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Julia Baranowsky, Petra Klose, Frauke Musial, Winfried Haeuser, Gustav Dobos, Jost Langhorst

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Qualitative Systemic Review of Randomized Controlled Trials on Complementary and Alternative Medicine Treatments in Fibromyalgia

Baranowsky J., Klose P., Musial F., Haeuser W., Dobos G., Langhorst J

Abstract

Objective: Identification, quality evaluation and summery on RCTs on complementary and alternative medicine as defined by the National Institute of Health with the exception of dietary and nutritional supplements.

Methods: A computerized search of databases from 1990 (year of publication of the ACR criteria for fibromyalgia) to July 2007 was performed. The RCTs were assessed by a methodological quality score.

Results: 23 RCTs issued from 1992 to 2007 on acupuncture, balneotherpy, thermotherapy, magnetic therapy, homeopathy, manual manipulation, Mind-Body medicine, diet therapy and music therapy were identified. The RCTs had an average group size of 25 with a number of groups ranging from two to four. The quality score assessment of the RCTs yielded a mean score of 51 out of 100.

Conclusions: The average methodological quality of the identified studies was fairly low. Best evidence was found for balneotherapy/hydrotherapy in multiple studies. Positive results were also noted for homeopathy and mild infrared hyperthermia in 1 RCT in each field. Mindfulness Meditation showed mostly positive results in two trials and acupuncture mixed results in multiple trials with a tendency towards positive results. Tendencies for improvement were furthermore noted in single trials of the Mesendieck system, connective tissue massage and to some degree for osteopathy and magnet therapy. No positive evidence could be identified for Qi Gong, Biofeedback, and Body Awareness therapy.

Abbreviations: FMS: fibromyalgia syndrome, RCT: randomized controlled trial, CAM: complementary and alternative medicine, FIQ: fibromyalgia impact questionnaire, TP: tender point, TPC: tender point count, VAS: visual analogue scale

Introduction

Fibromyalgia syndrome (FMS) is a chronic myosceletal pain disorder characterized by widespread pain and tenderness at marked sites of the body defined as the tender points. It is often accompanied by other characteristic symptoms as sleep disorders, fatigue or morning stiffness and associated with various syndromes as irritable bowel syndrome or depression (4). First formally defined by Smythe in 1977 (1) it has since then received several definitions (1, 2, 3) that varied in their emphasis of concomitant syndromes and the importance and number of tender points (4). Some authors have even doubted whether FMS should be at all considered as a distinct clinical entity (5, 6).

In 1990 the American College of Rheumatology endorsed the publication of a set of criteria for the classification of FMS by Wolfe at all (3). These criteria have since then provided a basis for most clinical studies investigating fibromyalgia. According to these criteria FMS can be diagnosed in about 2% of the U.S. population with prevalence in women in about of 3.4% and in men in about of 0.5% (7).

The pathophysiology of FMS remains unclear though research has revealed several physiologic and psychological features associated with FMS (8). However it is not clear whether these features are etiological or secondary to the desease (9).

As fibromyalgia is a chronic condition that often proves refractory to treatment, multidisciplinary symptom management is the main goal in fibromyalgia therapy (11, 12). Various guidelines for FMS treatment exist and have been issued as for instance the guidelines by the European League Against Rheumatism in 2007 as well as from the American Pain Association in 2005. However the conventional treatments often achieve only weak results (14) and especially pharmacological therapies bear the risks of side effects. Thus many fibromyalgia patients seek complementary or alternative medical treatment (CAM). The estimated percentage of CAM users among fibromyalgia patients varies according to the definition of complementary medicine applied and the population studied and is found to be from about 60% to 90% in the North American region (15, 16, 17).

The question as to which therapies should be considered as CAM treatments is controversial. The National Centre for Complementary and Alternative Medicine defines CAM as a group of diverse medical systems, practices and products that are not presently considered to be part of conventional medicine (18). The term ‘Alternative medicine’ furthermore means that it is being practised instead and the term ‘Complementary medicine’ that it is being practised together with conventional medicine. That usually implies no or little evidence by valid scientific studies as to their effects exist and as such evidence emerges these therapies are

integrated into conventional health care. Still in the ongoing process of evaluating CAM therapies by clinical trials and scientific research a group of studies remain that already have been evaluated and partly proven effective and are not yet fully recognised as conventional care.

Another concept of defining CAM medicine is one of a holistic approach to patients that involves both individual physical and spiritual dimensions (8). This concept is found in traditional medical approaches as for instance Traditional Chinese Medicine or more recently developed health systems as are part of the so called Mind-Body Medicine.

Thus reviews on CAM topics vary greatly in their choice of included and excluded therapy approaches. Several reviews have been issued on CAM therapies in fibromyalgia in the past years. Table 1 offers a selection of these reviews published since 2000.

Tbl.1

Most of the represented publications review both randomized controlled trials (RCTs) and non-RCTs. Though RCTs are considered as the strongest research basis for clinical recommendations in evidence based medicine, RCTs are particularly difficult to perform in many categories of CAM medicine. An individualized approach to the patient in diagnosis and therapy is often already part of the healing process itself. This makes standardization and the creation of control groups in order to rule out so called ‘placebo effects’ often very challenging and blinding of both patients and medical practitioners sometimes impossible. Thus it is not surprising that many authors comprise different study design to fully cover the field.

However as RCTs are considered as less liable to bias, there is also need for publications that focus on only this kind of clinical trials. In 2002 a methodologically impressing publication appeared that coved RCT research on non-pharmacological approaches in fibromyalgia (24). The authors concluded that many of the studies reviewed suffered from methodological shortcomings and worked with small study samples. Thus only moderate evidence for aerobic exercise approaches could be found. In 2003 another comprehensive review appeared that particularly focused on CAM in fibromyalgia and covered RCTs and controlled or sequential trials (22). The authors noted best evidence for acupuncture and some herbal and nutritional supplements. However since then some new clinical trials have appeared that make a new review on RCTs in fibromyalgia necessary.

This work aims to identify and review RCTs on CAM in fibromyalgia and offer both an overview over the field by tables and a summery on evidence in the different CAM categories. The possibility of metaanlysis was considered separately for every field of CAM presented but could not be performed due to heterogenic study designs and outcome measures.

Methods

The selection of potential CAM topics followed mostly the CAM definition of the NIH (18). However nutritional, herbal and hormonal supplements were found beyond the scope of this article and not included.

Articles were identified by a search of the following databases: Embase, Medline, Pubmed, PsychInfo, Cochrane central register of controlled trials and Cambase. Search was performed for publications till June 2007. The following terms acted as keywords: fibromyalgia, fibrosis, fibromyalgia syndrome, complementary medicine, alternative medicine, CAM, biologically based: energy medicine: reiki, johrei, qi gong healing touch, intercessory prayer, therapeutic touch, distant healing, putative energy, manipulative/body-based: Alexander technique, bowen, chiropractic, craniosacral therapy, feldenkrais, massage, osteopathic, reflexology, rolfing, trager bodywork, tui na, neural therapy, acupressure, acupuncture, mind-body medicine: meditation, imaging, placebo, expectancy, breathing exercise, whole medical systems: traditional Chinese medicine, ayurvedic, naturopathy, homeopathy, anthroposophy, herbal medicine, phytotherapy, balneotherapy, bath, junge bath, dietary, diet.

Titles and abstracts of the articles thus identified were checked for relevance to the CAM field and study category (RCT). Articles in English and German that fulfilled these inclusion criteria or for which the RCT-status remained unclear were obtained in full and scrutinized for the following inclusion criteria:

- Inclusion of fibromyalgia patients diagnosed by the ACR criteria. Confirmation of diagnosis by the ACR criteria comprised in the study protocol.
- Randomization performed. Studies that operated with a within-subject design were excluded. Studies that used a cross-over design were only included if the results of the period before the cross-over were presented separately.
- At least one of the interventions assessed by the study could be attributed to the CAM field.
- Between-group analysis on post treatment results was performed

An evaluation of the included studies was performed by a trial quality score according to 16 formal criteria.
This evaluation was adopted from an article issued in 2002 on non-pharmacological approaches in fibromyalgia (24). A similar quality score had been originally used in systemic reviews on neck and back pain (26, 27).
Two reviewers scored the included studies independently, discrepancies were resolved through discussion. When information on certain criteria was not given in the publication no points were allocated.

Tbl. 2

The results of the evaluation are presented in the tables containing the study summaries.

Results and Discussion

Overall 24 RCTs issued from 1992 to 2007 have been identified for this review. Nine clinical trials evaluated two or more different therapies or used some kind of treatment different to the actually evaluated one as a control (as for instance education groups). Four studies offered the same treatment regime for active and control groups with the addition of an intervention in question in the active group. Seven studies created some kind of ‘sham’ or ‘placebo’ treatment for their control groups and five studies compared an active treatment to usual care. The mean sample size of the studies was 57 and the mean group size 25 with the number of groups ranging from two to four.
21 trials offered some kind of pain measurement as an outcome and 12 of them used a visual analog scale (VAS) pain. Furthermore the FIQ, a tool specifically developed for the assessment of fibromyalgia, appeared eleven times as an outcome variable. Other often used assessment tools were tender point count, tender point dolorimetry and the Beck Depression Scale.
Only seven studies operated with a treatment versus placebo design that permitted patient blinding and in only two studies the success of the blinding procedure was assessed. 17

studies worked either with an assessor blinded to group allocation or with outcome measures obtained through questionnaires only.
The mean score of the trial quality assessment turned out to be fairly low with a mean value of 51. The highest average score was noted for homeopathy, music therapy and acupuncture studies with above 50 points and the lowest for the manual manipulation and diet fields with about 40 points.

Tbl. 3

Acupuncture

Acupuncture originally has been embedded into the theories of Traditional Chinese Medicine. TCM operates with the concept of Qi, often translated as vital energy or life energy that moves through certain channels of the body or meridians and can be influenced by needling of acupoints (28).
When acupuncture was introduced into modern medicine, different and newer forms of acupuncture as elctroacupuncure have been developed by biomedically trained physicians and its practitioners' attitudes vary in their emphasis of traditional theories. Clinical research has provided some evidence for the effectiveness of acupuncture in various clinical conditions though for many conditions the results are contradictory (29). Basic scientific research suggests several possible mechanisms of physiologic effects of acupuncture (30). Yet it still remains controversial whether the observed effects in clinical studies are due to the specific effects of acupuncture or to more general effects often referred to as 'placebo'. (29, 31)
A recently published qualitative review on acupuncture in fibromyalgia (20) (Tbl.1) evaluated 5 RCTs and concluded the results to be equivocal. According to the authors 3RCTs showed positive and 2 negative results. However it can be argued that actually 4 of the 5 RCTs showed some significant positive changes in favor of acupuncture treatment (including the later described study by Sprott(32))and thus a more explicit judgment in favor of acupuncture on the basis of the provided data could also be justified.
For this review we identified 4 clinical trials that complied with our inclusion criteria. Two RCTs had to be excluded due to the use of Mueller/Lautenschläger diagnosis criteria. (One of these studies (33) had positive results and one (34) significant changes in tender points but no significant changes in pain by treatment as compared to control.)

The studies identified vary in the treatment mode chosen (standardized or individually modified acupuncture, elctroacupuncure) and use different procedures for control groups.
For controls non-insertive sham acupuncture as used by Martin et al. (35) and by Assefi and colleagues (36) stands alongside with needle insertion away from acupoints as applied by Deluze et al. (37). This may be important because some findings suggest that needle insertion away from acupoints may also be effective in alleviating pain (38).
Two of the four identified clinical trials show significant improvements in such important outcome measures as FIQ and pain. These RCTs have scored relatively high in the applied method assessment. A study by Deluze and colleagues evaluated partly individualized acupuncture treatment for 3 weeks versus a non-acupoint needling control and found significant improvement in the majority of outcome variables as for instance in pain. However the authors did not perform a follow-up.
Martin et al. noted significant improvements in FIQ and pain up to 1 month follow-up in an active group that was treated with 6 sessions of standardized acupuncture when compared to a non-insertion control.
These results are questioned by a methodologically good trial by Assefi and colleagues that did not show any difference in outcome measures between acupuncture treatment designed for fibromyalgia and a pooled control that consisted of sham acupuncture, acupuncture for another syndrome and needle insertion away from acupoints.
Finally a study by Sprott adds equivocal results. The author compared an individualized acupuncture treatment for 3 weeks to sham acupuncture treatment with a disconnected laser instrument and usual care on a rather small patient sample and found a decreased number of tender points in the acupuncture group when compared to usual care and an increased pain threshold in the pre/post comparison of the acupuncture group but except for that no group differences.
Altogether the results seem contradictory. Two studies show results in favor of acupuncture in FMS, one against it and one yields equivocal results. The two positive and the negative trial show similar methodological quality, only the study by Sprott scores lower in the quality score.
As for the mode of acupuncture chosen, both the positive study by Martin et al. and the negative study by Assefi and colleagues used standardized acupuncture for fibromyalgia as active treatment. Some systematic differences can however be found in the control groups between the negative and the positive studies.

In the negative study by Assefi et al the pooled control group consisted of both non-insertive acupuncture as well as two groups of insertive needling of acupoints for another condition and away from acupoints. The two positive studies by Martin et al and Deluze et al. used either non-insertive acupuncture or acupuncture away from acupoints at a much lesser depth (25-10 versus 4-3 mm) and the study by Sprott applied a control treatment with a disconnected laser without any needling. Thus a possible explanation for the contradictions might be that the non-specific effects of needling were causing the pain alleviating effects and thus the control in the trial by Assefi was as effective as the treatment group. Particularly as the acupuncture treatment was standardized in two of the trials and fibromyalgia patients are often a heterogeneous group the non-specific effects might have prevailed.
Overall the results would create a positive tendency in favor of acupuncture.
But it is difficult to draw conclusions due to the different study designs.
More RCTs with comparative designs and follow-ups are needed to clarify the effects of acupuncture for fibromyalgia and to provide material for meta-analysis.

Tbl. 4

Balneotherapy/Thermotherapy

This group contains three different subgroups of therapies: thermal and mineral bath therapy, hydroelectric bath therapy and near infrared hyperthermia treatment.

There are different treatment modalities that use water, especially warm water, as a means. Balneotherapy operates with natural mineral water, hydrotherapy uses ordinary water, in hydrogalvanic bath therapy current application is involved and Spa treatment often comprises different therapy modalities as balneotherapy, massage and exercise. Several possible mechanisms of action of these therapies have been proposed (39).

Balneotherpy was traditionally offered in Spa Settings in Turkey, the Dead Sea area in Israel and in Europe to treat different rheumatic and pain deceases.
Four out of seven RCTs identified in this field examine the effects of balneotherapy. Three of these studies show some significant benefits by this intervention immediately after the end of treatment and at follow-up when compared to control (40, 41, 42) and one proves equal to pool based exercise (43).

The treatments described in these studies differ in constituents found in the mineral water as well as in therapy settings and the management of the control groups.
A study by Dönmez et al. (40) compares a stay at a Spa Center and treatment by balneotherapy in its course to usual care and finds significant improvement in such important outcome measures as pain and FIQ when compared to control. The results are maintained at follow-up up to 1 month in pain and tender point count and up to 6 month in FIQ. However they can also be attributed to the effects of the Spa stay that was not offered to the control group.
Two other studies address this problem by either offering a stay in a Spa hotel to the control group (Neumann et al. (41)) or treating the active group as outpatients (Evcik et al. (42)). Both studies show the effects of balneotherapy to be significantly superior to the controls in some variables. Especially the trial by Evcik and colleges shows some lasting effects. The authors compared balneotharpy to usual care and found significant improvements in favor of treatment in pain, tender point counts and FIQ that were maintained at 6 month follow-up. Finally Altan and colleagues (43) compare balneotherapy to pool exercise. Both groups showed within-group improvement in several outcome measures. Between-group difference was found only in Beck Depression Inventory in favor of the exercise group.

Hydroelectric therapy is examined in two studies. A study by Eksioglu et al. (44) finds joint treatment with Stanger bath therapy and amitrityline significantly superior to amitriptyline administration alone as measured by FIQ. Another study by Guenther and colleagues (45) compares hydro galvanic therapy to Jacobsen relaxation training and shows them to be equal in reducing various pain dimensions.

There seems to be evidence that fibromyalgia patients can benefit from various kinds of water therapy. Particularly for balneotherapy the results are encouraging. There is even some evidence that these results can be maintained at follow up. However the studies in this field vary in design, in methodological quality and mostly have relatively small sample sizes. Accordingly larger and more standardized studies are needed to evaluate further the clinical relevance of these therapies.
Beside the water therapy RCTs, a study by Brockow and colleagues (46) tests near infra-red hyperthermia in a rehabilitation setting on a comparatively large group of patients and finds significant improvements in pain, FIQ and depression as compared to an inpatient control. The significant pre/ post treatment improvements are not confirmed at follow-up but the

intergroup difference is maintained up to 6 month. These are promising results that yet have to be confirmed by other RCTs testing this approach.

Tbl. 5

Magnetic field treatment

Though there is little adequate scientific evidence for the effectiveness of static magnetic products on pain relief and eventual mechanisms of action, they are widely promoted and bought by patients (47, 48).

Two clinical trials examined the exposure of patients to a low static magnetic field during night-time as a therapeutic means but one had to be excluded due to a lack of between-group post-treatment analysis. (49)

The remaining clinical trial used hard magnetic sleeping pads that contained ceramic magnets as active treatment and sham pads without magnets as a placebo.

This 6-month-study by Alfano et al. (50) showed no significant differences in overall FIQ between sham and functional pad users but pain intensity by FIQ was significantly decreased by magnet pads as compared to controls and there were trends towards improvement in overall FIQ and other outcome measures in the treatment groups.

However the success of the patient blinding was not assessed in the study and it must be kept in mind that it might have been possible for the enrolled patients to discern a true magnet from a sham one and thus to undo the blinding.

Although the results are of moderate magnitude, there seems to be some tendency towards improvements of symptoms in fibromyalgia patients treated by magnetic pads whether by the some effect of the magnets or by an anticipation effect if blinding had been really unsuccessful..

As this trial has not shown any adverse effects and yet some hints at improvement further investigation might be useful to confirm these improvements and to estimate an eventual clinical relevance.

Tbl. 6

Homeopathy

Only one clinical trial evaluating homeopathy in fibromyalgia complied with our inclusion/ exclusion criteria as the ACR based diagnosis and was included into this review (51).
The 4 month double-blind trial by Bell used individually prescribed homeopathic remedies of daily, flexibly dosed LM potencies and placebo. The homeopaths were permitted to change prescription after a homeopathic visit at 2 month.
This study yielded a significant improvement in favor of the treatment group in tender point count and pain, quality of life and global health ratings.
These results show homeopathy to be a promising option in the treatment of fibromyalgia. Yet further clinical trials are needed to confirm these findings with bigger sample sizes and follow-ups and to create an eventual evidence-based basis for homeopathic treatment in fibromyalgia.

Tbl. 7

Manual Manipulation

Three studies evaluating manual manipulative treatment with a complementary medical background were identified for this review, one in chiropractic care, one in osteopathy and one in massage therapy.
Blunt et al. (52) examined a chiropractic approach to fibromyalgia with a relatively small sample of patients and short study duration but a rather intensive treatment program. No statistically significant between-group improvements were found. Some significant improvement was noted in pain levels and several ranges of motion in the within-group analysis of the treatment group. Accordingly there is so far little evidence that chiropractic care is effective in fibromyalgia but the small study sample limits the reliability of these results.
Another clinical trial by Gamber et al. (53) examined osteopathic manipulative treatment (OMT) with and without additional educational support against moist heat treatment and treatment as usual. The authors found an increase in tender point pain threshold in 3 tender points in favor of OMT group and improvements in some activities of daily living, some measures of perceived pain and perceived functional ability. Although the trial was of relatively long duration of 6 month, the study sample was rather small. Accordingly these findings can only serve as a pilot study for further investigation and cannot provide clear results as to the efficacy of osteopathy in fibromyalgia.

Massage has been historically considered as an option to treat pain and musculoskeletal disorders.
We identified one trial assessing massage as a treatment for FMS that complied with the inclusion criteria.
The study by Brattberg et al (54) tested the effects of regular sessions of connective tissue massage for 10 weeks versus a waiting list control and education control group and found significant improvements in FIQ and pain in the treatment group versus control. A 3 and 6 month follow-up revealed some lasting effect at 3 month that was almost gone at 6 month. As FIQ and pain are major outcome measures for fibromyalgia symptoms (24) this trial indicates a possible effect of massage for FMS. More studies would be needed to replicate these results.

Tbl. 8

Mind Body
The field of Mind Body Medicine comprises various approaches that aim to influence both the spiritual or emotional and the physical dimensions in a patient. Some of these therapies like Cognitive Behavioral therapy have become part of conventional medicine (18) but most are still considered part of CAM Medicine.
For this review we identified and included RCTs evaluating six therapeutical approaches in the Mind-Body category: Body Awareness therapy, Mindfulness Meditation, Qigong and Mensendieck System therapy, Biofeedback and Relaxation by Autogenic Training.
Overall there are rather positive though somewhat equivocal results for the effectiveness of Mindfulness Meditation and little to no evidence for the benefits of Body Awareness Therapy. One clinical trial provides some promising results in favor of Mesendieck System therapy. Qigong that only appeared as a co-treatment in the presented studies did not yet prove beneficial in fibromyalgia according to the identified RCTs.
Biofeedback showed no positive results in a pragmatic study and Autogenic Training was inferior to an Integrated Group Therapy approach in a study comparing these treatments.

The Mindfulness Meditation interventions examined in two clinical trials follow the Mindfulness Based Stress Reduction (MBSR) therapy developed by Kabat-Zinn. It combines stress reduction skills as sitting meditation, hatha yoga and a somatically focused technique called the body scan (55).
Sephton et al. (56) focused on the effects of MBSR on depressive symptoms in FMS.

A MBSR teaching and practicing program for 2 month was compared to treatment as usual. The MBSR therapy significantly reduced depressive symptoms in the active group versus control up to a 2 month follow-up.
Another study by Astin et al. (57) tested an integrated program of stress reduction based on MBSR and Qigong versus an education-support group as a control. No significant differences between groups were found though significant positive changes occurred in FIQ, Total Myalgic Score, Pain and Depression in both groups and were maintained at follow-up. This clinical trial was limited by a high attrition rate in the treatment period already. Furthermore the control program that consisted of 2.5 h long education sessions and free discussion might have acted as a successful intervention itself.
Considering the different control groups in these two trials it remains unclear whether the observed positive effects can be attributed to MBSR specifically. Yet there are some promising results especially as to a lasting effect in the follow-ups that would justify further investigation in this field.

Body Awareness Therapy (BAT) is evaluated in two clinical trials identified for this review. One investigates the effects of an integrated intervention of Body Awareness Therapy and Qigong and tests it versus a usual care control (58). Another pragmatic study compares BAT to Mensendieck System therapy (59).
The Mensendieck System created by Bess Mensendieck focuses on teaching patients to understand the concepts of functioning of their bodies by pedagogically designed exercises and aims to enable them to change suboptimal patterns of movement (59).
BAT was developed by the physiotherapist Gertrud Roxendal and combines exercises that aim to provide an enhanced body consciousness and management to patients (61).
Mannekorpi et al. evaluated a BAT plus Qigong intervention versus usual care control in a three month trial. The patients involved had a rather long history of symptoms of averagely 10 years. Though a significant change for the better was observed in the treatment group in Body awareness Scales there were no positive changes in symptoms measured by FIQ. Even an exacerbation of complains was noted in the pre/post analysis in FIQ depression and fatigue in the active group.
Kendall et al. performed a pilot study evaluating group sessions of BAT versus individual sessions of Mensendieck System over 20 weeks with a comparatively long follow-up of 18 month. Altogether Mesendieck group reported better scores in the significant variables. There were almost no positive changes in the pre/post analysis for BAT and in the between-group

analysis the Mesendieck group scored significantly better in FIQ and several Arthritis Self Efficacy Scale (ASES) and Coping Strategies Questionnaire (CSQ) subscales. There were still some subscales of CSQ and ASES that showed a significant difference in favor of Mensendieck System at 6 month and 18 month follow-up.
Accordingly there is yet no evidence provided by RCT that BAT is effective in FM. Mensendieck System showed positive results in one study that were still not completely extinguished at follow-up. These results would need replication to serve as evidence based criteria for broad clinical use.

Qigong, an ancient Chinese discipline of movement and breathing exercises, appears only as a co-treatment in integrated interventions with Body Awareness Therapy and with Mindfulness Meditation. In a joint intervention with BAT Qigong shows no positive results in either pre/post analysis or in the between-group comparison with a treatment as usual control in fibromyalgia symptoms. Together with Mindfulness Meditation it proves equal to an education support-group control yet pre/post analysis shows benefits in FIQ, pain and depression in both groups that are maintained at follow up. However as Mindfulness Meditation proved to be effective in fibromyalgia at least on depressive symptoms in another study by Sephton and colleagues it is not clear whether the intergroup results can be attributed to either a ‘placebo’ effect, the Mindfulness Meditation effects alone or to Qigong itself. Accordingly there is so far no RCT based proof for the effectiveness of Qigong in FMS.

Only one clinical trial based on the ACR diagnosis criteria was found to examine biofeedback for FMS patients (63).
Eight weeks of individual biofeedback training were compared to a group fitness training and usual care control. This trial did not show any benefits from either intervention in any outcome measure.
Keel et al (64) used Autogenic Relaxation training as a control treatment when investigating the benefits of Integrated Group Therapy for FMS patients and found Autogenic training to be significantly inferior to Integrated Group Therapy in decreasing pain and a tendency in favor of Integrated Group Therapy in overall patients’ improvement. Thus it must be concluded that there is yet no evidence in favor of effects of biofeedback or Autogenic training alone for FMS patients.

Tbl. 9

Vegetarian Diet

Only one RCT assessing the effects of vegetarian diet was identified.
The vegetarian diet was evaluated in a 6 weeks lasting study versus the administration of amitriptyline. Significant pre/post changes occurred only in pain scores in the diet group and the magnitude of pain decrease was significantly lower than in the amitriptyline group. No changes were observed for several other variables measuring common FMS symptoms.
Thus there is no RCT based proof that vegetarian diet is an effective treatment for fibromyalgia.

Tbl. 10

Music vibration therapy
Music therapy has historically been considered as a means for pain relief and is used by music therapists to alleviate pain.
We identified one pilot study evaluating music listening and application of musically fluctuating vibration to the body with a frequency in the sensitivity range of Panician corpuscle (PC) mechanoreceptors versus music listening and music vibration outside the range of PC receptors. No significant between group differences were noted. Both groups scored significantly better in tender point index after the intervention yet only the treatment group showed significantly better results in tender point pain threshold in the within-group analysis. Thus these results might hint at benefits for FMS patient by musically fluctuating vibration therapy. But as only one intervention session was performed on a relatively small sample of patients it is only a stimulus for further investigation in this field and does not provide evidence of clinical relevance.

Tbl. 11

Quality score

There is general acceptance and empirical evidence (67, 68) that some methodological features of designing, performing and reporting clinical trials affect their outcome and

perception. This makes some kind of assessment of quality of reported trials necessary. Thus a variety of different quality scales has been developed by different authors.
A critical overview of such quality scores and checklists for RCTs performed by Moher and colleagues (69) found these scores to be heterogenic. Findings have been reported that show different summery scores to yield contradicting results on the quality of the same trials. Jüni and colleagues demonstrated that when these different quality scores are used in metaanalysis they influence review results oppositely (70).
Jüni et al. and others (71) have pointed out that the quality of clinical trials is an equivocal term and can address either quality of reporting or quality of design. Thus different quality scores often address different quality dimensions without explicitly mentioning it.
The quality score applied in this review comprises both aspects of trial design and reporting. As it is only based on generally accepted criteria (26, 69) of which some but not all are based on empirical evidence it is itself liable to bias that it aims to address. Particularly the weight assigned to different criteria by different amounts of score points can produce some bias of quality assessment.
But as many of the RCTs presented appear to show some methodological flaws and the results in the different therapy fields are sometimes equivocal we consider a quality score to be a useful tool to further objectify these problems and to provide an additional means to interpret the given results.

Tbl. 12

Conclusions

This review does not include all RCTs on complementary medicine in fibromyalgia because of the limitation to RCTs using the ACR diagnostic criteria and the presence of other methodological features. This limitation was chosen in order to create a more homogeneous sample of patients in the primary studies but has led to the omission of some studies.
Although search of computerized databases has been thoroughly performed hand searching of references was not attempted. This might have likewise led to the omission of some relevant studies.
Many of the primary studies showed shortcomings in both study design and study reporting.

This is partly understandable because RCTs in some field of CAM are particularly difficult to design because of a lack of established placebo procedures and difficulties in blinding but it limits the strength of evidence of these studies nonetheless.

Follow-ups were often not performed or of short duration although they are particularly important in a chronic condition as fibromyalgia (24). Furthermore many publications did not contain information on randomization procedures or assessment blinding. These problems should be addressed in further research.

Beside the heterogenic control approaches different outcome measures are still one of the main obstacles to metaanlysis in this field. For instance most of the RCTs address pain as an outcome variable but use different procedures to evaluate it. As visual analog scales on pain are the most commonly used pain assessment they could be recommended for further research in order to standardize outcome measurement. Furthermore the use of specific recognized tools as the Fibromyalgia Impact Questionnaire could contribute to greater comparability.

The mean group size was rather low with 25 subjects per group. Group sizes in that range might have been often too low to detect statistically significant results.

It has been suggested that studies trying to detect significant effects in the field of acute pain analgesics require group sizes of at least 40 subjects per group to provide statistical reliability and of about 10 times as many patients in each group for clinical relevance (72). Although this estimate cannot be transferred unadjusted to the more complex field of chronic pain of fibromyalgia it might serve as further caution to the reliability of both positive and negative results of some of the reviewed studies.

Overall best evidence was found for balneotherapy and hydrotherapy interventions with mostly positive results in multiple studies.

Positive results were further found for mild infrared-hyperthermia treatment and homeopathy in one RCT for each field.

Mindfulness meditation was examined in two studies and showed positive results in the alleviation of depression in one study and scored equal to a control education treatment in another, however maintaining the positive within-group results in the follow-ups.

Equivocal results in multiple studies with positive results outnumbering the negative results were noted for acupuncture.

Improvement in some but not the greater part of the outcome variables in between-group analysis were found for the Mesendieck system, connective tissue massage, osteopathy and magnet therapy in 1 RCT for each field.

Vegetarian diet, autogenic training, a session of music vibration and chiropractics did not show to be superior to another intervention in a control group but resulted in some pre/post improvements.

So far no positive evidence in RCTs identified for this review was found for biofeedback , Body-Awareness therapy and Qi Gong for fibromyalgia patients.

References

1. Smythe HA, Moldofsky H (1977) Two contributions to the understanding of the 'fibrositis' syndrome. Bull Rheum Dis ▪▪▪:928–931 Medline.

2. Lautenschläger J, Brückle W, Seglias J, Müller W (1989) Lokasierte Druckschmerzen in der Diagnose der generalisierten Tendomyopathie (Fibromyalgie). Z Rheumatol 48:132–138 Medline.

3. Wolfe F, Smythe HA, Yunus MB, et al (1990) The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum ▪▪▪:160–172 Medline. doi:10.1002/art.1780330203

4. Raspe H, Croft P (1995) Fibromyalgia. Baillieres Clin Rheumatol ▪▪▪:599–614 Medline. doi:10.1016/S0950-3579(05)80261-4

5. Hadler NM (2003) 'Fibromyalgia' and the medicalization of misery. J Rheumatol ▪▪▪:1668–1670 Medline.

6. Cohen ML (1999) Is fibromyalgia a distinct clinical entity? The disapproving rheumatologist's evidence. Best Pract Res Clin Rheumatol ▪▪▪:421–425. doi:10.1053/berh.1999.0031

7. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L (1995) The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum ▪▪▪:19–28 Medline. doi:10.1002/art.1780380104

8. Hardy-Pickering R (2007) The use of complementary and alternative ther apies for fibromyalgia. Phys Ther Rev ▪▪▪:249–260. doi:10.1179/108331907X222930

9. **Adams, N. and Sim, J.,** *An overview of fibromyalgia syndrome : Mechanisms, differential diagnosis and treatment approaches- Physiotherapy*1998.

10. Abeles AM, Pillinger MH, Solitar BM, Abeles M (2007) Narrative review: the pathophysiology of fibromyalgia. Ann Intern Med ▪▪▪:726–734 Medline.

11. Goldenberg DL, Burckhardt C, Crofford L (2004) Management of fibromyalgia syndrome. JAMA ▪▪▪:2388–2395 Medline. doi:10.1001/jama.292.19.2388

12. Carville SF, Arendt-Nielsen S, Bliddal H, et al (2008) EULAR evidence-based recommendations for the management of fibromyalgia syndrome. Ann Rheum Dis ▪▪▪:536–541 Medline.

13. University of Texas, School of Nursing, Family Nurse Practitioner Program. Fibromyalgia treatment guideline. Austin (TX): University of Texas, School of Nursing; 2005 May. 13 p

14. **Noller, Vera and Sprott, Haiko,** *Prospective epidemiological observations on the course of the disease in fibromyalgia patients*.

15. (2007) **Lind, Bonnie K., Lafferty, William E., Tyree, Patrick Timothy, Diehr, Paula K. and Grembowski, David E.,** "Use of complementary and alternative medicine providers by fibromyalgia patients under insurance coverage. Arthritis Rheum ▪▪▪:71–76 Medline.

16. Wahner-Roedler DL, Elkin PL, Vincent A, et al (2005) Use of complementary and alternative medical therapies by patients referred to a fibromyalgia treatment program at a tertiary care center. Mayo Clin Proc ▪▪▪:55–60 Medline.

17. Pioro-Boisset M, Esdaile JM, Fitzcharles MA (1996) Alternative medicine use in fibromyalgia syndrome. Arthritis Care Res ▪▪▪:13–17 Medline. doi:10.1002/art.1790090105

18. **National Center for Complemntary and Alternative Medicine**: What is CAM medicine? NCCAM Publication No.D347. Updated February 2007

19. (2006) **Sarac, Aysegul Jale and Gur, Ali,** "Complementary and alternative medical therapies in fibromyalgia. Curr Pharm Des ▪▪▪:47–57 Medline.

20. Mayhew E, Ernst E (2007) Acupuncture for fibromyalgia--a systematic review of randomized clinical trials. Rheumatology (Oxford) ▪▪▪:801–804 Medline. doi:10.1093/rheumatology/kel406

21. Adams N, Sim J (2005) Rehabilitation approaches in fibromyalgia. Disabil Rehabil ▪▪▪:711–723 Medline. doi:10.1080/09638280400014709

22. Holdcraft LC, Assefi N, Buchwald D (2003) Complementary and alternative medicine in fibromyalgia and related syndromes. Best Pract Res Clin Rheumatol ▪▪▪:667–683 Medline. doi:10.1016/S1521-6942(03)00037-8

23. (▪▪▪) **Sierpina, Victor S and Carter, Ramona,** “Alternative and integrative treatment of fibromyalgia and chronic fatigue syndrome. Clin Fam Pract 4(44):853–872.

24. Sim J, Adams N (2002) Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia. Clin J Pain ▪▪▪:324–336 Medline.

doi:10.1097/00002508-200209000-00008

25. Crofford LJ, Appleton BE (2001) Complementary and alternative therapies for fibromyalgia. Curr Rheumatol Rep ▪▪▪:147–156 Medline. doi:10.1007/s11926-001-0010-9

26. Koes B, Bouter L, Beckerman H, van der Heijden G, Knipschild P (1991) Physiotherapy exercises and back pain. BMJ ▪▪▪:853 Medline.

27. Hurwitz EL, Aker PD, Adams AH, Meeker WC, Shekelle PG (1996) Manipulation and mobilization of the cervical spine. A systematic review of the literature. Spine ▪▪▪:1746–1759. discussion 1759-60 Medline. doi:10.1097/00007632-199608010-00007

28. Zheng L, Faber K (2005) Review of the Chinese medical approach to the management of fibromyalgia. Curr Pain Headache Rep ▪▪▪:307–312 Medline. doi:10.1007/s11916-005-0004-9

29. Ernst E (2006) Acupuncture--a critical analysis. J Intern Med ▪▪▪:125–137 Medline. doi:10.1111/j.1365-2796.2005.01584.x

30. Kaptchuk TJ (2002) Acupuncture: theory, efficacy, and practice. Ann Intern Med ▪▪▪:374–383 Medline.

31. Liu T "Acupuncture: What underlies needle administration?" *Evidence Based Complementary and Alternative Medicine,* 2008

32. Sprott H "Efficiency of acupuncture in patients with fibromyalgia," *Clinical Bulletin of Myofascial Pain,* 1998

33. Lautenschlaeger J, Schnorrenberger C, Müller W "Akupuntur bei generalisierter Tendomyopathie (Fibromyalgie-Syndrom)," *Deutsche Zeitschrift für Akupunktur,* 1989

34. Sprott H, Mennet P, Stratz T, Müller W (1993) Wirksamkeit der Akupunktur bei Patienten mit generalisierter Tendomyopathie (Fibromyalgie). Aktuelle Rheumatol ▪▪▪:132–135. doi:10.1055/s-2008-1047326

35. Martin DP, Sletten CD, Williams BA, Berger IH (2006) Improvement in fibromyalgia symptoms with acupuncture: results of a randomized controlled trial. Mayo Clin Proc ▪▪▪:749–757 Medline.

36. Assefi NP, Sherman KJ, Jacobsen C, et al (2005) A randomized clinical trial of acupuncture compared with sham acupuncture in fibromyalgia. Ann Intern Med ▪▪▪:10–19 Medline.

37. Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL (1992) Electroacupuncture in fibromyalgia: results of a controlled trial. BMJ ▪▪▪:1249–1252 Medline.

38. Bars L **Daniel und Willer, Jean-Claude,** "Pain modulation triggered by high-intensity stimulation: implication for acupuncture analgesia?" *international Congress Series*, 2002, 11-29.

39. Bender T, Karagulle Z, Balint GP, et al (2005) Hydrotherapy, balneotherapy, and spa treatment in pain management. Rheumatol Int ▪▪▪:220–224 Medline. doi:10.1007/s00296-004-0487-4

40. Donmez A, Karagulle MZ, Tercan N, et al (2005) SPA therapy in fibromyalgia: a randomised controlled clinic study. Rheumatol Int ▪▪▪:168–172 Medline. doi:10.1007/s00296-005-0623-9

41. Neumann L, Sukenik S, Bolotin A, et al (2001) The effect of balneotherapy at the Dead Sea on the quality of life of patients with fibromyalgia syndrome. Clin Rheumatol ▪▪▪:15–19 Medline. doi:10.1007/s100670170097

42. Evcik D, Kizilay B, Gokcen E (2002) The effects of balneotherapy on fibromyalgia patients. Rheumatol Int ▪▪▪:56–59 Medline. doi:10.1007/s00296-002-0189-8

43. Altan L, Bingol U, Aykac M, Koc Z, Yurtkuran M (2004) Investigation of the effects of pool-based exercise on fibromyalgia syndrome. Rheumatol Int ▪▪▪:272–277 Medline.

44. (2007) **Eksioglu, Emel, Yazar, Duygu, Bal, Ajda, Usan, Hicran Demir and Cakci, Aytul,** "Effects of Stanger bath therapy on fibromyalgia. Clin Rheumatol ▪▪▪:691–694 Medline.

45. Gunther V, Mur E, Kinigadner U, Miller C (1994) Fibromyalgia--the effect of relaxation and hydrogalvanic bath therapy on the subjective pain experience. Clin Rheumatol ▪▪▪:573–578 Medline. doi:10.1007/BF02242996

46. Brockow T, Wagner A, Franke A, Offenbacher M, Resch KL (2007) A Randomized Controlled Trial on the Effectiveness of Mild Water-filtered Near Infrared whole-body Hyperthermia as an Adjunct to a Standard Multimodal Rehabilitation in the Treatment of Fibromyalgia. Clin J Pain 23:67–75 Medline. doi:10.1097/AJP.0b013e31802b4f80

47. Ratterman R, Secrest J, Norwood B, Ch'ien AP (2002) Magnet therapy: what's the attraction? J Am Acad Nurse Pract ▪▪▪:347–353 Medline. doi:10.1111/j.1745-7599.2002.tb00135.x

48. Cepeda MS, Carr DB, Sarquis T, et al (2007) Static magnetic therapy does not decrease pain or opioid requirements: a randomized double-blind trial. Anesth Analg ▪▪▪:290–294 Medline. doi:10.1213/01.ane.0000230613.25754.08

49. Colbert AP, Markov MS, Banerji M, Pilla AA (1999) Magnetic mattress pad use in patients with fibromyalgia: a randomized double-blind pilot study. J Back Musculoskeletal Rehabil ▪▪▪:19–31.

50. Alfano AP, Taylor AG, Foresman PA, et al (2001) Static magnetic fields for treatment of fibromyalgia: a randomized controlled trial. J Altern Complement Med ▪▪▪:53–64 Medline. doi:10.1089/107555301300004538

51. Bell IR, Lewis DA 2nd, Brooks AJ, et al (2004) Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. Rheumatology (Oxford) ▪▪▪:577–582 Medline. doi:10.1093/rheumatology/keh111

52. Blunt KL, Rajwani MH, Guerriero RC (1997) The effectiveness of chiropractic management of fibromyalgia patients: a pilot study. J Manipulative Physiol Ther ▪▪▪:389–399 Medline.

53. Gamber RG, Shores JH, Russo DP, Jimenez C, Rubin BR (2002) Osteopathic manipulative treatment in conjunction with medication relieves pain associated with fibromyalgia syndrome: results of a randomized clinical pilot project. J Am Osteopath Assoc ▪▪▪:321–325 Medline.

54. Brattberg G (1999) Connective tissue massage in the treatment of fibromyalgia. Eur J Pain ▪▪▪:235–244 Medline. doi:10.1016/S1090-3801(99)90050-2

55. Kabat-Zinn J (1982) An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiatry ▪▪▪:33–47 Medline. doi:10.1016/0163-8343(82)90026-3

56. Sephton SE, Salmon P, Weissbecker I, et al (2007) Mindfulness meditation alleviates depressive symptoms in women with fibromyalgia: results of a randomized clinical trial. Arthritis Rheum ▪▪▪:77–85 Medline. doi:10.1002/art.22478

57. Astin JA, Berman BM, Bausell B, et al (2003) The efficacy of mindfulness meditation plus Qigong movement therapy in the treatment of fibromyalgia: a randomized controlled trial. J Rheumatol ▪▪▪:2257–2262 Medline.

58. Mannerkorpi K, Arndorw M (2004) Efficacy and feasibility of a combination of body awareness therapy and qigong in patients with fibromyalgia: a pilot study. J Rehabil Med ▪▪▪:279–281 Medline. doi:10.1080/16501970410031912

59. Kendall SA, Brolin-Magnusson K, Soren B, Gerdle B, Henriksson KG (2000) A pilot study of body awareness programs in the treatment of fibromyalgia syndrome. Arthritis Care Res ▪▪▪:304–311 Medline. doi:10.1002/1529-0131(200010)13:5<304::AID-ANR10>3.0.CO;2-P

61. Roxendal G Body awareness therapy and the body awareness scale. Gothenburg: Dept. Rehabilitation Medicine, University of Gothenburg; 1985.

63. van Santen M, Bolwijn P, Verstappen F, et al (2002) A randomized clinical trial comparing fitness and biofeedback training versus basic treatment in patients with fibromyalgia. J Rheumatol ▪▪▪:575–581 Medline.

64. Keel PJ, Bodoky C, Gerhard U, Muller W (1998) Comparison of integrated group therapy and group relaxation training for fibromyalgia. Clin J Pain ▪▪▪:232–238 Medline. doi:10.1097/00002508-199809000-00010

65. Azad KA, Alam MN, Haq SA, et al (2000) Vegetarian diet in the treatment of fibromyalgia. Bangladesh Med Res Counc Bull ▪▪▪:41–47 Medline.

66. **Chesky, Kris S, Russell, Jon I, Lopez, Yolanda und Kondraske, Goerge,** "Fibromyalgia Tender Point Pain: A Double-Blind, Placebo-Controlled Pilot Study of Music Vibration Using the Music Vibration Table," *Journal of Musculoskeletal Pain*, 1997,.

67. Colditz GA, Miller JN, Mosteller F (1989) How study design affects outcomes in comparisons of therapy. I: Medical. Stat Med ▪▪▪:441–454 Medline. doi:10.1002/sim.4780080408

68. Schulz KF, Chalmers I, Hayes RJ, Altman DG (1995) Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA ▪▪▪:408–412 Medline. doi:10.1001/jama.273.5.408

69. Moher D, Jadad AR, Nichol G, et al (1995) Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. Control Clin Trials ▪▪▪:62–73 Medline. doi:10.1016/0197-2456(94)00031-W

70. Juni P, Witschi A, Bloch R, Egger M (1999) The hazards of scoring the quality of clinical trials for meta-analysis. JAMA ▪▪▪:1054–1060 Medline. doi:10.1001/jama.282.11.1054

71. Berlin JA, Rennie D (1999) Measuring the quality of trials: the quality of quality scales. JAMA ▪▪▪:1083–1085 Medline. doi:10.1001/jama.282.11.1083

72. Moore RA, Gavaghan D, Tramer MR, Collins SL, McQuay HJ (1998) Size is everything--large amounts of information are needed to overcome random effects in estimating direction and magnitude of treatment effects. Pain ▪▪▪:209–216 Medline. doi:10.1016/S0304-3959(98)00140-7

Tbl. 1 CAM fibromyalgia reviews

Authors, year	specifics	Therapies reviewed	results
Hardy-Pickering, R. (8)	-Comprehensive, extensive introduction into the field of	RCTs and non-RCTs	Moderate evidence for acupuncture and balneotharpy, some evidence for massage, holistic movement therapies and chiropractics

	fibromyalgia and CAM: discussion of CAM terminology, CAM use and specifics of patients using CAM		
2008		-Energy therapies	
		-Balneothrapy	
		-Osteopathy, Chiropractic	
		-Acupuncture	
		-Homeopathy	
		-Holistic movement (only short and by reference)	
Sarac, J.S. and Gur, A. (19)	-Additional theoretical information on background and research on complementary treatments for which no clinical trials in FMS were identified by the authors	RCTs and non-RCTs	Best evidence for effectiveness noted by authors for magnesium, S-Adenosylmethionine and massage, Chlorella, biofeedback, relaxation evaluated in only one RCT with positive results, magnet therapy in multiple RCTs with mixed results. Homeopathy, botanical oils, balneothrapy, anthocyanidins and dietary modifications are noted to have positive results in studies with methodological flaws.
2006	- extensive information on nutritional, herbal and hormonal supplements	- Nutritional, herbal and hormonal supplements: St. John's worth, Siberian Ginseng, Valeria, Botanical oil, Melatonin, Magnesium, Serum Dehydroepiandosterone Sulphate, Nicotinamide Adenine Dehydrogenase, S-Adenosylmethionine, Growth hormone, Chlorella Pyrenoidosa, 5-Hydroxytryptophan combination therapy	
		- Dietary supplement	
		-Manual manipulative Technique	
		- Massage	
		-Homeopathy	
		-Ayurvedic	
		-Chiropractic Care	
		-Superficial Cold and Heat therapy	
		-Others: electroconvulsive therapy, hypnotherapy	
Mayhew,	-Systemic review	Only RCTs	Equivocal results:

E. and Ernst, E.	on acupuncture and elctroacupuncture in FMS		
-20	-Reviewed papers assessed by Jadad methodological score	-Acupuncture	3 RCTs positive results but mostly short-lived, 2 RCTs negative results, all positive RCTs used electroacupuncture.
2006		-Electroacupuncture	
Adams, N. and Sim, J. °	-Review on rehabilitation approaches in FMS, accordingly CAM and non-CAM therapies reviewed	RCTs and non-RCTs	Evidence for exercise therapy. Psychologically based interventions as CBT useful as part of multimodal programmes combined with exercise rather than alone.
-21	-Information on U.K. practitioners' views on FMS management	-Holistic movement therapies	For most CAM therapies results equivocal
2005		- Energy therapies	
		- Balneotherapy	
		- Osteopathic and Chiropractic manipulation	
		- non-CAM therapies:	
		-Exercise	
		- Educational, psychological and cognitive behavioral treatments	
		- Electromyographic biofeedback training	
		- Self-management education programmes	
		-Multimodal/ combination approaches	
Holdcraft, L.C., Assefi, N, Buchwald, D. (22)	- CONSORT Score:	RCTs and non-RCTs (controlled clinical trials, sequential trails)	Acupuncture, some herbal and nutritional supplements (Magnesium, S-Adenosyl-L-methionine) and massage therapy have the best evidence for effectiveness with FMS.
2003	standardized evaluation of the quality of methodology for each paper reviewed	- Acupuncture	Chlorella, biofeedback, relaxation have been evaluated in only one RCT with positive results,
	-Four level scale for strength of recommendation for each CAM category	- Homeopathy	Magnet therapy in multiple RCTs with mixed results.
		-Biologically based therapies:	Homeopathy, botanical oils, balneotherappy, anthocyanidins, dietary modifications have positive results from studies with methodological

			flaws.
		Magnesium, Botanical oils, Balneotharpy, S-Adenosyl-L-methionine, Chlorella pyrenoidosa, Anthocyanidins)	
		-Dietary modifications	
		-Manipulative and body-based systems:	
		Chiropractic Care, Massage	
Sierpina, V.S. and Carter, R. (23)	Review on CAM in fibromyalgia and Chronic Fatigue Syndrome	RCTs and non-RCTs	Recommendation for CBT and exercise in FMS therapy, moreover 5-Hydroxy-Tryptophan and S-Adenosyl-L-methionine.
2002		-Biofeedback	No robust evidence for other CAM therapies, but some Mind-Body therapies, Acupuncture, manipulative techniques as Chiropractic and massage are referred to as promising
		-Hypnotherapy	
		-Cognitive behavioral therapy (CBT)	
		-Meditation	
		-Exercise	
		-Multimodal and multidisciplinary programmes	
		-Chiropractic	
		-Massage	
		-Acupuncture	
		-Herbal Supplements	
		-Diet therapy	
		-Electrotherapy	
		-Homeopathy	
Sim, J. and Adams, N.	- Review on non-pharmacological interventions in fibromyalgia examined in RCTs	Only RCTs	No strong evidence for any intervention, preliminary support of moderate strength for aerobic exercise
-24	- assessment of reviewed papers by a methodological score based on 16 criteria	-Aerobic exercise	
2002		-Acupuncture, electroacupuncture and electrostimulation	
		-Educational and psychological interventions	
		-Other interventions:	
		hypnotherapy, massage, relaxation, chiropractic treatment,	

		pool exercise, electromyographic biofeedback, Vibration therapy, magnetic therapy, hydrotherapy	
Crafford, L. J. , Appleton, B. E. (25)	Additional information on background and research on treatments for which no clinical trials in FMS were identified by the authors , clinical trials on these approaches in other medical conditions described	RCTs and non-RCTs	The review describes the results of the CAM papers identified but mostly does not draw conclusions about overall effectiveness of CAM categories or give recommendations
2001		-Herbal and Nutritional Supplements:	
		Valeria, Ginseng, St. John's wort, Melatonin, Magnesium, Serum dehydroepiandosterone sulphate, Nicotinamide adenine dehydrogenase, Botanical oils	
		-Dietary Supplements	
		-Homeopathy-Mind-Body Medicine:	
		Cognitive-Behavioral therapy, hypnosis, guided imagery, biofeedback	
		-Acupuncture	
		-Manual manipulation:	
		Soft tissue massage, Stretching, Chiropractic, Osteopathic manipulation	
		-Electromyographic biofeedback training	
		-Electromagnetic field and magnet therapy	

Tbl. 1 Reviews on CAM therapies in fibromyagia

Tbl. 2 Quality rating

Criterion	Possible Score	Calculation (no. of points)
A. Homogeneity	**2**	**1:** description of inclusion and exclusion criteria
		1: restriction to a homogeneous study population
B. Comparability of relevant baseline characteristics	**5**	**1 points each:** comparability for duration of complains, value of outcome measures, age, sex, and distribution of symptoms
C. Randomization procedure	**4**	**2:** randomization procedure described

adequate		
		2: randomization procedure that excludes bias
D. Dropouts described for each study group separately	**3**	Information about each group and reason for withdrawal (no dropouts= **3**)
E. Loss to follow-up	**4**	Loss to follow-up: all randomized patients minus the number of patients at main moment of effect measurement for the main outcome measure, divided by all randomized patients, times 100 (<20% **2**; <10%, **2** additional)
F. Subjects in smallest group	**17**	Size of smallest group immediately after randomization:
		>50 patients, **8**;
		>100 patients, **9** additional
G. Intervention standardized and described	**10**	**5:** experimental treatment explicitly described;
		5: all other interventions explicitly described
H. Pragmatic study/control group adequate	**5**	Comparison with other treatment
I. Co interventions avoided	**5**	Other medical interventions avoided in the design of the study (except analgesics, general advice, or use at home of heat, rest, or a routine exercise)
J. Placebo-controlled	**5**	Comparison with placebo therapy
K. Patients blinded	**5**	**3:** Attempted blinding of patients with respect to the content of the interventions;
		2: blinding evaluated and fully successful;
L. Outcome measures relevant	**10**	Outcome measures used and reported:
		2 pain; **1,5** sleep quality; **1,5** fatigue;
		2 global measure of improvement;
		1 functional status; **1** return to work or normal activities; **1** use of medication and/medical services;
M. Blinded outcome assessment	**10** (or **15** when patient blinding not possible)	Effect measured by blinded assessor
N. follow-up period adequate	**5**	Including an effect measurement after 6 moth or longer
O. Intention-to-treat analysis	**5**	When loss to follow-up < 10%: all randomized patients for most important outcome measures and on most important moments of effect measurement minus missing values, irrespective of non-compliance or co interventions; when loss to follow-up >10%: intention to treat as well as an alternative analysis that accounts for missing values
P. Frequencies of most important outcomes presented for each group	**5**	For most important outcome measures and on the most important moments of effect measurement; in the case of (semi-) variables, presentation of mean or median with standard error or percentiles continuous

Tbl. 2 Quality score assessment

CAM field	Number of RCTs	Mean quality score	SD	CAM field	Number of RCTs	Me qua sco
Acupuncture	4	55	13	Manual Manipulation	3	43
Balneotherapy/Thermotherapy	7	54	9	Mind-Body-Field	6	48
Magnetic therapy	1	54	/	Diet	1	40
Homeopathy	1	58	/	Music therapy	1	59

Tbl. 3 Mean quality scores

Acupuncture

Author	Intervention	Control	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Assefi et al.	1. Standardized acupuncture for fibromyalgia	1. Standardized acupuncture for irregular menses	100	62	2×weekly for 12 weeks (24 treatments)	-VAS pain	No significant differences between fibromyalgia acupuncture and the pooled control groups in any outcome measure
		2. Needle insertion at points not recognized as acupoints	4 groups,			-VAS fatigue	
2005		3. Nonisertive, simulated acupuncture	6 month follow-up			-VAS sleep quality	
						-VAS overall well-being	
						-Medical Outcome Study 36-item Short-Form Health Survey	
Deluze et al.	1.electroacupuncture, 4 standardized points and ≥ 6 individual points,	1. points similar to acupoint treatment 20mm away from acupoints	70	50,5	2×weekly for 3 weeks (6 treatments)	- pain threshold	Significant improvement in treatment group in comparison to control in 5 out of 8 outcome measures including pain threshold which was considered main parameter
	depths: 10-25mm	Dephs: 3-4 mm	2 groups			- analgetics used	
1992						- VAS pain	
						- Regional pain	

						score	
						- sleep quality	
						- morning stiffness	
						- general state assessment by patient and physician	
Martin et al.	1. 3 treatment sessions 18, 3 treatment sessions 20 standardized acupoints	1.Similar acupoints with needles attached to bandages not piercing skin	50	68	6 treatments in a 2 to 3 week period	- FIQ	Significant improvement of FIQ(P=0,01) and MPI (p=0,03)in treatment group as opposed to control up to 1 month after treatment
			2 groups,			-modified Multidisciplinary Pain Inventory(MPI)	
2006			7 month follow up				
Sprott et al.	1. 6 acupuncture treatments 2 × week (individually chosen acupoints)	1. 6 treatments of individually chosen acupoints with a disconnected laser instrument	30,	39	3 weeks,	- VAS pain	Significant decrease in TP count as compares to the usual care but not to the sham acupuncture group.
			3 groups		2 month follow-up	- TP count	Sign. Pain threshold decrease in within-group analysis in scupuncture only but not sign. When compared to controls. Not maintained at follow-up-
1998		2. usual care				- TP pain threshold	

						- pain score	
						- interview on general health	

Tbl. 4 Acupuncture

Balneotherapy/Thermotherapy

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Altan et al.	1.balneotherapy in a pool (37°) for 35 min	1.pool based exercise for 35 min	50, 2 groups	56	12 weeks, 12 follow-up	1. VAS pain	No significant between-group differences except for BDI, which showed sign. improvement in the exercise group only.
						2. 5 point scale pain	Significant within-group improvement in most of the parameters at 12 weeks, partly maintained at follow-up.
2004						3. Morning stiffness	
						4. VAS fatigue	
						5. Fatigue 5 point scale	
						6. TP count	
						7. Global assessment by patient	
						8. Global assessment by physician	
						9. FIQ	
						10.Chair test	
						11. Beck Depression Inventory(BDI)	
Brockow et al.	1. Standard medical rehabilitation (MR) and mild near infra-red whole-body hyperthermia 2	1.MR only 2 × week	139, 2 groups	58	3 weeks, 6 month follow-up	1. McGill Pain Questionnaire	Significant improvements in treatment group in MPG, pain intensity, FIQ abridged, FIQ and TP

	× week up to 38°						assessment as compared to MR only. Between – group difference maintained at follow-up.
						(MPG)	
2007						2. Pain intensity	
						3. FM-related quality of life by FIQ	
						4. FIQ	
						5. Mean TP pain threshold	
						6. TP count	
						7. total TP pain intensity	
Dönmez et al.	1. Spa-Centre stay and thermal pool bath (37°) for 20 min 6 × week (12 sessions) and pressured shower with thermal water or classical massage (15min) every day alternately	2. treatment as usual	30, 2 groups	60	2 weeks, 9 month follow-up	1. VAS pain	Significant difference between Spa group and control at the end of treatment in FIQ, pain, TPC, fatigue and patients' global assessment. Maintained up to 1 month in pain, TPC and up to 6 month in FIQ
						2. FIQ	
2005						3. TP count	
						4. Beck Depression Inventory(BDI)	
						5. VAS sleep	
						6. VAS fatigue	
						7. VAS gastrointestinal symptoms	
						8. VAS anxiety	
						9. Patient's global assessment	
Eksioglu	1.amitriptyline	1.amitriptilyne	50, 2	61	8 weeks,	1. TP count	Significant

et al.	10mg/day for 2 weeks and 10 Stanger bath sessions (hydroelectric bath), 20 min each, in a 2 week period	10mg/ day for 8 weeks	groups		2 month follow up		difference in favour of Stanger bath group after 8 weeks in FIQ.
						2. FIQ	
2007							
Evcik et al.	1. thermal bath sessions (36°-60°) for 20 min, 5 × week for three weeks (15 sessions)	2. treatment as usual	42, 2 groups	36	3 weeks, 6 month follow-up	1. VAS pain	Significant improvements in treatment group in VAS pain, FIQ, BDI and TPC compared to control, maintained up to 6 month in pain, TPC and FIQ.
						2. FIQ	
2002						3. Beck Depression Inventory	
						4. TP count	
Guenther et al.	1. hydrogalvanic bath therapy (36°-37°) for 20 min, 2 ×.week for 5 weeks (10 sessions)	2. Jacobson relaxation training: 4 sessions in 3 weeks and auditory tape given to patients to continue daily for 2 weeks	25, 2 groups	51	5 weeks	1. Variety of different scales evaluating pain intensity, quality and pain behaviour	Only between group difference: sign. higher decrease in pain intensity in the period from breakfast till lunch in bath group
1994							
Neumann et al.	1. 10 day stay at a spa hotel at the Dead Sea and bath therapy in a sulphur pool(37°), 20 min sessions, frequency not mentioned	1. 10 day stay at a spa hotel at the Dead Sea	48, 2 groups	56	10 days, 3 month follow-up	VAS:	Both group improved in pain, fatigue and global well being up to 3 month follow-up. Patients in balneotherapy group reported significantly lower levels of

							anxiety and depression at the end of treatment and in functioning status up to 3 month follow-up.
						1. Pain	
2001						2. Fatigue	
						3. Sleep	
						4. Gastro-enterological complains	
						5. Global well-being	
						7. Helplessness scale	
						8. Depression and anxiety subscales out of Arthritis Impact Measurement Scales	
						9. Quality of Life by SF-36	

Tbl. 5 Balneotherapy/Thermotherapy 1

Magnetic therapy

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Resu
Alfano et al.	1. whole-body – exposure to a low, uniform magnetic field of negative polarity by a magnetic sleep-pad	3. Sleep pads with sham magnets	119, 4 groups	54	6 month	1. TPcount	Signi pain funct comp signi in ot meas tende impr varia the a
2001	2. whole body-exposure to a low static magnetic field that varied spirally and in polarity	4. treatment as usual				2. dolorimetry	
						3. FIQ (modified)	

Tbl. 6 Magnetic therapy

Homeopathy

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Bell et al. 2004	1. Individually chosen homeopathic remedy : oral daily liquid LM(1/50000)	2. placebo: oral daily liquid	62, 2 groups	57,5	4 month, outcome assessed partially at 3 and partially at 4 month	1. TP count	Significant improvement in active group in TPC and TP pain on palpation, Appraisal of FM scores, global health ratings and helpfulness of treatment as compared to placebo group.
						2. TP pain on palpation	
						3. McGill Pain Ratings	
						4. Appraisal of FM quality of life scale	
						5. Profile of Mood States scale(POMS)	
						5. Global health self-rating	
						6. treatment helpfulness ratings	

Tbl. 7 Homeopathy 1

Manual Manipulation

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Blunt et al. 1997	1. chiropractic treatment 3-4 × week	2. treatment as usual	21, 2 groups	45	4 weeks	1. TP dolorimetry	No statistically significant differences between groups were

							achieved.
						2. Various ranges of motion	Sign. Within-group improvements were noted in various ranges of motion and pain levels in the active group.
						3. Strength teasting	
						4. VAS pain	
						5. Pain Diagram	
						6. Oswestry Disability Index(ODI)	
						7. Neck pain disability index	
Brattberg et al.	1. 15 connective tissue massage treatments in 10 weeks	2. control group: 50% waiting-list control, 50% education group program	52, 2 groups	38.5	10 weeks, 6 month follow-up	1. VAS pain	Significant improvements in current pain, quality of life by FIQ and depression as compared to control. After 3 month 30% and after 6 month 90% of the pain-relieving effect was gone.
						2. Disability Rating Index	
1999						3. Sleep disturbance Scale	
						4. Anxiety and Depression Scale (<had)	
						5. Quality of Life Scale by Fugl-Meyer	
						6. Quality of Life by FIQ	
						7. FIQ	
						8. Quality OF Life Scale (QOLS)	

Gamber et al.	1. weekly osteopathic manipulative treatment for 15- 30 min	3. moist heat treatment	24, 4 groups	46,5	6 month	1. pain threshold dolorimentry	Significant improvements in osteopathic manipulation groups when compared to controls in pain threshold in 3 tender points, some subcategories of perceived pain, attitude towards treatment, activities of daily living and chronic pain attitudes.
						2. Chronic Pain Experience Inventory	
2002	2. weekly osteopathic manipulative treatment and teaching	4. treatment as usual				3. Present Pain intensity rating scale	
						4. Self evaluation Questionnaire	
						5. Stanford Arthritis Center Disability and Discomfort Scales	
						6. Health Assessment Questionnaire	
						7. Center for Epidemiologic Studies Depression Scale	

Tbl. 8 Manual Manipulation 1

Mind Body

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Astin et al.	1. Mindfulness meditation	2. Education-support-group	128, 2 groups	67	8 weeks, follow-up at 16	1. TP count	No significant between-group

	training and Qigong, 2,5 h group sessions weekly	sessions for 2,5 h weekly			and 24 weeks		differences on any study outcome. Within-group analysis showed sign. improvements in FIQ, pain and depression in both groups. These results were maintained at follow-up.
						2. Total Myalgic score	
2003						3. FIQ	
						4. 6 minute walk test	
						5. Beck Depression Inventory	
						6. Medical care history	
						7. Coping Strategies Questionnaire	
Keel et al.	1. 15 × 2 hour sessions of integrated group therapy (information, instruction in self- control strategies, gymnastics, relaxation and group discussion) once a week.	2. 15 × 45-60 min sessions of Autogenic Training	32, 2 groups	36,5	15 weeks, 3 month follow-up	1. General Symptom Checklist	Average pain intensity had significantly decreased in integrated group therapy patients versus autogenic training. Overall more patients with integrated group therapy treatment showed a tendency towards improvement.
						2. Concurrent treatment:	
1998						- medication	
						- physical therapies	
						Results	

						achieved by scores based on patient's treatment diaries:	
						3. daily active time in hours	
						4. daily rest (daytime)	
						5. disturbed sleep	
						6. average pain intensity	
Kendall et al.	1. Mesendieck System (MS): 18 × 40 min individual sessions of Mesendieck System education and exercises and 2 group sessions	2. Body Awareness Therapy (BAT): 19 × 90 min group sessions	20, 2 groups	46,5	20 weeks, 6 and 18 month follow-up	1. VAS	MS group had significantly better scores in FIQ, ASES pain and others and some CSQ subscales than the BAT group. At 6 month MS group still reported better scores than BAT group in ASES pain and several CSQ variables, at 18 month in ASES function and ASES others.
						- pain	
2000						-muscle stiffness	
						- fatigue	
						- global health	
						2. FIQ	
						3. Coping Strategies Questionnaire (CSQ)	
						4. Arthritis Self Efficiency Scale	
						5. Quality of Life Scales	
						6. Disability	
						7. Treatment Utility	

						Questionnaire	
Mannekorpi et al.	1. Body Awareness and Qigong therapy group sessions for 1,5 h	2. treatment as usual	36,	35	3 month	1. Body Awareness Rating Scale	No improvements in FIQ or functional test.
			2 groups			2. FIQ	Significant improvement for movement harmony (BARS) for treatment group in between group analysis.
2004						3. Hand grip test	
						4. Chair test	
						5. Semi – standardized interview with treatment group	
Sephton et al.	1. Mindfulness Meditation group sessions 18 × 2,5h, 1 day lod retreat and material for home practice	2. waiting list control	91,	34	2 month follow-up	1. Beck Depression Inventory with cognitive and somatic depression subscales	Significant reduction of depressive symptoms as compared to control, effects maintained at follow-up
			2 groups				
2007							
van Saanten et al.	1. 60 min fitness training group sessions (mostly aerobic) twice a week for 24 weeks	2. individual 30 min sessions of biofeedback training twice weekly for 8 weeks	143, 3 groups	71.5	24 weeks	1. VAS:	Worsening of fitness status in all groups in pre/post analysis was noted. Apart from these results no significant changes in outcome measures.
		3. treatment as usual				- pain	

		cintrol					
2002						- fatigue	
						2. TP count	
						3. TP dolorimetry	
						4. physical fitness by bicycle ergometer peak workload	
						5. Arthritis Impact Measurement Scales (AIMS)	
						6. Sickness Impact profile (SIP)	
						7. Symptom Checklist 90 Revised (SCL-90)	
						8. Patient's global assessment	
						9. Rating of the intervention	
						10. Amount of additional therapy	

Tbl. 9 Mind-Body therapy

Diet

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures	Results
Azad et al. 2000	1. Vegetarian diet (provided vegetarian meals)	2. 10 -25 mg of amitriptyline per day, tittered up to 100mg per day in the course of study	78, 2 groups	40	6 weeks	1. VAS	Within-group analysis yielded a significant improvement in all variables in amitrityline group and only in VAS pain in diet group. The magnitude of pain decrease was significantly in favor of amytriptyline group.
						- pain	
						- fatigue	
						- insomnia	
						- non-	

						restorative sleep	
						2. TP count	

Tbl. 10 Diet therapy

Music therapy

Author	Intervention	Control/ other interventions	No of Subjects, No of groups	Score	Duration	Outcome measures
Chesky et al. 1997	1. 30 min session of music listening and musically fluctuating vibration (60 to 300Hz, in the sensitivity range of PC-mechano-receptors)	2. 30 min session of music listening and musical vibration (constant 20 Hz, known to be outside of the sensitivity range of PC mechanorezep tors)	26, 2 groups	59	1 session	1. VAS pai
						2. TP index
						3. TP avera dolorimetry threshold (T

Tbl. 11 Music therapy

Author	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Sum
Assefi	1	4	4	3	2	0	10	5	0	5	5	8	10	5	0	0	62
Deluze	1	4	4	3	0	0	10	0	0	5	3	5 1/2	10	0	0	5	50,5
Martin	2	1	4	3	4	0	10	0	0	5	5	9	10	5	5	5	68
Sprott	0	0	0	3	4	0	10	0	0	5	3	4	10	0	0	0	39
Altan	2	4	0	3	4	0	10	0	0	5	0	8	15	0	0	5	56
Brockow	2	3	4	3	4	8	10	5	0	0	0	4	0	5	5	5	58
Dönmez	2	5	4	3	4	0	10	0	0	0	0	7	15	5	0	5	60
Eksioglu	2	4	4	3	4	0	10	5	5	0	0	4	15	0	0	5	61
Evcik	1	4	0	3	4	0	5	0	5	0	0	4	0	5	0	5	36
Guenther	2	3	0	3	4	0	10	5	0	0	0	4	15	0	0	5	51
Neumann	2	4	0	3	4	0	10	5	0	0	0	8	15	0	0	5	56
Bell	1	4	4	3	2	0	10	0	0	5	3	5,5	10	0	5	5	57,5
Alfano	2	3	4	3	0	0	10	5	0	5	3	4	10	0	0	5	54
Blunt	2	3	4	3	4	0	5	0	0	0	0	4	15	0	0	5	45
Brattberg	1	3	0	3	4	0	5	5	0	0	0	7,5	0	5	0	5	38,5
Gamber	2	1	4	3	4	0	5	5	0	0	0	7,5	15	0	0	0	46,5
Astin	2	5	4	3	0	8	10	5	0	0	0	5	15	5	0	5	67
Keel	2	3	0	3	2	0	10	5	0	0	0	6,5	0	0	0	5	36,5

Kendall	1	4	4	3	2	0	10	5	0	0	0	7,5	0	5	0	5	46,5
Mannekorpi	0	4	0	3	0	0	5	0	0	0	0	3	15	0	0	5	35
Sephton	2	5	4	3	0	0	5	0	5	0	0	0	0	0	5	5	34
Van Santen	2	4	0	3	2	8	10	5	0	0	0	7,5	15	5	5	5	71,5
Azad	1	3	4	3	4	0	10	5	0	0	0	5	0	0	0	5	40
Chesky	2	3	0	3	4	0	10	5	0	0	3	9	15	0	0	5	59

Tbl. 12 Quality score for each RCT