strength of recommendation	Level of Evidence	Strength of recommendation
Aerobic exercice	I	A	IIb	C	Ia	A
Cognitive-behavioral therapy	I	A	IV	D	Ia	A
Amitriptyline	I	A	Ib	A	Ia	A
Cyclobenzaprine	I	A	*	*	Ia	C
Multicomponent therapy	I	A	*	*	Ia	A
Tramadol	II	B	Ib	A	IIb	C
Balneotherapy	II	B	IIa	B	IIb	B
Patient education alone	II	B	*	*	Ia	Not B
Hypnotherapy	II	B	*	*	IIb	B
Biofeedback	II	B	*	*	IIb	Not B
Massage therapy	II	B	*	*	IIb	B
Anticonvulsants	II	B	Ib	A	IIb	B
SSRI (Fluoxetine)	II	B	Ib	A	IIb	B
SNRI (Duloxetine)	II	B	Ib	A	IIb	B
Opioids	III	C	IV	Not D	IV	Not C
Acupuncture	II	C	*	*	Ia	Not A
Trigger point injection	III	C	*	*	IV	Not C

Not = Not recommended.
* No statement.

treatment, some physical therapies (e.g. acupuncture, massage), or psychological therapies other than CBT.

Whereas APS and AWMF used the data of systematic reviews and meta-analyses to support their recommendations, EULAR performed its own statistical analyses by calculating effect sizes of pain visual analog scales (VAS) and function assessed by the fibromyalgia impact questionnaire (Burckhardt et al., 1991).

EULAR used the criteria of placebo-controlled studies. Indeed, this criteria is a very relevant criteria for pharmacological studies, however it is less appropriate in the evaluation of non-pharmacological treatments. Using of a placebo group as control group has been shown to lead to the overestimation of the effects of psychological pain therapy (Thieme et al., 2007). No panel members from the field of psychology and psychosocial medicine were included on the EULAR committee who might have been able to explain issues that are specific to nonmedical treatments.

There were relately few differences between APS and AWMF. These can likely be explained by the fact that systematic reviews demonstrating an ineffectiveness of patient education as single intervention and acupuncture and a RCT demonstrating the superiority of CBT versus self-monitoring in adolescents at the end of therapy were published subsequent to the publication of the APS guidelines (Burckhardt, 2005; Mayhew and Ernst, 2007; Kashikar-Zuck et al., 2005).

The strength of the recommendation for cyclobenzaprine was downgraded by AWMF due to the fact that this drug is not licensed in Germany. Although the sources of evidence did not differ (only one non-controlled study was available), APS recommended trigger point injections (level C), whereas AWMF did not recommend this treatment. This different recommendation highlights the influence of expert opinions and the composition of the steering committee and the panel. A multidisciplinary approach to the management of FMS was proposed by all three guidelines reviewed whereby APS and AWMF recommended beside pharmacological treatment, physiotherapy, and psychological pain treatment, in particular.

We recommend a regular update of the existing guidelines and the development of new guidelines that adhere to the national clearing house standards for developing guidelines, such as complete provision of the literature and giving the highest level of evidence to systematic reviews and meta-analyses of RCTs. The recommendations should focus on all of the treatments frequently used by FMS patients, including complementary and alternative medicine (CAM). The developmental process of establishing guidelines for the management of FMS should include patients and a balanced composition of work groups and panels, resulting in a consensus based on scientific societies, rather than single persons. Finally, recommendations should be tailored to the health system of each country.

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