English Version of "Methodenreport zur Erstellung der Leitlinie".
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W. Häuser[1, 2] · H. Wang[3] · K. Bernardy[4] · I. Kopp[5]
[1] Department of Internal Medicine I, Klinikum Saarbrücken GmbH, Saarbrücken
[2] Department of Psychosomatic Medicine and Psychotherapy, Klinikum rechts der Isar, Technische Universität München
[3] Department of Orthopedics, Trauma Surgery and Spinal Cord Injury, Clinic for Orthopedics and Trauma Surgery, Heidelberg University Hospital, Heidelberg
[4] Department of Pain Management, Clinic of Anaesthesiology, Intensive Care, Palliative and Pain Medicine, BG University Hospital Bergmannsheil Bochum, Ruhr-University of Bochum
[5] AWMF- Institute of Medical Knowledge Management, Philipps-University, Marburg

Methodological fundamentals used in developing the guideline

On June 15, 2010, the board of the German Association of Pain Therapy ("Deutsche Interdisziplinären Vereinigung für Schmerztherapie", DIVS) decided to update the interdisciplinary S3 guidelines on fibromyalgia syndrome (FMS) by the Association of the Scientific Medical Societies ("Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften", AWMF; registration no. 041/004). The task of initiating and coordinating the update process as well as literature search and compilation of evidence reports was assigned to the general secretary of DIVS, W. Häuser, MD.

Materials and methods

Basics

The guideline update was carried out according to the rules of the AWMF in Germany [1], the methodology for national guidelines for health treatment [2] and the standards of the German instrument for the evaluation of guidelines ("Deutschen Instruments zur methodischen Leitlinienbewertung", DELBI) [7, 14]. Methodical advice was contributed by Professor Ina Kopp, MD, leader of the AWMF Institute of Medical Knowledge Management. The complete timeline of the development and consensus process can be found in **Tab. 1**.

Mixture of the guideline group: participation of interest groups

Participation of scientific societies

The executive committee of DIVS decided to invite scientific societies who represent medical specialties treating FMS patients to participate in the guideline development. Scientific societies that do represent medical specialties treating FMS patients were not invited. When an association agreed to participate, its board was asked to confirm its present member in the FMS guideline steering board or to delegate a new competent member. The task of the steering board consisted of the definition of objectives to be reached, issues to be covered, methodology to be used, voting procedures for the delegates to be used in the consensus process concerning guideline subjects, algorithms and quality indicators. All invited associations, which already participated in the first version of the guideline, agreed to continue participating with the exception of German Association of General and Family Medicine ("Deutschen Gesellschaft für Allgemein- und Familienmedizin", DEGAM). DEGAM stated their refusal with conceptual and process-related aspects and the consequences for family doctors to keep up with the update and implementation (email dated Jun 10, 2010). The participating associations and their delegates can be found in **Tab. 2**.

Participation of patients

The two largest German FMS patient self-help organizations, the German League of People against Rheumatism ("Deutsche Rheuma-Liga") and the German Fibromyalgia Association ("Deutsche Fibromyalgie-Vereinigung"), pursued membership in the steering board respectively and obtained one vote each in the consensus process, similar to a scientific society.

Composition of working groups: additional experts

The presidents of the participating associations were asked to confirm their members of the first version of the guideline and/or to delegate new members.

The nomination should be based on experience with treatment and/or research of FMS. Furthermore they were asked to choose from all types of care (outpatient, inpatient and rehabilitation care) and to look after a balanced relation of hierarchies and gender. The workgroups and their leaders can be found in **Tab. 3**.

The first two authors contributed equally to the manuscript.

Tab. 1 Overview of workflow and time flow of the development and consensus trial for updating of the guideline

Category	Contents	Period
Preparation	Drafting of proposals for methods (Guideline coordinator and Institute of Knowledge Management of AWMF)	Jun 2010–Aug 2010
	Convention of the steering board for the guidelines	By Sept 30, 2010
	Consensus of the steering board for methods of the development of the guidelines	
	Nomination of members of the workgroup by the steering board of the professional associations and patient organizations	By Dec 30, 2010
Drafting of recommendations	Establishment of search terms and definitions for systemic literature research by guideline coordinators	By Nov 30, 2010
	Literature research by guideline coordinators	By Jan 15, 2011
	Data extraction by guideline coordinators	By Feb 28, 2011
	Formulation of suggestions include references (1st version)	By Mar 30, 2011
	Revision of recommendations and references by respective working groups	By May 30, 2011
	Formulation of recommendations (2nd version) and references by workgroup leader and guideline coordinator	By Jul 30, 2011
	Anonymous online vote of the second version of all suggestions by all participants (Delphi methods)	By Sept 15, 2011
	Formulation of suggestions (3rd version) by workgroup leader and guideline coordinator	By Oct 30, 2011
	Consensus conferences: plenary meeting for vote of suggestions (4th version)	Nov 10 and 24, 2011
	Revision of respective chapters by guideline coordinator, workgroup leader and steering board according to decisions by the consensus meetings and final passing of text by steering board	By Jan 31, 2012
	Annotation of guidelines by boards of each participating professional associations	Feb 15–Mar 26, 2012
	Submission of guidelines to AWMF	Apr 13, 2012
	Acceptance of guidelines by AWMF	Apr 19, 2012
	Publication as special edition in *Der Schmerz*	June 2012

AWMF Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften.

Tab. 2 Participating medical and psychological scientific associations and patient self-help organizations and delegates from steering board

- Association of the Scientific Medical Associations in Germany (AWMF): Prof. Dr. med. Ina Kopp
- German Fibromyalgia Federation (DFV): Margit Settan
- German Association of Neurology (DGN): Prof. Dr. med. Claudia Sommer
- German Association of Orthopaedics and Traumatology (DGOOC): Prof. Dr. med. Marcus Schiltenwolf
- German Association of Physical Medicine and Rehabilitation (DGPMR): Dr. med. Andreas Winkelmann
- German Association for Psychosomatic Medicine and Psychotherapy (DGPM) and German Council for Psychosomatic Medicine (DKPM): Univ. Prof. Dr. med. Peter Henningsen
- German Association for Psychiatry and Neurology: Univ. Prof. Dr. med. Karl J. Bär
- German Association of Psychological Pain Therapy and Pain Research (DGPSF): Univ. Prof. Dr. soc. Dipl. Psych. Kati Thieme
- German Association of Rheumatology (DGRh): Univ. Prof. Dr. med. Wolfgang Eich
- German Association for the Study of Pain (DGSS): Dr. med. Bernhard Arnold
- German League of People against Rheumatism: Sabine Eis
- Association of Children and Adolescence Rheumatology (GKJR): Dr. med. Renate Häfner

DFV Deutsche Fibromyalgie-Vereinigung, **DGN** Deutsche Gesellschaft für Neurologie, **DGOOC** Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie, **DGPMR** Deutsche Gesellschaft für Physikalische Medizin und Rehabilitation, **DGPM** Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie, **DKPM** Deutsches Kollegium für Psychosomatische Medizin, **DGPPN** Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde, **DGPSF** Deutsche Gesellschaft für Psychologische Schmerztherapie und -Forschung, **DGRh** Deutsche Gesellschaft für Rheumatologie, **DGSS** Deutsche Gesellschaft zum Studium des Schmerzes, **GKJR** Gesellschaft für Kinder- und Jugendrheumatologie.

The task of the workgroup members consisted of revising results found in the literature search and data extraction, writing recommendations and background reports, creating drafts for the steering board in a concerted manner and attending consensus conferences. To take part in consensus meetings conflicting interests needed to be declared and the membership in the work-groups needed to be performed actively.

Complete attendance to all voting meetings on drafts for the consensus conferences was regarded as the minimal requirement for an active membership. Five persons (3 delegates from the German Fibromyalgia Association, 1 delegate from the German Association of Neurology, 1 delegate from the German Society for the Study of Pain) were excluded from the guideline group before the consensus conferences because of failure to meet the requirement of active membership.

Some characteristics of members of the working groups can be found in **Tab. 4**.

Compared to other medical German guidelines the well-balanced ratio of gender and hierarchy has to be pointed out.

Editorial independence: dealing with conflicting interests

Developing a guideline for the health sector needs professional expertise as well as commercial independence. A declaration of each member involved in the development of the guideline is crucial for its high quality and public credibility.

All members involved in the development of the guideline signed a declaration from AWMF about potential conflicting interests.

Financial and other relevant conflicting interests with respect to third parties that might have any material presence in the contents of the guideline can be found in **Tab. 5**.

Potential conflict of interests resulted from execution/participation in studies about therapies based on drugs or physical/psychological treatments, discipleship of psychotherapeutic techniques, membership (as manager or employee) of a clinical facility where FMS patients are treated.

From the point of view of the steering board the guideline group was balanced with respect to its interests (medical, psychological, physical and complementary therapies and affiliation). Potential conflicting interests of individuals in the consensus conferences could be neutralized to the greatest possible extent by transferring their votes to other members of their association.

Financing of the guideline

The guidelines were financed by DIVS and the participating associations. There was no support (neither direct nor indirect) of any kind from commercial organizations. The cost of 10,000 Euro for the guideline development (internet platform, external moderation of the consensus conferences) was paid by DIVS. The expenses for traveling to the consensus conferences were paid by the members themselves or their associations. Travel and other expenses were budgeted according to the rules of national law and regulations in the universities. All members of the guideline group worked as non-profit, without any payment.

Abstract · Zusammenfassung

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W. Häuser · H. Wang · K. Bernardy · I. Kopp

Methodological fundamentals used in developing the guideline

Abstract

Background. The scheduled update to the German S3 guidelines on fibromyalgia syndrome (FMS) by the Association of the Scientific Medical Societies ("Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften", AWMF; registration number 041/004) was planned starting in March 2011.
Materials and methods. The development of the guidelines was coordinated by the German Interdisciplinary Association for Pain Therapy ("Deutsche Interdisziplinären Vereinigung für Schmerztherapie", DIVS); 9 scientific medical societies and 2 patient self-help organizations participated. Eight working groups with a total of 50 members were evenly balanced in terms of gender, medical field, potential conflicts of interest and hierarchical position in the medical and scientific fields.Literature searches were performed using the Medline, PsycInfo, Scopus and Cochrane Library databases (until December 2010). The grading of the strength of the evidence followed the scheme of the Oxford Centre for Evidence-Based Medicine. The formulation and grading of recommendations was accomplished using a multi-step, formal consensus process. Efficacy, risks, patient preferences and applicability of therapies available were summarized into a balance sheet. The guidelines were reviewed by the boards of the participating scientific medical societies.
Conclusion. The guidelines will be published in several forms: complete and short scientific versions, clinical practice and patient versions.The English full-text version of this article is available at SpringerLink (under "Supplemental").

Keywords
Fibromyalgia syndrome · Guideline · Methods · Association of the Scientific Medical Societies in Germany · German Association of Pain Therapy

Methodenreport zur Erstellung der Leitlinie

Zusammenfassung

Hintergrund. Die planmäßige Aktualisierung der S3-Leitlinie zum Fibromyalgiesyndrom (FMS; AWMF-Registernummer 041/004) wurde ab März 2011 vorgenommen.
Material und Methoden. Die Leitlinie wurde unter Koordination der Deutschen Interdisziplinären Vereinigung für Schmerztherapie (DIVS) von 9 wissenschaftlichen Fachgesellschaften und 2 Patientenselbsthilfeorganisationen entwickelt. Acht Arbeitsgruppen mit insgesamt 50 Mitgliedern wurden ausgewogen in Bezug auf Geschlecht, medizinischen Versorgungsbereich, potenzielle Interessenkonflikte und hierarchische Position im medizinischen bzw. wissenschaftlichen System besetzt.Die Literaturrecherche erfolgte über die Datenbanken Medline, PsycInfo, Scopus und Cochrane Library (bis Dezember 2010). Die Graduierung der Evidenzstärke erfolgte nach dem Schema des Oxford Center for Evidence Based Medicine. Die Formulierung und Graduierung der Empfehlungen erfolgte in einem mehrstufigen, formalisierten Konsensusverfahren. Wirksamkeit, Risiken, Patientenpräferenzen und Umsetzbarkeit von Therapieverfahren wurden in einer Bilanz zusammengefasst. Die Leitlinie wurde von den Vorständen der beteiligten Fachgesellschaften begutachtet.
Schlussfolgerung. Die Leitlinie wurde als Lang-, Kurz-, Kitteltaschen- und Patientenversion veröffentlicht.

Schlüsselwörter
Fibromyalgiesyndrom · Leitlinie · Methoden · Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) · Deutsche Interdisziplinäre Vereinigung für Schmerztherapie (DIVS)

Methodology for creating recommendations

Technical support: Internet-based development of proposals for the recommendations of the guideline

To save time and money the development

Tab. 3 Working groups and their speakers

Definition, classification, epidemology and diagnosis: Univ. Prof. Dr. med. Wolfgang Eich (DGRh), Univ.-Prof. Dr. med. Peter Henningsen (DKPM)
Etiopathogenesis and pathophysiology: Prof. Dr. med. Claudia Sommer (DGN), Univ. Prof. Dr. soc. Dipl.psych. Kati Thieme (DGPSF)
Nationwide care principle and patient education: Univ. Prof. Dr. med. Wolfgang Eich (DGRh), PD Dr. med. Frank Petzke (DGSS)
Drug therapy: Univ. Prof. Dr. med. Karl-Jürgen Bär (DGPPN), Prof. Dr. med. Claudia Sommer (DGN)
Psychotherapy: Prof. Dr. med. Volker Köllner (DGPM), Univ. Prof. Dr. soc. Dipl. psych. Kati Thieme (DGPSF)
Physiotherapy and physical therapy: Dr. med. Martin Offenbächer (DGMPR), Prof. Dr. Marcus Schiltenwolf (DGOOC)
Multidisciplinary therapy: Dr. med. Bernhard Arnold (DGSS), Dr. med. Andreas Winkelmann (DGMPR)
Alternative and complementary therapies: Prof. Dr. med. Jost Langhorst (DKPM), Professor Dr. phil. Frauke Musial (DGSS)
Children and adolescents: Dr. med. Renate Häfner (GKJR), Prof. Dr. med. Boris Zernikow (DGSS)

DGN Deutsche Gesellschaft für Neurologie; **DGOOC** Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie; **DGPM** Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie; **DGPMR** Deutsche Gesellschaft für Physikalische Medizin und Rehabilitation; **DGPPN** Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde; **DGPSF** Deutsche Gesellschaft für Psychologische Schmerztherapie und -Forschung; **DGRh** Deutsche Gesellschaft für Rheumatologie; **DGSS** Deutsche Gesellschaft zum Studium des Schmerzes; **DKPM** Deutsches Kollegium für Psychosomatische Medizin; **GKJR** Gesellschaft für Kinder- und Jugendrheumatologie.

Tab. 4 Constitution of guideline working groups

Gender	
Women	20 (40.0%)
Men	30 (60.0%)
Level of care	
General practitioner	5 (10.0%)
Secondary care	14 (28.0%)
University institutions	21 (42.0%)
Rehabilitation	6 (12.0%)
Patients	4 (8.0%)
Hierarchy	
Residence/scientific employee	8 (16.0%)
Senior physician/leading psychologist	20 (40.0%)
Chief physician/university professor	13 (26.0%)
General practitioner	5 (10.0%)
Patients	4 (8.0%)
Speciality	
Medicine	40 (80.0%)
Psychology	4 (8.0%)
Physiotherapy	2 (4.0%)
Patients	4 (8.0%)

of recommendations was carried out on an internet platform (http://www.leitlinienentwicklung.de/). Here the leaders of the working teams and coordinator of the guideline published the necessary working materials and had the right to formulate recommendations. Comments and discussions about these recommendations could be given here by the team members and in a separated section by the members of other working groups. For this, every working group received its own forum. In addition, teleconferences and email communication were used. Due to the organization of the preparatory work, meetings were not necessary until the consensus conferences.

Guideline research

Research about existing international guidelines for FMS was carried out by the guideline coordinator in the databases http://www.g-i-n.net and http://www.guideline.gov. A search for the keywords "Fibromyalgia"[MeSH] AND (guideline OR consensus) resulted in 156 hits in Pubmed, 3 hits in http://www.g-i-n.net and 19 hits in http://www.guideline.gov. Ten interdisciplinary consensus documents about diagnosis and/or therapy of FMS were found [3, 5, 6, 8, 11, 12, 13, 16, 22, 27]. The described consensus processes and the defined evidence were structured very differently. The reference lists of the documents were compared with the current findings.

Literature search

The literature search was carried out using keywords, which had been worked out by the team leaders and the guideline coordinator, by the guideline secretary in the databases Medline (via search Pubmed from inception to Dec. 31, 2010), PsycInfo (from inception to Dec. 31, 2010), Scopus (from inception to Dec. 31, 2010) and Cochrane Library (The Cochrane Database of Systematic Reviews, The Cochrane Central Register of Controlled Trials CENTRAL, from inception to Dec. 31, 2010).

To find yet unpublished studies in order to avoid publications bias, the database of the US National Institutes for Health (http://www.clinicaltrials.gov) was searched.

In Medline the following search strategy was used:

a) "Fibromyalgia"[MeSH]
b) For the work group "Therapeutic procedure" the following Pubmed search filter (category "therapy") which was optimized for sensitive/wide search (sensitivity/specificity of 99%/70%) was used for localization of randomised, controlled trials (RCTs):((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]) (Pubmed 2010).
c) For the work group "Definition, classification and prognosis" the Pubmed searchfilter Diagnosis/broad [filter] and (Prognosis/Broad[filter]) was used.
d) For the work group "Etiopathogenesis and Pathophysiology" the search filter "best one term strategy" risk (T) of Oxford Centre for Evidence Based Medicine was used (Review"[Publication Type] OR "Review Literature"[MeSH]).

For the search in SCOPUS and PsycInfo the keywords "Fibromyalgia" and "randomized contolled trial" in combination of the working group-specific Medline

Tab. 5 Financial and other potential conflicts of the guideline participants (according to the guidelines of AWMF)

Name	Consultant, referee or paid collaboration on scientific advisory board of a health business venture (such as pharmaceutical industry, medical products company) or of commercially orientated institutes or an insurance	Honorary for lecture and training course or paid author or co-author of assignment from a company in the fields of health care or insurance	Financial benefits (third-party funds) for research projects or direct finance of persons from the ventures in the fields of health care, commercially orientated assignment institutes or insurance	Owner interest in drugs/medical products (such as patent, copyright, selling licence)	Owner of business contingent, holding, fonds with share/participation in a company in the health care field	Personal relationship to the authorized delegate of a company in health care field	Member of relevant associations/professional institutions regarding guideline development, member of parliament in the context of guideline or politic, academic (e.g. affiliations to certain "schools"), scientific or personal interests that can reason potential conflicts.
Rieke Alten (DGRh)	Abott, BMS, Novartis, Merck, Pfizer	Abott, BMS, Novartis, Merck, Pfizer	Abott, BMS, Novartis, Merck, Pfizer				Association of Physical and Rehabilitative Medicine
Bernhard Arnold (DGSS)							Board member BVSD
Karl-Jürgen Bär (DGPPN)		Eli-Lilly, Janssen, Pfizer	Eli-Lilly				
Kathrin Bernardy (DGPSF)							Graduated as a Psychoanalytical University Professor; psychotherapy training in behavior therapy
Michael Bernateck (DGRh)							
Wolfgang Brückle (DGRh)							DGPMR, Professional Institute of Rheumatology
Marcus Burgmer (DKPM)							
Guido Bürk (GKJR)							
Wolfgang Eich (DGRh)		Pfizer					Deutsche Gesellschaft für Rheumatologie
Ulrike Eidmann (DRL)							
Sabine Eis (DRL)							
Rita Engelhardt (DGOOC)							
Erich Friedel (DFV)					Kommanditist Vitalis Medical Resort GmbH		
Kerstin Gerhold (GKJR)		Bristol-Myers Squibb					
Wolf Greiner (DGPPN)							Training in psychodynamic psychotherapy
Renate Häfner (GKJR)		Abott, Pfizer					DGRh

Tab. 5 Financial and other potential conflicts of the guideline participants (according to the guidelines of AWMF) (Forsetzung)

Name	Consultant, referee or paid collaboration on scientific advisory board of a health business venture (such as pharmaceutical industry, medical products company) or of commercially orientated institutes or an insurance	Honorary for lecture and training course or paid author or co-author of assignment from a company in the fields of health care or insurance	Financial benefits (third-party funds) for research projects or direct finance of persons from the ventures in the fields of health care, commercially orientated assignment institutes or insurance	Owner interest in drugs/medical products (such as patent, copyright, selling licence)	Owner of business contingent, holding, fonds with share/participation in a company in the health care field	Personal relationship to the authorized delegate of a company in health care field	Member of relevant associations/professional institutions regarding guideline development, member of parliament in the context of guideline or politic, academic (e.g. affiliations to certain "schools"), scientific or personal interests that can reason potential conflicts.
Winfried Häuser (DIVS)		Falk-Foundation, Janssen-Cilag					Trainer for medical hypnosis and autogenic training DGÄHAT; trainer for systemic therapy SG
Peter Henningsen (DKPM)		Eli-Lilly					Training in psychoanalytic–interactional therapy and clinical hypnosis
Hans-Jürgen Hesselschwerdt (DGOOC	Bayer	Bayer, MSD					Board member of the Professional Association of Specialists in Orthopedic Surgery Board member of Professional Institute of Consultants for Orthopaedic and Traumatology
Toni Hospach (GKJR)							
Arnold Illhardt (GKJR)							
Winfried Jäckel (DGRh)	AQUA		Old age insurance, statutory health insurance companies,Rehabilitation centers				German Association of Rehabilitation Science, DRL
Klaus Klimczyk (DGOOC)		Mundipharma, MSD					
Volker Köllner (DKPM)		Actelion, Astra Zeneca, Bayer, Glaxo Smith Kline					APS, DGMP, DGPPR, DGK, ICPR, DGRW, GMA, DEGPT, DGSS, DÄVT; AG Social Democrats in health care
Ina Kopp (AWMF)							
Edeltraud Kühn (DRL)							
Hedi Kühn-Becker (DGSS)							DGS, DÄVT, IGPS

Tab. 5 Financial and other potential conflicts of the guideline participants (according to the guidelines of AWMF) (Forsetzung)

Name	Consultant, referee or paid collaboration on scientific advisory board of a health business venture (such as pharmaceutical industry, medical products company) or of commercially orientated institutes or an insurance	Honorary for lecture and training course or paid author or co-author of assignment from a company in the fields of health care or insurance	Financial benefits (third-party funds) for research projects or direct finance of persons from the ventures in the fields of health care, commercially orientated assignment institutes or insurance	Owner interest in drugs/medical products (such as patent, copyright, selling licence)	Owner of business contingent, holding, fonds with share/participation in a company in the health care field	Personal relationship to the authorized delegate of a company in health care field	Member of relevant associations/professional institutions regarding guideline development, member of parliament in the context of guideline or politic, academic (e.g. affiliations to certain "schools"), scientific or personal interests that can reason potential conflicts.
Jost Langhorst (DKPM)		Alere, Falk-Foundation, Repha, Merckle Recordati	Repha, Techlab, Falk				Board member of German Association of Herbal Medicine Training in psychodynamic psychotherapy
Harald Lucius (DGN)		Eli-Lilly, Grünenthal				Stefan Frauke (Grünenthal)	DGSS, BVSD, mindfulness-based stress trainer
Martina Moog-Egan (DGSS)	Neuro-Orthopedic Institute, Adelaide						
Kirsten Mönkemöller (GKJR)							Working Group of Paediatric Psychosomatic Medicine
Frauke Musial (DGSS)							
Martin Offenbächer (DGPMR							Working Group of Pain Therapy in Bavaria, Professional Institute of Rehabilitation
Frank Petzke (DGSS)	Cilag-Janssen, Johnson u. Johnson, Grünenthal	Eli-Lilly, Grünenthal	UCB, Pierre Fabre				Board member of DGSS, DGAI, BVSD, BDA
Matthias Richter (GKJR)							DGP
Marcus Schiltenwolf (DGOOC)							BVSD, DIVS, Training in psychodynamic psychotherapy
Tobias Schmidt-Wilcke (DGSS)							
Elisabeth Schnöbel-Müller (GKJR)							DGKGM, DGKJPP, Paediatric Psychosomatic Medicine
Dagmar Seeger (DGSS)							
Margit Settan (DFV)							
Claudia Sommer (DGN)	Allergan, Astellas, Eli-Lilly	Astellas, Baxter, Behring, Genzyme Grünenthal, Pfizer	Bayer				DGSS

Tab. 5 Financial and other potential conflicts of the guideline participants (according to the guidelines of AWMF) (Forsetzung)

Name	Consultant, referee or paid collaboration on scientific advisory board of a health business venture (such as pharmaceutical industry, medical products company) or of commercially orientated institutes or an insurance	Honorary for lecture and training course or paid author or co-author of assignment from a company in the fields of health care or insurance	Financial benefits (third-party funds) for research projects or direct finance of persons from the ventures in the fields of health care, commercially orientated assignment institutes or insurance	Owner interest in drugs/medical products (such as patent, copyright, selling licence)	Owner of business contingent, holding, fonds with share/participation in a company in the health care field	Personal relationship to the authorized delegate of a company in health care field	Member of relevant associations/professional institutions regarding guideline development, member of parliament in the context of guideline or politic, academic (e.g. affiliations to certain "schools"), scientific or personal interests that can reason potential conflicts.
Michael Späth (DGRh)		Eli Lilly, MSD, Pfizer, Pierre Fabre, Abbott, Roche, UCB					
Kati Thieme (DGPSF)							APS, DGS; Psychological Psychotherapy, Psychologic Pain Therapy
Thomas Tölle (DGN)	Astellas, Eli-Lilly, Grünenthal, Mundipharma, Pfizer	Astellas, Eli-Lilly, Grünenthal, Pfizer					DGSS
Nurcan Üçeyler (DGN)							
Martin von Wachter (DKPM)							DGSS, IGPS; Systemic and Psychodynamic Psychotherapy
Haili Wang (DGOOC)							
Martin Weigl (DGPMR)							Board member DGPMR; DGSP
Thomas Weiss (DKPM)		Pizer					DGM; Training in psychoanalysis and systemic therapy
Andreas Winkelmann (DGPMR)							
Eva Winter (DGSS)	Grünenthal	Mundipharma					
Boris Zernikow (DGSS)	Grünenthal, Janssen, Schwarz	Grünenthal, Janssen, Mundipharma, Nycoma					DGSS, DGS, DGKJM

AWMF Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften; **BDA** Berufsverband Deutscher Anästhesisten; **BVOU** Berufsverband der Fachärzte für Orthopädie und Unfallchirurgie; **BVSD** Berufsverband der Ärzte und Psychologischen Psychotherapeuten in der Schmerz- und Palliativmedizin in Deutschland; **DÄVT** Deutsche Ärztliche Gesellschaft für Verhaltenstherapie; **DeGPT** Deutschsprachige Gesellschaft für Psychotraumatologie; **DFV** Deutsche Fibromyalgie-Vereinigung; **DGÄHAT** Deutsche Gesellschaft für Ärztliche Hypnose und Autogenes Training; **DGAI** Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin; **DGKJ** Deutsche Gesellschaft für Kinder- und Jugendmedizin; **DGKJP** Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie; **DGMP** Deutsche Gesellschaft für Medizinische Psychologie; **DGN** Deutsche Gesellschaft für Neurologie; **DGOOC** Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie; **DGPM** Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie; **DGPMR** Deutsche Gesellschaft für Physikalische Medizin und Rehabilitation; **DGPPN** Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde; **DGPPR** Deutsche Gesellschaft für Klinische Psychotherapie und Psychosomatische Rehabilitation; **DGPSF** Deutsche Gesellschaft für Psychologische Schmerztherapie und -Forschung; **DGRh** Deutsche Gesellschaft für Rheumatologie; **DGRW** Deutsche Gesellschaft für Rehabilitationswissenschaften; **DGS** Deutsche Gesellschaft für Schmerztherapie; **DGSP** Deutsche Gesellschaft für Sportmedizin und Prävention; **DGSS** Deutsche Gesellschaft zum Studium des Schmerzes; **DIVS** Deutsche Interdisziplinäre Vereinigung für Schmerztherapie; **DKPM** Deutsches Kollegium für Psychosomatische Medizin; **DRL** Deutsche Rheuma-Liga; **GKJR** Gesellschaft für Kinder- und Jugendrheumatologie; **GMA** Gesellschaft für Medizinische Ausbildung; **IGPS** Interdisziplinäre Gesellschaft für Psychosomatische Schmerztherapie; **SG** Systemische Gesellschaft.

search terms were used. For the search in the Cochrane Library and NIH database the search terms "Fibromyalgia" in combination with the working group-specific Medline search words were used. The working group-specific search terms and the number of hits are listed in Tab. 6.

Selection of articles found and index completion

The search results were matched with the indices of the guidelines and adjusted when needed. Furthermore randomized controlled studies that could not be found in the databases but that were known to working group-members were included. Additionally, German publications not listed in the databases listed above were reviewed if they were considered to be relevant according to the opinion of the coordinator of the guidelines or members of the working groups.

Inclusion and exclusion criteria

The search results were analyzed by the guideline coordinator and the working group-leaders based on the titles and abstracts by applying defined include/exclude criteria (filters). Filter 1 excluded search results when the following criteria matched: problem not covered, no controlled study, animal study, no complete publication, case report, letter to the editor, double publication. For the remaining studies the complete version (fulltext) was ordered. Filter 2 used the same criteria as filter 1, this time on the complete text. In cases of disagreement whether to include or exclude a publication, simple majority decided. The considerably relevant publications were used for the guideline text.

Inclusion criteria

- Diagnosis of FMS according to defined criteria
- In studies about therapy procedures: randomized studies with control groups, which checked a single therapy procedure. For the control groups the following selection order was used: medical or psychological placebo, usual therapy, waiting list, no therapy and any other kind of active therapy. For therapy procedures often used in Germany and worth an annotation, controlled studies without randomization or case series were used, if no RCTs were available.
- In the studies for etiology and pathophysiology: prospective cohort studies or systematic reviews of cross-sectional studies (case–control studies, ecologic studies, case series). If in the view of the guidelines none of these types of studies were available for etiological factors which were assumed to be relevant, case–control studies or case series were consulted for analysis. Irrespective of the language used a publication was included.

Exclusion criteria

- No defined criteria for the diagnosis of FMS
- In studies about therapy procedures: randomized studies with combined therapies (e.g. acupuncture with amitriptyline) (with the exception of the multimodal therapy); experimental studies (duration <1 week and/or application only 1 or 2 times, e.g. experimental studies about drugs or hypnosis)
- Studies without randomizing or controls
- In the studies for etiology and pathophysiology: case–control studies, ecological studies, case series

Archiving

The search strategies were stored electronically. The hits were stored electronically. All studies that were used in the recommendations of the working groups were available to all participants in full-text form on a password-protected noncommercial internet platform.

Data extraction and analysis

The steering board decided that evidence reports (systematic summary and meta-analysis) about every therapy procedure should be written, when

a) at least 2 randomized controlled studies with at least 50 participants (necessary for quantitative data analysis were available *and/or*
b) they were so frequently used in Germany, that they should be checked anyway. In cases where none or only 1 RCT was available, controlled studies or case series were used. In cases with only one RCT with a positive result, the therapy was classified as "due to inadequate data neither a positive nor negative recommendation can be given". In cases with only one RCT with a negative result, where the therapy might cause essential harm to the patient, it was negatively recommended.

All used studies were analyzed according to a consistent schema: number of patients in experimental and control groups, duration, applied doses, exclusion criteria and methodology were extracted from the studies by the guideline secretary and presented to the work groups in Word and Excel files. The extracted data was checked by the leader/members of the work teams. Discrepancies were resolved by consensus.

Methodical basics of the recommendation

Criteria for the levels of evidence. For the classification of the levels of evidence (EL) the Oxford classification was used (see Tab. 7; [23]). In a hierarchy of evidence, meta-analyses and systematic reviews of randomized controlled trials (RCT) have the highest evidence level in this guideline about therapies, because they bear the smallest risk of bias on the results. Based on the literature search and planned database analysis, an evidence level 1 was expected for many therapeutic procedures; therefore, a Delphi procedure was fixed a priori by the steering board so that the quantity and quality of evidence level 1a can be evaluated and the grading of evidence which is not good enough for evidence level 1a can be eventually conducted.

Criteria of quality of evidence. Insufficient quantity was set for evidence obtained from ≤4 studies with <200 participants, effectual quantity for evidence obtained from >4 studies with >200 participants.

Criteria of quality of evidence. The following criteria for internal validity (methodological quality) and risk of bias were set by the steering board:

Tab. 6 Search terms and hits in databases for therapeutic procedure of FMS

	Medline	CENTRAL	SCOPUS	PsycINFO	NIH	Hand search
Complementary and alternative therapies						
Search terms						
Acupuncture ("Acupuncture therapy"[MeSH] OR "Acupuncture"[MeSH])	43	20	244	18	15	0
Body awareness and meditative exercise therapy (e.g., qigong, tai chi): ("Breathing Exercises"[MeSH] OR body awareness therapy OR Tai Chi OR feldenkrais therapy OR Sign-Chi-Do OR Neuromuscular Integrative Action OR Eurhythmy)	20	10	73	4	10	0
Diet "Diet Therapy"[MeSH] OR "Diet, Vegetarian"[MeSH] OR fasting cure	6	9	2	1	9	0
Homeopathy "Homeopathy"[MeSH]	16	1	3	0	1	0
Melatonin "Melatonin"[MeSH]	7	1	24	2	0	0
Mindfulness based stress reduction Mindfulness based stress reduction	2	2	0	0	2	2
Music therapy "Music Therapy"[MeSH]	0	0	24	10	1	0
Nutritional supplements ("Dietary Supplements"[MeSH] OR "Anthocyanins"[MeSH] OR "Carnitine"[MeSH] OR "S-Adenosylmethionine"[MeSH] OR "Tryptophan" OR "Vitamins"[MeSH])	48	12	52	8	10	0
Reiki ("Therapeutic touch"[MeSH Terms])	3	3	9	2	2	0
Dance therapy "Dance therapy"[MeSH]	0	1	0	6	2	0
Drugs						
Search terms Medline						
"Analgesics" "Drug therapy"[MeSH]	174 149	4 2	15 16	5 25	55 189	
Acetaminophen (paracetamol) "Acetaminophen"[MeSH]	14	7	0	0	5	1
Anesthetics						
Local anesthetics (("Anesthetics, Local"[MeSH] OR "EMLA"[Substance Name] OR "Prilocaine"[MeSH] OR "Dibucaine"[MeSH] OR "Bupivacaine"[MeSH])) OR "Lidocaine"[MeSH]))AND "Fibromyalgia"[MeSH] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])	32	0	0	0	10	3
Ketamine Ketamine[MeSH]	12	5	0	0	0	0
Acetsalicyl acid "Aspirin"[MeSH]	6	2	0	0	0	0
Antidepressants						
(("Antidepressive Agents"[MeSH] OR "Antidepressive Agents, Tricyclic"[MeSH] OR "Amitriptyline"[MeSH]) OR "Clomipramine"[MeSH]) OR "Dothiepin"[MeSH]) OR "Doxepin"[MeSH]) OR "Imipramine"[MeSH])	33	20	6	18	26	0
(("Milnacipran"[Substance Name] OR dual serotonin and noradrenaline reuptake inhibitor))	6	11	2	2	15	1
"Duloxetine"[Substance Name]	8	8	8	1	19	2
(("Mirtazapine"[Substance Name] OR "venlaxafine"[Substance Name]))	1	0	0	0	0	0
("Serotonin Uptake Inhibitors"[MeSH] OR "Citalopram"[MeSH]) OR "Fluoxetine"[MeSH]) AND "Paroxetine"[MeSH]) OR "Sertraline"[MeSH])	15	15	100	0	0	0
Monoamine Oxidase Inhibitors"[MeSH]	2	2	23	0	0	0

Tab. 6 Search terms and hits in databases for therapeutic procedure of FMS (Forsetzung)

	Medline	CENTRAL	SCOPUS	PsycINFO	NIH	Hand search
Anticonvulsants (("Anticonvulsants"[MeSH] OR "Anticonvulsants "[Pharmacological Action] OR "Hydantoins"[MeSH] OR "Carbamazepine"[MeSH] OR "pregabalin"[Substance Name]) OR "gabapentin "[Substance Name]) OR "oxcarbazepine"[Substance Name]) OR "lamotrigine"[Substance Name]) OR "Valproic Acid"[MeSH]) OR "topiramate"[Substance Name]))	109	10	9	6	24	1
Antipsychotics (("Antipsychotic Agents"[MeSH] OR "Ritanserin"[MeSH] OR "olanzapine"[Substance Name] OR "quetiapine"[Substance Name]))	10	0	3	0	4	0
Antiviral substances "Antiviral Agents"[MeSH]	4	1	0	0	0	0
Hypnotics, sedatives and tranquilizer ("Hypnotics and Sedatives"[MeSH] OR "Barbiturates"[MeSH] OR "Benzodiazepines"[MeSH]" OR GABA Modulators"[MeSH] OR "Tranquilizing Agents"[MeSH] OR "Nitrazepam"[MeSH] OR "Flurazepam"[MeSH] OR "zopiclone"[Substance Name] OR "zolpidem"[Substance Name "Central Nervous System Depressants"[MeSH]))	100	15	38	2	16	1
Calcitonin "Calcitonin"[MeSH]	3	0	0	0	0	1
Cannabinoids (("Cannabinoids"[MeSH] OR "Tetrahydrocannabinol"[MeSH])	6	0	0	1	3	0
Dopamine (("Dopamine"[MeSH] OR "Dopamine Agents"[MeSH]) OR "ropinirole"[Substance Name]))	19	0	15	0	22	0
Glucocorticosteroids "Glucocorticoids"[MeSH]	9	0	0	1	1	1
Hormones (("Hormones"[MeSH] OR "Growth Hormone-Releasing Hormone"[MeSH] OR "Human Growth Hormone"[MeSH] OR "Gonadal Steroid Hormones"[MeSH] OR "Luteinizing Hormone"[MeSH] OR "Thyroid Hormones"[MeSH] OR "Selective Estrogen Receptor Modulators"[MeSH]))	84	14	1	1	12	4
Interferons "Interferons"[MeSH]	2	3	0	0	0	0
Metamizol ("Dipyrone"[MeSH] OR "metamizole magnesium"[Substance Name])	0	0	1	0	1	0
Non-steroidal anti-inflammatory agents (("Anti-Inflammatory Agents, Non-Steroidal"[MeSH] OR "Cyclooxygenase Inhibitors"[MeSH]) OR "Ibuprofen"[MeSH]) OR "Diclofenac"[MeSH])) AND "Fibromyalgia"[MeSH] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])	64	6	2	0	7	0
Muscle relaxants (("Muscle Relaxants, Central"[MeSH] OR "cyclobenzaprine"[Substance Name]) OR "Chlormezanone"[MeSH]) OR "tetrazepam"[Substance Name]) OR "Methocarbamol"[MeSH]) OR "flupirtine"[Substance Name])) AND "Fibromyalgia"[MeSH]	32	1	2	0	4	6
Opioids (("Analgesics, Opioid"[MeSH] OR "Buprenorphine"[MeSH] OR "Codeine"[MeSH] OR "Fentanyl"[MeSH] OR Hydromorphone[MULTI] OR "Morphine"[MeSH] OR "Oxycodone"[MeSH] OR "Tilidine"[MeSH] OR "Tramadol"[MeSH])) AND "Fibromyalgia"[MeSH] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])	50	5	10	0	9	0
Serotonin receptor antagonists (("Serotonin 5-HT1 Receptor Antagonists"[MeSH] OR "Serotonin 5-HT2 Receptor Antagonists"[MeSH] OR "Serotonin 5-HT4 Receptor Antagonists"[MeSH] OR "Serotonin 5-HT3 Receptor Antagonists"[MeSH])) OR "tropisetron"[Substance Name]))	25	9	4	0	0	0

Tab. 6 Search terms and hits in databases for therapeutic procedure of FMS (Forsetzung)

	Medline	CENTRAL	SCOPUS	PsycINFO	NIH	Hand search
Sodium oxybate "Sodium Oxybate"[MeSH]	5	0	0	0	8	1
Central nervous stimulants "Central Nervous System Stimulants"[MeSH]	5	0	0	0	3	0
Physical therapy and physiotherapy						
Search terms Medline						
Aerobic training "Exercise"[MeSH]	33	55	16	118	50	3
Balneo therapy (("Balneology"[MeSH] OR "Hydrotherapy"[MeSH] OR "Climatotherapy"[MeSH]))	32	21	83	1	14	2
Chiropractic ("Manipulation, Chiropractic"[MeSH]	4	2	17	0	2	0
Whole-body hyperthermia Whole-body hyperthermia OR warmth stimulation	4	1	3	1	1	1
Hyperbaric oxygenation "Hyperbaric oxygenation"[MeSH]	1	1	7	0		0
Cryotherapy "Cryotherapy"[MeSH]	3	1	32	0	0	0
Craniosacral therapy "Craniosacral massage"[MeSH] OR craniosacral therapy	24	0	3	0	0	2
Strength training "Resistance Training"[MeSH] OR strength training	16	6	23	2	8	2
Laser therapy "Laser therapy"[MeSH]	6	9	40	1	0	0
Local thermal therapy ("Electric Stimulation Therapy"[MeSH]" OR "ultrasonic therapy"[MeSH Terms] OR "diathermy"[MeSH Terms] OR "short-wave therapy"[MeSH Terms])	6	5	44	0	0	1
Lymph drainage Manual lymph drainage OR lymph drainage	1	2	3	0	1	0
Magnetic field therapy ("Magnetic field therapy"[MeSH] OR static magnetic fields)	5	3	12	6	4	0
Massage "Massage"[MeSH]	18	13	193	8	6	1
Physiotherapy "Physical Therapy Modalities"[MeSH]	250	133	48	16	0	0
Quadrant intervention Surgical Quadrant-Pain-Intervention	0	0	0	0	0	3
Stretching (Flexibility training OR stretching exercises)	29	17	24	1	14	0
Transcutaneous electrical nerve stimulation (TENS) "Transcutaneous Electric Nerve Stimulation"[MeSH]	11	1	14	3	2	0
Transcranial magnetic stimulation Transcranial magnetic stimulation	4	3	29	5	4	0
Multidisciplinary pain therapy						
Search terms Medline						
("Rehabilitation"[MeSH] OR multidisciplinary treatment OR multimodal therapy OR combined modality therapy)	260	104	68	191	23	4
Patient education and communication						
Search terms Medline						
Patient education and self management ("Education"[MeSH] AND "Self Care"[MeSH])	10	48	691	135	30	0
Patient-orientated communication (shared-decision making OR patient-centred approach)	7	3	3	2	5	0
Psychotherapy						
Search terms Medline						

Tab. 6 Search terms and hits in databases for therapeutic procedure of FMS (Forsetzung)

	Medline	CENTRAL	SCOPUS	PsycINFO	NIH	Hand search
General psychotherapy						
"Psychotherapy, Group"[MeSH]	6	0	51	0	3	0
"Psychotherapy"[MeSH]	143	0	543	81	5	0
"Mind-body therapies"[MeSH]	67	2	40	2	5	0
Biofeedback "Biofeedback"[MeSH]	15	5	89	33	5	0
Relaxation therapy ("Relaxation Therapy"[MeSH] OR "Autogenic Training"[MeSH])	25	3	150	15	6	3
Hypnosis and conducted imagination ("Hypnosis"[MeSH] OR "Guided Imagery"[MeSH]	16	2	13	21	2	0
Cognitive (and) behavior therapy ("Behavior Therapy"[MeSH] OR "Cognitive Therapy"[MeSH] OR "Desensitization, Psychologic"[MeSH] OR "Aversive Therapy"[MeSH] OR ("Desensitization, Psychologic"[MeSH] OR "Eye Movement Desensitization Reprocessing"[MeSH] OR "Implosive Therapy"[MeSH])	109	27	127	91	85	0
Therapeutic writing Written emotional disclosure	2	2	6	3	0	0
Psychoanalytic therapy "Psychoanalytic Therapy"[MeSH] OR Interpersonal therapy	6	0	9	5	1	0

Search strategy Pubmed:Fibromyalgiesyndrom: "Fibromyalgia"[MeSH]RCTs: Pubmed search filter (category "therapy"), optimised for sensitive/broad (sensitivity/specificity 99%/70%): ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])http://www.ncbi.nlm.nih.gov/books/NBK3827/#pubmedhelp.Clinical_Queries_FiltersAND "Fibromyalgia"[MeSH] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]))**NIH** US National Institutes of Health.

- randomisation (1: efficient, 0: inefficient, the code for imprecise information is 0),
- treatment assignment is concealed to patients (1: efficient, 0: inefficient, the code for imprecise information is 0),
- blinding (1: efficient, 0:inefficient, the code for imprecise information is 0) and
- intention-to-treat analysis (1: yes, 0: no).

The methodological quality was controlled by criteria of Tulder Scores [29]. An adequate randomisation was assumed in case of a computer-generated random sampling list or closed and light tight envelops covering the treatment assignment. A randomisation according to birthday, date of hospital admission, an alternative admission into a study and no information about the type of randomisation are deemed as inadequate. An adequate concealment of treatment allocation was accepted, if it was conducted by an independent person (e.g. central independent unit, hospital pharmacist) who did not participant in the study or via closed envelope. Open randomization tables or no information were evaluated as inadequate. In pharmacological studies information about identical appearance of verum medication and placebo was accepted as adequately blind. Because a blinding of the therapist in non-drug studies is not possible, the information that the evaluator of study results was not involved in the choice of patients and treatment should be explicitly mentioned and chosen as criteria of adequate blinding. A total score (0–4) was composed of four criteria. A high methodological quality was accepted at a total score of 4, a moderate quality at 2–3, and a low quality score at 0–1.

The following criteria for external validity were fixed by the steering board:

- inclusion of common somatic comorbidity of FMS: inflammatory rheumatic diseases (0: no, 1: yes) and
- Inclusion of common mental disorders (depressive and anxiety disorders) (0: no, 1: yes)

The categories of quality of evidence are listed in **Tab. 8**.

Low quality evidence was presumed in case of low methodological quality and low external validity, high quality evidence was presumed in case of high methodological quality and high external validity, moderate quality evidence was presumed in case of all quality combinations which did not fulfill the criteria of low and high methodological quality.

Based on the criteria of quantity and quality of evidence grading 1a the following criteria were defined to downgrade the level of evidence of a therapy procedure:

- 1 level: at least 1 of the following criteria: low methodological quality of RCTs, inefficient database (≤4 studies with 200 participant), evidence of selective publication study results,
- 2 levels: at least 2 of the following criteria: low methodological quality of RCTs and inefficient database (≤4 studies with 200 participants), evidence of selective publication study results.

Criteria of efficacy. As the endpoints for the evaluation of efficacy (benefit) the "key domains" (endpoint) of FMS accepted in specialist and patient consensus (Omeract 7) were chosen for criteria of efficacy: pain, sleep, fatigue, quality of life [20].

Tab. 7 Methodological quality of scientific documents: classification of evidence grading for studies of therapy, etiology and prevention (adapted from [23])

Level	Therapy/prevention, etiology/ adverse reactions	Prognosis	Diagnosis	Differential diagnosis/symptoms prevalence study
1a	*SR* (with homogeneity[a])	*SR* (with homogeneity[a]) concluded cohort studies; CDR[b] validated in different populations	*SR* (with homogeneity[a]) of level 1 diagnostic studies; CDR[b] with 1b studies of different clinical centres	*SR* (with homogeneity[a]) of prospective cohort studies
1b	*Individual RCT* (with small confidence interval[c])	*Individual cohort studies with* ≥80% post-observation rating; CDR[b] validated in a single population	*Validation cohort studies*[d] with good[e] reference standard, or tested CDR[b] in a clinical center	*Prospective cohort studies* post- observation rate[f]
1c	All or none[g]	All or none case series	Absolute SpPins and SnNouts[h]	All or none case series
2a	*SR* (with homogeneity[a]) of *cohort-studies*	*SR* (with homogeneity[a]) of *retrospective cohort studies* or untreated control groups in RCTs	*SR* (with homogeneity[a]) of level>2 *diagnostic studies*	*SR* (with homogeneity[a]) of 2b and better studies
2b	*Single cohort studies* (concluded RCT with poor quality; e.g.<80% post-observation rate)	*Retrospective cohort studies* or post-observation rate of untreated control patients in a RCT; Derivation of a CDR[b] or only validated in a part of control sample[i]	*Explorative*[d] *cohort studies* with good[e] reference standard; CDR[b] after derivation or only validated in a part of the control sample[i] or basis data	*Retrospective cohort studies*, or low post-observation rate
2c	*Results research; ecological studies*	*Results research*		*Ecological studies*
3a	*SR* (with homogeneity[a]) of *case–control studies*		*SR* (with homogeneity[a]) of level 3b and better studies	*SR* (with homogeneity[a]) of level 3b and better studies
3b	*Single case–control studies*		*Non-consecutive studies* or without consistent use of reference standards	*Non-consecutive cohort study* or very limited population
4	*Case series* (and qualitatively poor cohort and case–control studies)	*Case series* (and qualitatively poor prognostic cohort studies)	*Case–control study*, poor or independent reference standard	*Case series* or obsolete reference standard
5	*Expert opinion* without critical analysis or based on physiological or experimental research or "basic principles"	*Expert opinion* without critical analysis or based on physiological or experimental research or "basic principles"	*Expert opinion* without critical analysis or based on physiological or experimental research or "basic principles"	*Expert opinion* without critical analysis or based on physiological or experimental research or "basic principles"

The users can use a minus symbol ("–") for the grading that lacks for a conclusive answer, because **either** there is a single result with broad confidence interval [e.g. absolute risk reduction (ARR) is not statistically significant in a RCT, but the confidence interval excluded the clinical relevant adverse reaction and usage] **or** there is a systemic review with concerning (and statistic significant) heterogeneity. Such evidence is inconsistent and can be generated, therefore, only on the recommendation of level D.[a]Homogeneity is meant for a systemic review without considerable variance (heterogeneity) related to results between respective studies. Not all systemic reviews with statistic significant heterogeneity should be necessarily concerning and not all distressing heterogeneities have to be statistically significant. As above mentioned, studies with concerning heterogeneity should be added to the last level of the recommendation.[b]Clinical Decision Rule (CDR): algorithm or item system, which guides a prognostic evaluation or diagnostic category.[c]See explanatory note 2 as help for understanding, classification and handling of studies with wide confidence interval.[d]Validation studies test the quality of specific diagnostic tests, based on the formerly developed evidence. An explorative study collects information and investigates all data (e.g. with a regression analysis) for searching factors that are significant.[e]Good reference standards are independent from the test. They are used blind or objectively in patients. Poor reference standards are used by chance and are still independent from the test. The usage of non-independent reference standards implicates a study of level 4 (if the test is included in the reference or the test influences the reference).[f]Good post-observation rate of a study for differential diagnosis is >80% at adequate time for the incidence of alternative diagnosis (e.g. 1–6 months acute, 1–5 years chronic).[g]Relevant, if all patients died before the therapy was available and some of them have survived after the therapy was available; or if some of patients died before the therapy was available and nobody died after the therapy was available.[h]"The absolute SpPin" is a diagnostic result whose specificity is so high so that a positive result includes the diagnosis. An absolute SnNot is a diagnostic result whose sensitivity is so high that a negative result excludes the diagnosis.[i]The validation of a part of the sample is reached if all information is collected in an arm which is artificially divided into a derivation and validation group.[j]"Qualitatively poor cohort studies" was meant for those studies which have not clearly defined the control group and/or the exposition and results were not measured in the same objective manner in both groups (exposed and not exposed) and/or no adequate disturbing factors have been identified and controlled and/or there was no adequate post-observation rate. "Qualitatively poor case–control studies" are meant for those which had no defined control group and/or the exposition and results have not been measured in the same objective manner (blinded) in both groups (cases and controls) and/or no adequate confounding factors have been identified and controlled.[k]Good, better and poor refer to the comparison between treatments in terms of their clinical risks and benefits.[l]Treatments with higher benefits are likewise good, but more convenient or better at the same or less cost. Treatments with lower benefit are equally good, but more expensive or worse.[m]"Qualitatively poor prognostic cohort studies" are meant for those where the probability sampling is distorted and patients who already have results were preferred or the measurement of results was performed in <80% of the study population or the results was measured by unblinded, not objective methods or the confounding factors were not corrected. **CDR** clinical decision rule; **RCT** randomized, controlled trial; **SR** systematic review.

Tab. 8 Ratings of quality of evidence

Symbol	Text	Criteria
Methodological quality		
+++	High	≥25% of studies with high and/or ≥50% of studies with moderate quality
++	Moderate	≤25% studies with high and/or ≥25–50% of studies with moderate quality
+	Low	<25% of studies with moderate quality
External validity (transferability of study results to patients in routine clinical care)		
+++	High	≥50% of studies included patients with comorbid anxiety or depressive disorder and/or inflammatory rheumatic diseases
++	Moderate	≥25% of studies included patients comorbid anxiety or depressive disorder and/or inflammatory rheumatic diseases
+	Low	<25% of studies included patients comorbid anxiety or depressive disorder and/or inflammatory rheumatic diseases

- Pain: current pain measured on a numeric or visual analogue scale, other measures or time units (e.g. the last 7 days)
- Sleep: validated total score (e.g. Pittsburg Sleeping Questionnaire), numeric or visual analogue single score
- Fatigue: validated total score (e.g. Multidimensional Fatigue Index), numeric or analogue single scale
- Health-related life quality: total score of Fibromyalgia Impact Questionnaire, other total score of validated quality of life instruments, numeric or visual analogue single scale of global feeling.

As measure of efficacy, the effect size [standardized mean difference (SMD)] of the therapy procedure versus control group was chosen at final treatment and if available at follow-up of the outcomes outlined above.

In the case of several potential control groups, the choice was carried out in following order:

- drug therapy: pharmocological placebo, non-pharmaocological placebo, other active therapy, common therapy, no therapy,
- non-drug therapy: attention control, waiting list, therapy as usual, other active therapy, no therapy.

The effect sizes were calculated using software RevMan version 5.1 of Cochrane Collaboration [25] by a random effects model. The classification of effect sizes was performed according to Cohen (0–0.2: not substantial; 0.2–0.5: low; 0.5–0.8: moderate; >0.8 strong; [9]). The heterogeneity of the effect sizes was determined by I^2 statistic. I^2>50% was evaluated as substantial heterogeneity [17]. A consistence of study results was accepted, when there was a significant test of overall effect in the case of a meta-analysis or there were consistent results in the case of non-controlled studies or case series.

The steering board was aware that the group mean does not reflect the individual response. Persons whose response is clinically relevant (at least 30% pain reduction; responder) have probably a relevant higher response to the therapy procedure (inclusive placebo) than the average person. Therefore, responder rate would have been more suitable than effect sizes and would be easier to understand by patients and therapist than the standardized mean differences [21]. Because the responder rate was predominantly reported in new drug studies (in line with approval procedures) and only in a few nonpharmacologic studies, the database did not allow that responder analysis be used to evaluate the efficacy of a therapy procedure.

Criteria for evaluating the efficacy are shown in **Tab. 9**.

Criteria of risks. Potential lethal or irreversible physical and psychological harm during the therapy were defined as essential risks. The subjectively relevant side effects such as negative consequences in activities of daily life were chosen as important risks. The frequency of serious and subjective relevant side effects was documented in the analysed RCTs in contrast to the control group. Furthermore, for the determination of each drug's harms, the warning notice about prescription information from the US Food and Drug Administration and the side effects from the Red List and for nonpharmacologic procedure information from the literature which were known to the members of working group were used.

Criteria of patient's preferences. As an identifiable measure in almost all controlled studies, the relative total dropout rate in the active therapy and control groups and the relative risk of treatment dropout were calculated by a random effects model (method of inverse variance [17]). The dropout rate due to side effects was not chosen as a measure, because the dropout reasons were not explicitly detailed in most nonpharmacological studies.

Criteria of practicability/applicability.

- In the case of drugs: was the drug approved for therapy of FMS and/or its common comorbidities (anxiety, depression) in Germany?
- In the case of nonpharmacologic procedures: was the procedure available in clinical routine care with the necessary structure quality and was it included in the service catalogue of statutory health insurance?

The above mentioned evaluation criteria of therapy procedure were entered into a balance sheet.

Ethical duties. Ethical duties were defined based on patient charter and professional standards.

Grading of evidence and recommendations—criteria for downgrading and upgrading. The grading of recommendations (**Tab. 10**) was carried out according to the approach of the national guidelines [14]. The evidence levels are relevant for determining the strength of recommendations: the higher the evidence level, the stronger the recommendation. As a rule, a recommendation strength A (strong recommendation) was argued for evidence level I, a recommendation strength B to evidence level II and open recommendation to evidence level III, IV and V (**Fig. 1**). In addition, the ethical

Tab. 9 Benchmark of efficacy and criteria of grading of recommendation

Criteria of efficacy		
Symbol	**Text**	**Criteria evidence-based medicine**
+++	High	Efficacy at two endpoints at final treatment and at follow-up compared to controls
++	Moderate	Efficacy in one endpoint at follow-up and/or at two endpoints at final treatment compared to controls
+	Low	Efficacy at one endpoint at final treatment compared to controls
–	None	No difference and/or inferiority in all endpoints compared to controls
Efficacy is assumed, if the SMD (therapy vs. control group) at clinical endpoints is >0.2 according to Cohen's categories.		
Criteria of risks (harms)		
Symbol	**Text**	**Expert criteria**
–––	High	Serious side effects >1% and/or subjectively relevant adverse events >10% compared to controls
––	Moderate	Serious side effects >1% and/or subjectively relevant side effects 5–10% compared to control group
–	Low	No serious side effects and subjectively relevant side effects not different to control group
Criteria of patient's preferences		
Symbol	**Text**	**Criteria**
+++	High	Dropout rate in RCTs <10% and/or relative risk of study dropout significantly lower compared to controls
++	Moderate	Dropout rate in RCTs 10–25% and/or no significant difference in relative risk of study dropout compared to controls
+	Low	Dropout rate in RCTs>25% and/or relative risk of study dropout significantly higher compared to controls
Criteria of feasibility		
Symbol	**Text**	**Criteria**
+++	Completely	Approved for FMS in Germany (drugs) and included in capacity catalog of statutory and private health insurance companies *and* available in Germany in routine care
++	Limited	Approved for common comorbidities of FMS in Germany (drugs) *and* available in routine care with limits, not included in capacity catalog of statutory and private health insurance companies (non-pharmacological procedures)
+	Low	Not approved for FMS (drugs) *and* not included in capacity catalog of statutory and private health insurance companies and not available in routine care (non-pharmacological procedures)
FMS fibromyalgia syndrome; RCT randomised, controlled trials, SMD standard mean difference.		

Tab. 10 Recommendation grading for a therapy

Strength of recommendation	**Formulation**	**Meaning**	**Symbol**
Strong positive recommendation	Shall	Most of patients shall receive the therapy	↑↑
Positive Recommendation	Should	The majority of patients should receive the treatment. Based on medical rationale and/or patient's preferences many patients will not receive the therapy.	↑
Open	Can be applied	Data exposure unclear. Some of patients can receive the therapy	←→
Clinical Consensus Point (CCP)	Standard in the treatment	Recommendation as good clinical practice in consensus and based on the clinical experience of the guideline group as a treatment standard for which no experimental research is possible or aimed	CCP
Negative recommendation	Shall not	The majority of patients shall not receive the intervention	↓
Strong negative recommendation	Should not	Most of patients should not receive the therapy	↓↓

duties, the clinical relevance of effect measures and effect sizes of the studies, an explict balancing of potential benefits and harms, the applicability of the study results to the whole patient population and the practicability in all levels of care were considered in addition to evidence for the assignment of strength of recommendations. Corresponding to these consensus aspects, an upgrading and downgrading of recommendations compared to the evidence level could be performed. A priori criteria of upgrading and downgrading of recommendations were defined by the steering board via a Delphi procedure, so that the conducted upgrading and downgrading could be kept transparent.

The criterion for a negative recommendation was defined as follows:

- negative recommendation: no evidence of efficacy compared with controls in all 4 endpoints,
- strong negative recommendation: inferiority compared with controls in at least one endpoint and no superiority compared to controls in the remaining endpoints.

Upgrading of recommendation strength of a therapy procedure:

- upgrading of 1 level: at least 2 of the following 3 criteria: low risks or high patient acceptance (dropout rate <10% in studies), high practicability in Germany and ethic duties,

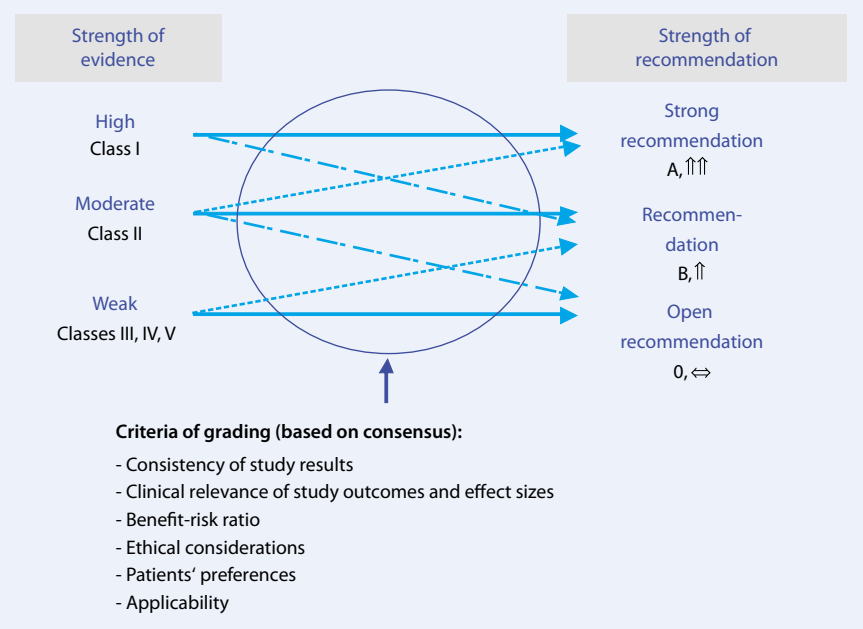

Fig. 1 ▲ Relationship between strength of evidence and strength. [a]According to Oxford Centre of Evidence-based Medicine [23]; [b]Strength of recommendation in the Programme for National Supply Guideline [7]. (Modified from [1])

- upgrading of 2 levels: all 3 criteria.

Downgrading of recommendation strength of a therapy procedure:

- downgrading of 1 level: at least 2 of the 3 following criteria: high risks or low patient acceptance (dropout rate>25% in studies), low practicability in Germany and ethic duties,
- downgrading of 2 levels: all 3 criteria.

As additional recommendation category, the clinical consensus point (CCP) was borrowed from the national guidelines on unipolar depression [14].

Classification of strength of consensus. Based on the literature knowledge from members of the steering board, it could be foreseen that several topics of the guidelines could not be answered based on the clinical studies (e.g. extent of diagnostics, type of the supply chain) or that controversial aspects on several topics were probable. Therefore, it was decided that the consensus strength for individual recommendations should be specified in addition to the evidence and recommendation grading [18].

It was also decided that every single vote will be adjudicated at the consensus conference of every association and patient self-help organization, so that the evaluation of consensus strength will be simplified and the consensus processing will be advanced. Both psychosomatic associations received together one vote. The members of the two associations of the patient self-help organizations should cast their vote according to an internal vote based on the majority. If no majority could be reached, the member of the steering board was authorized to make a decision. In addition, it was possible possibility that a vote not be given (e.g. due to lack of expertise) or a justified minority vote be specified. The guideline coordinator (W. Häuser) and the moderator of consensus conference (I. Kopp) had no voting rights. The consensus strength was classified as in the former guidelines (**Tab. 11**; [18]).

Results

Consensus conferences

The results of the individual online votes with comments and suggestions concluded by the guideline coordinators and workgroup leaders were forwarded to the members via e-mail. The consensus conference took place on November 10, 2011 (24 members) and on November 24, 2011 (22 members) in Heidelberg, Germany. The members who could not participate in the conference were asked to cast their votes and/or suggestions to other members of the steering group of their association.

- Part 1: short presentation
  - introduction of the procedure of the formal consensus process by the moderator
  - the audience had opportunity to ask questions about the methodical procedure
- Part 2: structured consensus determination
  - chapter by chapter proceeding, request of every keynote or recommendation individually by the moderator
  - registration of statements from the plenum by the moderator
  - clarification and justification of alternative suggestions
  - preordination about first draft and all alternatives
  - identification of discussion points and dissents
  - debate and discussion
  - final voting

The discussion and voting were directed by Prof. I. Kopp. The vote was by a show of hands. Documentation of the procedures and the results was performed by Ms. S. Engels.

After agreement on the recommendations, the guideline coordinator revised the final draft, identified the key recommendations, formulated the quality aims and created a short version. Additionally, the clinical algorithms of the first guidelines for diagnosis and graded therapy of FMS was revised by a structured logic analysis (clinical algorithm structural analysis) using the software ALGO [24] and modified after consultation with members of the steering group. The final vote was carried out in a Delphi procedure of the steering group and workgroup leaders.

External review and enacting

The final manuscript was sent to the steering boards with the request for comments and authorization. By request, a member

Tab. 11 Classification of consensus. (Adapted from [18])

- Strong consensus: agreement of >95% of members
- Consensus: agreement of >75–95% of members
- Majority: agreement of 50–75% of members
- No consensus: agreement of <50% of members
- A minority vote with reasons is possible

from every association involved was asked for an appraisal of the guidelines. An external review was performed by Prof. Dr. E. Genth (DGRh), Associate Prof. Dr. HA. Halder (DGOOC), Prof. Dr. JP Haas (GKJR) and Prof. Dr. W. Koppert (DGSS). Formal change requests of the associations for the guideline text were considered. The comments of DGRh are published in a special document in the appendix to the methods reports of the guideline on the AWMF homepage (http://www.awmf.org/leitlinien/detail/ll/041–004.html).

Furthermore, the following associations and organizations were requested for comment and acceptance: German Association of General Medicine and Family Medicine ("Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin", DEGAM) and Central Organization of Physiotherapists ("Zentralverband der Physiotherapeuten/Krankengymnasten", ZVK). The ZVK accepted the guidelines. The external reviewer was Ms. A. Heck-Darabi (Dipl. Biologist and Physiotherapist). Formal change requests of ZVK were considered. The constant guideline committee of DEGAM declined to support the guideline. The letter from DEGAM and its comments are published in a special document in the appendix of guideline methods reports on the AWMF homepage by the guideline steering board (http://www.awmf.org/leitlinien/detail/ll/041–004.html).

Approximately 80 FMS patients who were asked by the German Rheumatism League, the DFV and 3 pain therapy outpatient departments commented on the pilot versions of the patient guidelines verbally or in written form. In a Delphi procedure, the patient spokespersons who were involved in generating the patient guidelines decided which suggestions should be considered for modification.

Acceptance by AWMF

The guideline updating was declared on April 10, 2012 in AWMF and accepted on April 19, 2012 by AWMF (AWMF Registration No. 041/004).

Discussion

Practicability and confirmability

Health economic aspects were not comprehensively formed in sparse data situations. An explicit consideration of costs was not performed. The guideline group hopes that, with consideration of the positive and negative recommendations of the guidelines, the direct treatment costs will be reduced by the reduction of prescription of drugs or physical therapy which are not recommended by the guidelines. Cost-intensive inpatient multidisciplinary programmes may lead to a cost reduction in the medium term.

A study about cost efficacy in German-speaking areas by CBT/OBT calculated a saving of $3,933 of hospital cost per patient per year and a cost-reduction in the field of outpatient care of $1,840 per patient per year [26]. The previous and current guidelines included information about inpatient and outpatient treatment and supply coordination.

Inappropriate or obsolete procedures were identified in the chapter diagnosis because of the suggestion to outline necessary and unnecessary exclusion diagnostics and those in the chapter therapies due to negative recommendations.

The concerned questions were handled in the thematically divided chapters of the guidelines. According to the recommendations, the comments contain the explanation and citation which is adducted as evidence. The evidence table (contents, methodical quality and external validity of studies) and the quantitative data synthesis (meta-analysis) with the Forest plots are provided in the appendix (available online in the Evidence Report).

Dissemination and implementation

The guideline (pocket version, short version, complete version), the methods report and evidence report are available on the web site of AWMF (http://www.awmf.org/leitlinien/detail/ll/041–004.html).

In addition to publication of the full scientific version of the current guidelines in *Schmerz*, an extract of of the guidelines that is relevant for the respective specialties will be published by the respective member of steering committee as first author in the German journals of pediatrics, neurologist, orthopaedics, psychotherapist and Journal of Rheumatology (respectively, *Monatsschrift Kinderheilkunde*", "*Der Nervenarzt*", "*Der Orthopäde*", "*Der Psychotherapeut*" and "*Zeitschrift für Rheumatologie*"). A summary of the guidelines will be submitted for the category "memorandum" of the German Medical Journal ("*Deutschen Ärzteblatt*").

A patient version of the guidelines was developed by the spokepersons of the German Rheuma-League in cooperation with the guideline secretary and under orientation of the national supply guidelines. It is in available on the websites of the self-help organizations (http://www.rheuma-liga.de; http://www.firomyalgie-fms.de) and of the AWMF. The contents of the new guidelines will be printed in the member journals of both self-help organizations.

The presentation of the guideline recommendations was performed at the German Congress of Psychosomatic Medicine and Psychotherapy in March 2012 in Munich, Germany. The guidelines will be introduced at a symposium of the Annual European Congress of Rheumatology in June 2012 in Berlin, at the Congress of the German Association of Rheumatology in September 2012 in Bochum and at the German Pain Congress in October 2012 in Mannheim, Germany.

The following arrangements are planned for international distribution of the guidelines: a lecture and a poster will be held at the Congress of European League against Rheumatism (EULAR) in June 2012 in Berlin and at the World Pain Congress in August 2012 in Mailand, respectively. An English summary of the

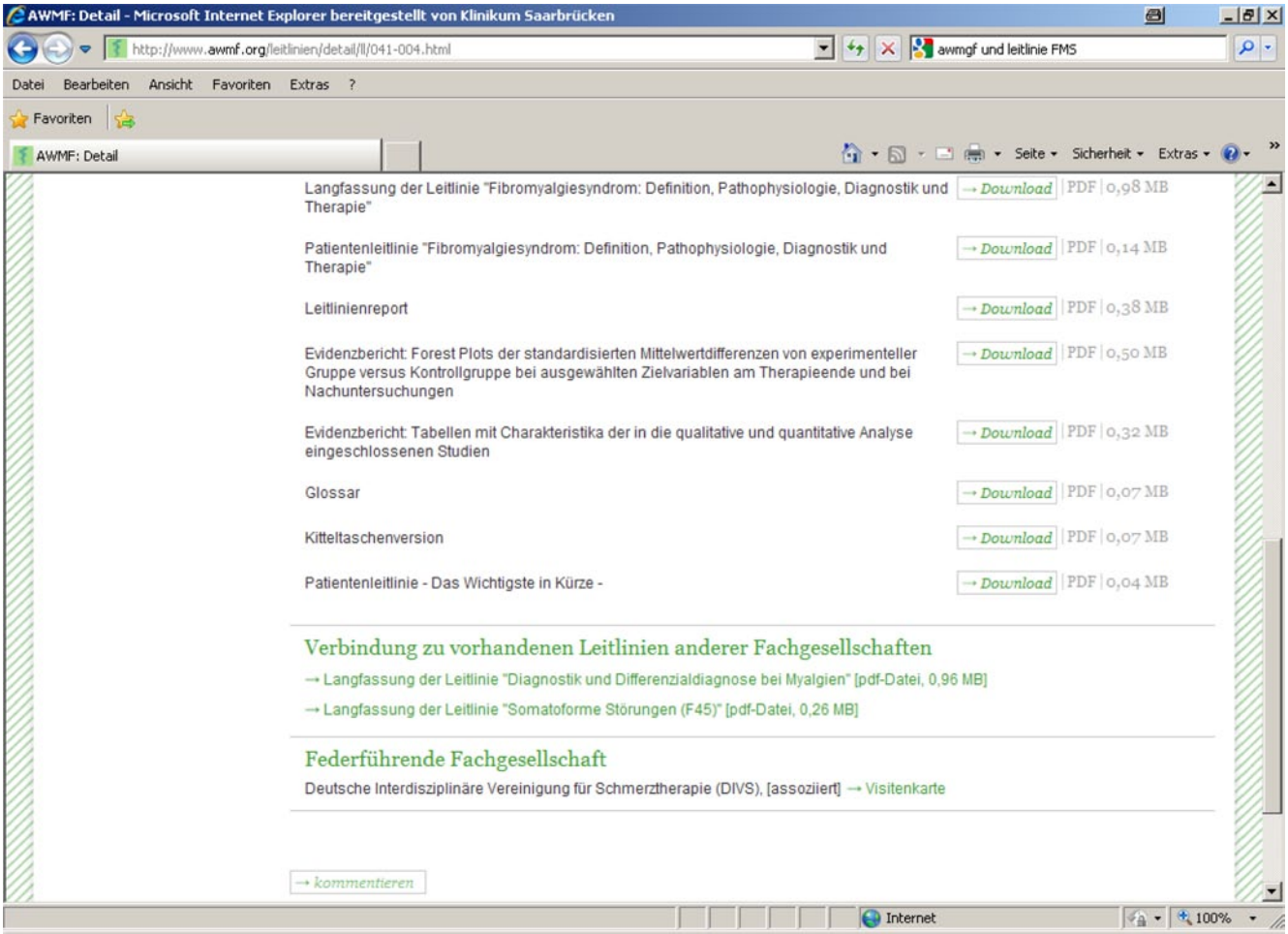

Fig. 2 ▲ Screenshot of the comments function on the AWMF homepage

guideline will be published in *German Medical Science*, an open access journal of AWMF. The English translation of the contribution for this special issue is "open access" accessible via databank Medline. The updated version of the guideline is available via the homepage of the international guideline network (http://www.g-i-n-net).

Evaluation of the guidelines

The implementation of the guidelines should improve treatment satisfaction and the quality of life of FMS patients. Because a guideline is formally considered as a thesis, it should be evaluated during an adequate period whether the aims are reached. The following evaluation-steps are planned:

a) Interview of members of the German League of People against Rheumatism and of the German Fibromyalgia Federation in 2013 whether the acceptance of the symptoms have been changed by the physicians due to guideline conformal therapy recommendations since the first publication of guideline in 2008.
b) Analysis of data from the Barmer health insurance company [19] whether the frequency of guideline conformal prescriptions has increased since the first publication of the guideline in 2008.
c) The areas which were not edited in the guidelines and perceived barriers should be discussed in the context of audits by the guideline members with local quality circles (psychotherapy, pain therapy) and inpatient institutions (psychosomatic medicine, pain therapy). A common strategy for better guideline implementation should be developed.
d) The practicability of the short and pocket version of the guidelines in practice will be tested in a pilot study (local quality circles).

Duration of validity and updating proceeding

The guideline is valid till April 2017. At that time point an inspection of the whole manuscript is intended for identification of revision requirement. Interim knowledge which can necessitate the update of individual chapters or recommendations will be observed by the steering board. Relevant abstracts of all new publications about FMS in Medline supplied by an automatic electronic search will be classified for relevance for the guidelines by the guideline secretary. Advice is welcome from guideline users and can be sent to the coordinator (whaeuser@klinikum-

saarbruecken.de) or submitted via the homepage of AWMF (Fig. 2).

New relevant and accepted knowledge which conflicts with the guidelines should be notified within 3 months in the special journals of the participating associations and an addendum to the guidelines should be provided on the homepage of AWMF. Relevant and accepted knowledge will be supposed, if the approval status of a recommended or not recommended medication for FMS is different from the guidelines (e.g. market withdrawal or permit), for warning notices for the recommended drugs by the guidelines or if there are at least two new randomised controlled studies with high methodological quality and external validity with at least 50 participants per study arm which can lead to an update of the current recommendation strength. The date of publication, the date of next planned revision and the registration of the planned and/or interim updating will be indicated in the publically accessible contents of AWMF registers.

Methodological differences compared to the first version of the guideline

The analysis of the available literature was refined and the foundation for the recommendations were differentiated compared to the first guideline [4] which was limited to the narrative (qualitative) reporting of the existing studies and review articles. The foundation for evaluation of efficacy was the main results as reported by the authors. In the current version, the predefined outcomes of the publications as defined by the guideline group were analyzed. This approach showed that positive results were selectively generated in several studies (e.g. in the abstract) and negative results could be found in the tables of the full publications. The current methodology led to a more negative evaluation of several therapy procedures compared to the first version of the guideline (e.g. cognitive behavior therapy and therapeutic writing as monotherapy).

The a priori definition of criteria of up- and downgrading of evidence and of recommendation strength was chosen, so that decisions of consensus were made transparent and the influence of individual opinions on the consensus conference was minimized.

In the first version, an open recommendation was given in the case of integration of the procedure into a multidisciplinary therapy concept even if the data were missing. This approach for complementary and alternative proceeding was not used in the current version.

The current therapy algorithm includes stepwise therapy according to severity of FMS in reference to the S3 guidelines on unspecific/functional/somatoform bodily complaints [15].

Limitations of evidence-based medicine

Although it was possible to search in the NIH databank, it is possible that studies with negative results were not published and the efficacy of individual therapy was overrated by the current guidelines. Data extraction for the studies was limited due to following reasons: type of randomization, treatment concealment and blinding of the outcome assessor were not described in many studies—also in several large RCTs for drugs which were approved by the US Food and Drug Administration for therapy of FMS. Because we did not receive information about the methodology from the study authors required during previous systematic reviews, we used the information which was included in the publications. Thus, the methodological quality could be underestimated.

The inclusion and exclusion criteria in many studies were not explicitly specified. The evaluation of the representativeness of studies is, therefore, not loaded. The outcome measures pain, fatigue, sleep and life quality were documented in several studies, but not reported. Some of the authors responded to requests, some of them did not.

Standard deviations were not reported in several studies and had to be calculated from mean values from other studies. In several studies only the mean for meta-analysis was used. Thus, the quantitative data analysis was associated with uncertainty.

In nearly all nonpharmocological studies only group mean values were reported. Information such as how many patients had a 30% or 50% of pain reduction were found only in large RCTs of drugs which led to the approval of several drugs for therapy of FMS by the US Food and Drug Administration. The group mean value does not correctly reflect an individual's response to a drug, because only few patients have the group mean value [21].

Barriers in practicing the guidelines and possible solutions

The general acceptance of the guidelines is not given by delegates of psychosocial disciplines who reject the construct (diagnostic label) "FMS" and give those patients a diagnosis of somatoform pain disorder or masked depression [28]. Both guideline groups hope to the end of the labeling debate on somatic symptoms without explanation by a somatic disease factor, because an assimilation of the recommendations of FMS guidelines with those of unspecific/functional/somatoform bodily symptoms [15] was performed.

Financial incentives of the standard evaluation rules ("einheitlichen Bewertungsmaßstabs", EBM) and schedule of fees ("Gebührenordnung für Ärzte", GOÄ) foster the performance of invasive procedures which were not recommended for FMS. Communication with patient (information, shared decision making) are poorly reimbursed in the nonpsychotherapeutic field. Selective contracts of health insurances with a team of health care providers who are better paid for therapies that are recommended in the guidelines and the exclusion of therapies that are not recommended in the guidelines can overcome the limitation of the compensation scheme [19].

The availability of multidisciplinary therapy programmes is limited in several areas in Germany. The self-help organizations, cooperating with local interdisciplinary medical supply centers and possibly supported by selective contracts, can enlarge the treatment offers. The implementation of the active therapy procedures (aerobic exercise, meditative exercise therapy) which is marked with strong recommendation in the guidelines can be limited due to patients' preferences (preferred passive physical therapy, unrealistic hope of drugs) and comorbidity of pa-

tients (e.g. depressive apathy in major depression, advanced knee osteoarthritis). The development of a tailored therapy programme for subgroups of patients is urgently needed.

Corresponding address

W. Häuser
Department of Internal Medicine I,
Klinikum Saarbrücken GmbH
Winterberg 1, 66119 Saarbrücken
Germany
whaeuser@klinikum-saarbruecken.de

Conflict of interest. Potential conflicts of interest are listed in Tab. 5 of this article.

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