Cognitive–behavioural therapies and exercise programmes for patients with fibromyalgia: state of the art and future directions

S van Koulil, M Effting, F W Kraaimaat, W van Lankveld, T van Helmond, H Cats, P L C M van Riel, A J L de Jong, J F Haverman and A W M Evers

Ann Rheum Dis 2007;66;571-581; originally published online 17 Aug 2006; doi:10.1136/ard.2006.054692

REVIEW

Cognitive–behavioural therapies and exercise programmes for patients with fibromyalgia: state of the art and future directions

S van Koulil, M Effting, F W Kraaimaat, W van Lankveld, T van Helmond, H Cats, P L C M van Riel, A J L de Jong, J F Haverman, A W M Evers

Ann Rheum Dis 2007;**66**:571–581. doi: 10.1136/ard.2006.054692

This review provides an overview of the effects of non-pharmacological treatments for patients with fibromyalgia (FM), including cognitive–behavioural therapy, exercise training programmes, or a combination of the two. After summarising and discussing preliminary evidence of the rationale of non-pharmacological treatment in patients with FM, we reviewed randomised, controlled trials for possible predictors of the success of treatment such as patient and treatment characteristics. In spite of support for their suitability in FM, the effects of non-pharmacological interventions are limited and positive outcomes largely disappear in the long term. However, within the various populations with FM, treatment outcomes showed considerable individual variations. In particular, specific subgroups of patients characterised by relatively high levels of psychological distress seem to benefit most from non-pharmacological interventions. Preliminary evidence of retrospective treatment analyses suggests that the efficacy may be enhanced by offering tailored treatment approaches at an early stage to patients who are at risk of developing chronic physical and psychological impairments.

Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome characterised by widespread pain and tenderness in at least 11 of the 18 so-called tender points. Patients frequently report sensations of fatigue, sleep disturbances, morning stiffness, symptoms associated with irritable bowel syndrome and affective distress.[1] The prevalence of FM in Western countries varies between 2% and 10% and the majority of the patients is female.[2 3] Most patients report a high degree of impairment in their daily functioning. In comparison with other chronic pain conditions, patients with FM report higher levels of pain and functional disability and judge their quality of life as poorer.[4–6] Moreover, they make extensive use of health services, thus leading to high costs for medical and societal care.[7] The syndrome's pathology is not well understood, and to date no treatment has proven effective in fully alleviating its symptoms.

Over the past few decades, a wide range of potential treatments has been applied and evaluated. Pharmacological therapies primarily comprise analgesics, antidepressants, anticonvulsants, hormone therapy or a combination of these drugs. A recent review of the various treatments showed that tricyclic antidepressants—for example, amitriptyline and cyclobenzaprine—are the most promising in reducing pain and sleep problems in patients with FM.[8] However, it has been argued that many patients report symptoms of drug intolerance and consequently discontinue taking them.[9] Furthermore, the treatment effects disappear as soon as the treatment regimen is ended. Medication mainly focuses on short-term relief of symptoms, whereas non-pharmacological interventions aim to address the long-term consequences of the disease, such as disability, psychological distress, muscular deconditioning and weakness. Interventions mainly consist of elements of cognitive–behavioural therapy (CBT), exercise training, or a combination of the two. Overall, reviews have shown non-pharmacological approaches to be more effective than pharmacological treatments.[10 11] Several meta-analyses have specifically examined the effects of non-pharmacological interventions for patients with FM. It is concluded that the combination of CBT and exercise training is the most effective treatment.[8 10 12 13] Non-pharmacological interventions such as CBT and exercise programmes are generally based on biopsychosocial models of FM and chronic pain.

Rationale of CBT and exercise programmes

Biopsychosocial models describe the transition of acute to chronic pain, independent of a biomedical cause, as in FM. In acute pain, three response systems are involved: behavioural reactions (eg, avoidance behaviour), cognitive reactions (eg, increased attention to bodily sensations and catastrophising) and physiological reactions (eg, an elevated autonomous arousal and muscle tension). All are appropriate adaptive short-term reactions to acute pain, but they become less functional and even detrimental when applied long term and in response to chronic pain.[14–16] Avoidance behaviour has been described as an important aspect contributing to the aggravation of pain. This behaviour is affected by classic and operant learning processes, and is an prominent factor of the fear–avoidance model.[17 18] The key concept of the model is fear of pain following the

See end of article for authors' affiliations

Correspondence to: S van Koulil, Department of Medical Psychology 840, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands; s.vankoulil@mps.umcn.nl

Accepted 4 August 2006
Published Online First 17 August 2006

Abbreviations: CBT, cognitive–behavioural therapy; FIQ, Fibromyalgia Impact Questionnaire; FM, fibromyalgia; RA, rheumatoid arthritis

sensation of acute pain—for example, pain experienced during or after a road accident. People may react to this pain-related fear with avoidance or withdrawal of activities in order to prevent or escape pain. Cognitions such as the expectation that an activity will lead to pain or an increase in pain may also trigger avoidance behaviour.[19 20] Avoidance behaviour is easily reinforced by the belief that one has successfully prevented increments in pain. As long as activities are avoided, it is impossible to refute the belief that activity will lead to pain. Catastrophising is another important cognitive factor that plays a role in chronic pain.[18 21] People who have exaggerated negative interpretations of pain show elevated levels of pain-related fear. Moreover, there is evidence that fear of pain intensifies attention to bodily sensations, triggering hypervigilance to pain.[22] Long-lasting avoidance of activities can lead to changes in the musculoskeletal system caused by physical deconditioning and impairments in muscle coordination, also called the disuse syndrome.[23] The resultant deficient physical condition may in turn exacerbate the pain problem. Physiological reactions to pain such as heightened muscular tension and increased autonomic arousal may also lead to higher levels of pain and functional disability in the long term.[14] Furthermore, this autonomic arousal could be misinterpreted as evidence of physical harm and subsequently lead to more avoidance behaviour.[24] This habitual pattern of physiological, behavioural and cognitive reactions to pain might be generalised to various other situations and areas independent of objective pathology and intensity of pain. Patients with high levels of avoidance behaviour have been shown to have a tendency to restrict their daily and social activities and withdraw from work, which will negatively affect long-term pain outcomes.[15 16 25] Social factors, such as external reinforcements from the patient's social network, can further reinforce and maintain avoidance behaviour. In addition, avoidance may also include withdrawal from positive reinforcers such as leisure activities which in turn can exacerbate psychological distress and reduce their quality of life.[20] A vicious cycle has thus been established.

There has been incidental evidence from experimental and prospective studies for the various factors of biopsychosocial models in FM. For example, higher levels of pain and depression and a lower quality of life in FM could be prospectively predicted by catastrophising.[26] Experimental studies have shown that patients with FM tend to display hypervigilance for aversive stimuli such as pain or for bodily sensations in general.[27 28] Furthermore, a large number of cross-sectional studies underline the relevance of cognitive behavioural factors in FM. Crombez and colleagues[29] found that patients with FM reported higher vigilance to pain and more intense catastrophic thinking than other patients with chronic pain.[29] Catastrophising has been found to be associated with higher levels of disability[30] and pain.[31] Finally, fear of pain is associated with an increased susceptibility to pain[32 33] and greater disability and depressed mood[33] in patients with FM. Studies on mediators of change in CBT treatment of patients with FM and chronic pain also provide evidence for possible mediating effects of specific cognitive behavioural factors. For example, several studies have shown that reductions in catastrophising and helplessness are related to and partly mediate CBT treatment outcomes of, for example, disability and depression in chronic pain.[34–36] Although these findings are by no means conclusive and clearly warrant additional longitudinal and experimental research, these results deliver a preliminary theoretical basis that non-pharmacological treatments consisting of CBT and exercise programmes can be beneficial for patients with FM.

Attempts have been made to direct non-pharmacological treatments to these cognitive behavioural factors. Treatments that include exposure or graded activity elements, for instance, aim at changing the patient's pain experience and disability by challenging their avoidance behaviour through disproving the cognition that activity will lead to pain or an increment of pain. Furthermore, interventions have focused on curbing the negative interpretation of pain by challenging catastrophic cognitions through cognitive restructuring. Another approach suggests that involving a support person from the patient's social network in the intervention could help the patient to deal with reinforcements of their pain behaviour that they receive from their social networks and facilitate the implementation of coping skills. Exercise training exploits muscle-strengthening and aerobic exercises in order to break the deconditioning cycle. Most studies on non-pharmacological interventions in FM include one or more of the aforementioned therapeutic elements.[37] However, a major problem in the treatment of patients with FM is that most of the non-pharmacological treatments are thus far not systematically based on this rationale. In general studies include a broad range of unspecified CBT techniques that are not directly focused on specific dysfunctional cognitive behavioural mechanisms for patients with FM.

Purpose of this study

Meta-analyses have shown that the effects of non-pharmacological interventions for patients with FM are, in general, limited and there appears to be a high individual response variation.[12 13] This underlines the need for a better understanding of the factors that predict and enhance the efficacy of the treatment for FM. To evaluate the merit of CBT and exercise training in FM and to identify patient and treatment characteristics that might contribute to an optimisation of treatment outcome, various strategies have been adopted. Experimental and prospective studies have been conducted to find empirical evidence for the theoretical rationale for CBT and exercise in FM. Other designs have evaluated the effectiveness of randomised, controlled trials of CBT and exercise in FM, and yet others have tried to identify factors that help predict the success of treatment. In this review, we provide an overview of empirical studies of non-pharmacological treatment in patients with FM. The effects of CBT and exercise training targeting patients with FM are described for the main outcomes of pain, disability and mood. Furthermore, we have screened the studies included in our review for specific treatment or patient characteristics that may enhance the efficacy of the treatment. We elaborate on this issue by proposing and discussing other potentially promising aspects of future non-pharmacological FM interventions based on recent developments in other populations with chronic pain, and provide recommendations for future research.

METHODS

The electronic bibliographic databases we used in our search for relevant studies for the review included MEDLINE (1966–January 2006), PsychINFO (1806–January 2006), EMBASE (1980–January 2006) and Cochrane Library (1993–January 2006). The keyword ''fibromyalgia'' was used in combination with the terms ''randomised'', ''clinical controlled trial'', ''clinical trial'', ''randomised controlled trial'', ''cognitive therapy'', ''CBT'' and ''exercise''. In addition, reference sections and review papers on non-pharmacological treatments of FM were screened manually. To be included in our review, the following criteria were needed to be met: (1) evaluation of non-pharmacological interventions for patients with FM founded on recognised diagnostic criteria[1 38]; (2) interventions comprising elements of CBT and/or exercise programmes; (3) a randomised, controlled study design with a control group that received no treatment, a standard default treatment or an

intervention that was not expected to yield clinically relevant effects (eg, non-specific treatment group/placebo control group); and (4) effect analyses of interaction effects or separate *t* tests based on the three outcome measures—namely, pain, disability and mood. If a research group published more than one article evaluating the same intervention, the most recent publication was included in the review. In all, 30 studies met the inclusion criteria (table 1[39–68]), and their findings were evaluated by reviewing the short-term and long-term effects on the three specified outcome measures. The factor pain was assessed by means of various instruments, including visual analogue scales (VAS), myalgic scores, tender points and subscales of questionnaires (eg, the Fibromyalgia Impact Questionnaire (FIQ) and the Multidimensional Pain Inventory (MPI)). Disability was determined using tests of physical fitness (eg, 6 min walk, perceived extortion, flexibility test) and subscales of questionnaires such as the FIQ physical function scale and the physical activity scale of the Arthritis Impact Measurement Scales (AIMS). Finally, assessment of the outcome variable mood included VAS, questionnaires for psychological distress in general, such as the Beck Depression Inventory and the Symptom Checklist-90-Revised, and subscales of questionnaires for FM and other chronic pain conditions (eg, FIQ depression and anxiety scale, AIMS depression and anxiety scales, MPI affective distress scale).

RESULTS

Effects of CBT and exercise programmes

To find empirical support for non-pharmacological treatments for patients with FM, studies have examined the efficacy of specific therapeutic approaches such as CBT and exercise training programmes, as well as combinations of the two approaches. The findings of the randomised controlled trials our search generated are reviewed below.

Cognitive–behavioural therapy

CBT is one of the most prevalent treatments for patients with FM. A distinction can be made between single-method interventions such as education and relaxation programmes, and multimethod CBTs that incorporate various methods and skills from cognitive behavioural approaches.

Educational programmes provide information about active self-management of pain, coping, relaxation techniques, the importance of physical activity and social support, and individual strategies for behavioural change. Three studies investigated the effect of education as a single-method intervention[39–41] and found the educational programmes to yield some benefits for the patients' self-efficacy[39] and pain-coping skills.[40] However, the programmes were not effective in diminishing pain and disability nor in improving mood. The only study that conducted a follow-up failed to find any treatment effect.[41] Other single-method CBTs are relaxation techniques—for example, progressive relaxation, biofeedback and autogenic training—which are used in patients with FM to diminish muscular tension and interrupt the pain–tension cycle. The three studies that investigated the effects of relaxation failed to find any results for disability or mood[42–44]; two studies reported improvements on pain[42 43] although the effect had not been maintained at follow-up.[42] However, the study of Ferracioli *et al*[43] may have been underpowered to detect effects due to its small sample size.

Multimethod CBT typically consists of a combination of various therapeutic elements, such as cognitive restructuring, pain-coping skills, problem-solving techniques, goal setting, increasing activity levels, activity pacing, stress management and adjustment of pain-related medication, and frequently also comprises educational and relaxation components. Five studies evaluated the outcome of multimethod CBTs.[40 45–48] Two studies found no effects on pain, disability and mood,[40 45] while three studies reported varying effects.[46–48] Wigers *et al*[46] reported the multimethod CBT to be initially effective in diminishing pain and depression, but this improvement was not sustained during the 4-year follow-up. Another CBT study aimed at improving physical functioning proved effective in reducing disability 1 year after treatment.[47] Finally, Thieme *et al*[48] reported in their evaluation of a behavioural pain treatment for patients with FM that, compared with the control group, pain, disability and mood had all largely improved in the experimental group and the effects were maintained at the 15-month follow-up.

Exercise training

In the past few decades many studies on effects of exercise training programmes in patients with FM have been conducted. Exercise training programmes include aerobic exercise, strength training, flexibility exercises and hydrotherapy. Although the programmes vary, all have some of the following basic elements: a gradual build-up of strength and endurance, emphasis on the importance of frequent exercise and a moderately intense exercise programme. Because they facilitate the exercises and minimise post-exercise pain, pool exercises and hydrotherapy are occasionally part of the training programmes.

Aerobic exercise is the most widely used exercise intervention and comprise various types of exercises such as cycling, walking and aerobic dancing. Ten studies investigated the effect of aerobic exercise,[41 46 49–56] and six of these found improvements on disability.[46 49–51 53 56] Pain relief[46 50 56] and changes in mood[49 52 56] were rarely mentioned, and one study even reported an increase in disability.[52] Only three studies conducted follow-up assessments[41 46 55] of which one showed limited long-term improvements in pain and disability.[55] Strength training has been investigated three times in randomised, controlled trials[57–59] and positively affected disability in two of the three studies,[58 59] although no effects on mood or pain were found. However, the study of Kingsley *et al*[58] could be biased, due to high dropout rates in the experimental group. Finally, five studies evaluated aerobic exercise in combination with muscle-strength training and obtained mixed results.[42 44 60–62] Three studies demonstrated a decrease in pain and disability[42 60 62] and these effects were maintained at follow-up.[42 62] In addition, two studies reported a lesser worsening of disability levels in the intervention group compared with the control group.[44 61]

Combinations of CBT and exercise training

Six studies examined the effectiveness of education in combination with exercise.[39 41 63–66] Two reported effects for disability, such as an enhanced physical condition.[63 64] Only in one study did patients also report of an improvement in pain and mood.[64] Of the three studies that included follow-up assessments,[41 65 66] two studies found long-term effects on pain and disability[65 66]; and one also on mood.[65] The improvements on pain and disability in the study of Zijlstra and colleagues[66] were only apparent at the 3-month follow-up and not at 6 and 12 months.

Relaxation combined with exercise training appeared to be effective in diminishing pain and disability in daily life, and the effects were maintained at the 1-year follow-up.[42] However, in this study, pain alleviation was largely accounted for by a deterioration of the control group.

Although only two trials have been conducted with interventions that combined multimethod CBT and exercise training, the available findings look promising.[67 68] Patients reported post-treatment improvements on pain, disability and mood,[68] and at the 3-month follow-up, they reported less pain.[67]

Predictors of treatment outcome of CBT and exercise programmes

From this and previous reviews it appears that, overall, the effects of non-pharmacological interventions in patients with

Table 1 Randomised, controlled trials of non-pharmacological interventions for patients with fibromyalgia

Author, year	n (completing), mean age (years), % women	Follow-up assessment	Control group, n (completing)	Intervention	Treatment characteristics: individual/group; inpatient/ outpatient; duration	Intervention group n (completing)	Outcome measures	Effects		Comments
								Post	Follow-up	
Buckelew, 1998[42]	119 (101), 44.0, 91	Post 3 mo 1 yr 2 yr	Education, 30 (27)	Relaxation (biofeedback)	Individual and group; outpatient; 1x wk for 6 wk indiv and 1x mo for 2 yr group	29 (25)	Pain Disability Mood	+ 0 0	0 0 0	Long-term effect of relaxation+exercise on pain was only evident at 3 mo, not at the 1-yr and 2-yr follow-ups
				Exercise training (aerobic and strength)	Individual and group; outpatient; 1x wk for 6 wk indiv and 1x mo for 2 yr group	30 (26)	Pain Disability Mood	+ + 0	0 + 0	
				Relaxation + exercise training	Individual and group; outpatient; 1x wk for 6 wk indiv and 1x mo for 2 yr group	30 (23)	Pain Disability Mood	+ + 0	+ + 0	
Burckhardt, 1994[39]	99 (86), 46.5, 100	Post	Waiting list, 35 (30)	Education	Group; outpatient; 1x wk for 6 wk	31 (28)	Pain Disability Mood	0 0 0	NA NA NA	
				Education + exercise training (aerobic)	Group; outpatient; 1x wk for 6 wk	33 (28)	Pain Disability Mood	0 0 0	NA NA NA	
Cedraschi, 2004[65]	164 (129), 49.3, 93	6 mo	Waiting list, 80 (68)	Education + exercise training (aerobic)	Group; outpatient; 2x wk for 6 wk	84 (61)	Pain Disability Mood	NA NA NA	+ + +	Dropout >20%: control 15%, intervention 27.4%
Da Costa, 2005[62]	80 (61), 50.8, 100	Post 3 mo 9 mo	Treatment as usual, 41 (33)	Exercise training (aerobic, strength and flexibility)	Individual; home-based; 12 wk and 4 sessions with physical therapist	39 (28)	Pain Disability Mood	+ 0 0	+ + 0	Dropout >20%: control 19.5%, intervention 28.2%
Ferraciocioli, 1987[43]	12 (12), 57.0, 100	Post	False biofeedback relaxation, 6 (6)	Relaxation (biofeedback)	Group; outpatient; 2x wk, 15 sessions in total	6 (6)	Pain Disability Mood	+ 0 0	NA NA NA	No between-group analyses
Gowans, 1999[63]	45 (41), 45.5, 78	Post	Waiting list, 22 (21)	Education + exercise training	Group; outpatient; 2x wk for 6 wk	23 (20)	Pain Disability Mood	0 + 0	NA NA NA	
Gowans, 2001[49]	51 (31), 47.9, 90	Post	Treatment as usual, 24 (16)	Exercise training (aerobic, pool exercises)	Group; outpatient; 3x wk for 23 wk	27 (15)	Pain Disability Mood	0 + +	NA NA NA	Dropout >20%: control 33.3%, intervention 44.4%
Jones, 2002[57]	68 (56), 47.8, 100	Post	Flexibility exercises, 34 (28)	Exercise training (strength)	Group; outpatient; 2x wk for 12 wk	34 (28)	Pain Disability Mood	0 0 0	NA NA NA	
Keel *et al*, 1998[67]	32 (27), 49.0, 89	Post 3 mo	Relaxation, 16 (13)	CBT + exercise training (stretching and aerobic)	Group; outpatient; 1x wk for 15 wk	16 (14)	Pain Disability Mood	0 0 NA	+ 0 NA	(a) Positive post-treatment trend for pain, significant at follow-up; (b) predictor of treatment success: shorter disease duration

Table 1 Continued

Author, year	n (completing), mean age (years), % women	Follow-up assessment	Control group, n (completing)	Intervention	Treatment characteristics: individual/group; inpatient/ outpatient; duration	Intervention group n (completing)	Outcome measures	Effects		Comments
								Post	Follow-up	
King, 2002[41]	170 (95), 46.1, 100	Post 3 mo	Waiting list, 39 (18)	Education (1)	Group; outpatient; 1x wk for 12 wk	48 (21)	Pain Disability Mood	0 0 NA	0 0 NA	Dropout >20% Control 53.8%, intervention (1) 56.3%
				Exercise training (aerobic) (2)	Group; outpatient; 3x wk for 12 wk	46 (30)	Pain Disability Mood	0 0 NA	0 0 NA	(2) 34.8%
				Education + exercise training (aerobic) (3)	Group; outpatient; 3x wk for 12 wk	37 (26)	Pain Disability Mood	0 0 NA	0 0 NA	(3) 29.7%
Kingsley, 2005[58]	29 (20), 46.0, 100	Post	Waiting list, 14 (12)	Exercise training (strength)	Group; outpatient; 2x wk for 12 wk	15 (8)	Pain Disability Mood	0 + NA	NA NA NA	Dropout >20%: control 14.3%, intervention 46.7%
Lemstra, 2005[68]	79 (72), 49.4, 84.8	Post	Treatment as usual, 36 (36)	CBT + exercise training	Group; outpatient; 24 sessions in 6 wk	43 (36)	Pain Disability Mood	+ + +	NA NA NA	
Mannerkorpi, 2000[64]	69 (58), 46.0, 100	Post	Treatment as usual, 32 (30)	Education + exercise training (pool exercise)	Group; outpatient; education 1x mo for 6 mo, exercise 1x wk for 6 mo	37 (28)	Pain Disability Mood	+ + +	NA NA NA	
Martin, 1996[60]	60 (38), 44.8, 97	Post	Relaxation, 30 (20)	Exercise training (aerobic and strength)	Group; outpatient; 3x wk for 6 wk	30 (18)	Pain Disability Mood	+ + NA	NA NA NA	Dropout >20%: control 33.3%, intervention 30%
McCain, 1988[50]	42 (38), 42.2, % unknown	Post	Flexibility exercises, 22 (20)	Exercise training (aerobic)	Group; outpatient; 2x wk for 20 wk	20 (18)	Pain Disability Mood	+ + 0	NA NA NA	
Mengshoel, 1992[51]	35 (25), 33.7, 100	Post	Treatment as usual, 17 (14)	Exercise training (aerobic)	Group; outpatient; 2x wk for 20 wk	18 (11)	Pain Disability Mood	0 + NA	NA NA NA	Dropout >20%: control 17.6%, intervention 38.9%
Nicassio, 1997[45]	86 (71), 53.1, 89	Post 6 mo	Education, 38 (35)	CBT	Group; outpatient; 1x wk for 10 wk	48 (36)	Pain Disability Mood	0 0 0	0 0 0	
Nichols, 1994[52]	24 (19), 49.4, 92	Post	Treatment as usual, 12 (9)	Exercise training (aerobic)	Group; outpatient; 3x wk for 8 wk	12 (10)	Pain Disability Mood	0 − +	NA NA NA	
Norregaard, 1997[54]	38 (23), 49.1, % unknown	Post	Thermotherapy, 8 (7)	Exercise training (aerobic) (1)	Group; outpatient; 3x wk for 12 wk	15 (5)	Pain Disability Mood	0 0 0	NA NA NA	Dropout >20%: control 12.5%, intervention (1) 66.7%
				Exercise training (gymnastic exercises and stretching) (2)	Group; outpatient; 2x wk for 12 wk	15 (11)	Pain Disability Mood	0 0 0	NA NA NA	(2) 26.7%

Table 1 Continued

Author, year	n (completing), mean age (years), % women	Follow-up assessment	Control group, n (completing)	Intervention	Treatment characteristics: individual/group; inpatient/ outpatient; duration	Intervention group n (completing)	Outcome measures	Effects		Comments
								Post	Follow-up	
Richards, 2002[55]	136 (112), 46.5, 92.6	Post 3 mo 9 mo	Relaxation and flexibility exercises, 67 (55)	Exercise training (aerobic)	Group; outpatient; 2x wk for 12 wk	69 (57)	Pain Disability Mood	0 0 NA	+ + NA	
van Santen, 2002[44]	143 (118), 44.7, 100	Post	Treatment as usual, 29 (28)	Relaxation (biofeedback)	Individual; outpatient; 2x wk for 8 wk	56 (43)	Pain Disability Mood	0 0 0	NA NA NA	
				Exercise training (aerobic and strength)	Group; outpatient; 2x wk for 24 wk	58 (47)	Pain Disability Mood	0 + 0	NA NA NA	
Schachter, 2003[53]	143 (102), 41.8, 100	Post	Discussion group, 36 (31)	Exercise training (aerobic, long bout of exercise)	Individual; home-based; 1x day, 10–30 min, 3–5 times wk for 16 wk (1)	51 (36)	Pain Disability Mood	0 0 0	NA NA NA	Dropout >20%: Control 13.9%, intervention (1) 29.4% (2) 37.5%
				Exercise training (aerobic, short bout of exercise)	Individual; home-based; 2x day, 5–15 min, 3–5 times wk for 16 wk (2)	56 (35)	Pain Disability Mood	0 + 0	NA NA NA	
Thieme, 2003[48]	63 (61), 47.3, 100	Post 6 mo 15 mo	Standard treatment: education and relaxation, 21 (21)	CBT	Group; inpatient; daily during 5 wk (75 h total)	42 (40)	Pain Disability Mood	+ + +	+ + +	Predictor of treatment success: group of highly distressed patients
Valkeinen, 2005[59]	26 (26), 59.5, 100	Post	Treatment as usual, 13 (13)	Exercise training (strength)	Group; outpatient; 2x wk for 21 wk	13 (13)	Pain Disability Mood	0 + NA	NA NA NA	
Valim, 2003[56]	76 (60), 45.9, 100	Post	Flexibility exercises, 38 (28)	Exercise training (aerobic)	Group; outpatient; 3x wk for 20 wk	38 (32)	Pain Disability Mood	+ + +	NA NA NA	
Verstappen, 1997[61]	87 (72), 45.2, 100	Post	Treatment as usual, 29 (27)	Exercise training (aerobic and strength)	Group; outpatient; 2x wk for 6 mo	58 (45)	Pain Disability Mood	0 + NA	NA NA NA	
Vlaeyen, 1996[40]	131 (105), 44.0, 88	Post 6 mo 12 mo	Waiting list, 43 (39)	CBT	Group; outpatient; 2x wk for 6 wk	49 (36)	Pain Disability Mood	0 0 0	0 0 0	Follow-up effects of CBT only in comparison with education and not with control group
				Education	Group; outpatient; 2x wk for 6 wk	39 (30)	Pain Disability Mood	0 0 0	0 0 0	
Wigers, 1996[46]	60 (44), 44.0, 92	Post 4 yr	Treatment as usual, 20 (16)	CBT	Group; outpatient; 2x wk for 6 wk, 1x wk for 8 wk	20 (13)	Pain Disability Mood	+ 0 +	0 0 0	(a) Positive effect of exercise training on pain and disability in comparison with both the controls and CBT; (b) predictor of treatment success: continued exercising during follow-up
				Exercise training (aerobic)	Group; outpatient; 3x wk for 14 wk	20 (15)	Pain Disability Mood	+ + 0	0 0 0	

Table 1 Continued

Author, year	n (completing), mean age (years), % women	Follow-up assessment	Control group, n (completing)	Intervention	Treatment characteristics: individual/group; inpatient/outpatient; duration	Intervention group n (completing)	Outcome measures	Effects: Post	Effects: Follow-up	Comments
Williams, 2002[47]	145 (122), 47.4, 90	1 yr	Treatment as usual, 69 (60)	CBT	Group; outpatient; 6 sessions in 4 wk	76 (62)	Pain Disability Mood	NA NA NA	0 + NA	
Zijlstra, 2005[66]	134 (113), 47.4, 95.5	3 mo 6 mo 1 yr	Treatment as usual, 76 (61)	Spa therapy, education + exercise training (aerobic exercise)	Group; inpatient (Tunisia), 7–8x spa therapy, 7x exercise and 7x education in 19 days	58 (52)	Pain Disability Mood	NA NA NA	+ + 0	Long-term effect of intervention on pain was evident only at 3 mo, not at the 6-mo and 1-yr follow-ups

CBT, cognitive behavioural therapy; mo, months; NA, not assessed; post, post-treatment; wk, week; yr, year. + = positive effect on at least one of the outcome measures (pain, disability and mood); 0 = no effects on the outcome measures (pain, disability and mood); − = negative effect on at least one of the outcome measures (pain, disability and mood).
The results all concern completers' analyses with the exception of one study that solely conducted an intention-to-treat analysis.[55] follow-up, minimum of 3 months after treatment.

FM are relatively limited. Various studies included in the review offered probable explanations for the lack of treatment effects: a large individual variation in patients' treatment response,[44 47] lack of long-term adherence to the exercise regimen,[63] inclusion of patients with prolonged duration of symptoms,[54 65] and patients who were too severely depressed to respond to treatment.[39 43] Only four studies carried out additional analyses to identify treatment and patient characteristics that could predict treatment response.[46 48 67 69] Thieme and coworkers[48] conducted additional analyses to explain the gains on pain, disability and mood following their multimethod CBT, and showed that a subgroup of highly distressed patients with a high impact of the disease on daily life had responded best. This suggests that highly distressed patients with FM are most susceptible to the CBT intervention, and that treatment effects could be improved by selecting this specific group of patients. In their 4-year follow-up evaluation of an aerobic exercise programme, Wigers *et al*[46] demonstrated that particularly those participants who had continued exercising reported the least pain. This would imply that long-term compliance is crucial in maintaining the positive effects of exercise training. Keel *et al*,[67] assessing combined multimethod CBT and exercise, found that the individuals who benefited most from the treatment were patients with a significantly shorter history of complaints. These preliminary findings underline the importance of initiating treatment shortly after diagnosis. Sociodemographic and psychosocial variables appeared to be significant predictors of the success of treatment in the intervention study of King and colleagues.[69] However, only a small percentage of the variance was explained by these variables, which may be due to the heterogeneity of FM. In addition, the percentage of responders was very low, suggesting that present treatments are not effective for a large group of patients. The results of this study should be interpreted with caution, due to the high dropout rate.

DISCUSSION

From this review of non-pharmacological treatment in patients with FM, it is apparent that interventions such as CBT and exercise training have a limited effect on the outcome measures, namely, pain, disability and mood. Only a few studies showed improvement after CBT methods and techniques, and even then the positive effects frequently disappeared in the long run. It was mostly multimethod CBT treatments that yielded improvements, suggesting that these are more effective than specific CBTs such as education and relaxation programmes. A recent study by Thieme *et al*,[48] which evaluated a multimethod CBT programme aimed at behavioural pain treatment, is potentially promising. Their patients reported less pain, disability and psychological distress after treatment, and these results were sustained in the longer term. The findings on exercise programmes indicate that exercise may be useful in reducing disability in daily life on account of patients' enhanced physical fitness. However, the technique seems less effective in decreasing pain and psychological distress, although trials did show that the fear of patients with FM that exercising will exacerbate their pain was not justified. Exercise training seems to be effective in diminishing disability in daily life but it is unclear whether these effects are maintained for extended periods. Additional psychological maintenance training could help establish long-term compliance with the exercise regimens. Although no evidence was found for the efficacy of a combination of exercise training and CBT been higher than that of interventions of only exercise training or only CBT, combination treatments have only been incidentally studied. Moreover, the outcomes might be improved if more targeted psychological interventions such as multimethod CBT are used

in addition to exercise training.[68] Four studies conducted additional analyses to identify those factors that could be vital to improve treatment outcomes. King and coworkers[69] showed that sociodemographic and psychosocial variables were relevant in predicting the success of treatment, but the explained variance was relatively small. The other studies found that early intervention,[67] selection of patients with high levels of distress and tailored treatment[48] as well as continued exercising[46] are promising indicators of the success of treatment.

As for methodological issues, the distinction between single-method interventions such as education and relaxation programmes and multimethod CBT is somewhat artificial. Some of the education programmes, for example, were more comprehensive than others and also trained patients in relaxation and coping techniques. Furthermore, comparing the evaluated studies was difficult due to many differences in content and timing, outcome measures and statistical analyses. Other methodological characteristics also varied greatly between the studies reviewed—for example, description of the content of the treatment, therapist training, quality of control condition.[70] In addition, a publication bias towards positive results cannot be completely ruled out, although in general the primary effects of the studies reported were rather limited. With regard to the methodological quality of the studies, the small sample size and hence low statistical power of some studies makes it hard to detect significant effects.[43 51 52 54 58 59 67] Results could also be biased due to high dropout rates, particularly in treatment groups, suggesting that the treatment was not matched to the patient's needs.[41 49 51 53 54 58 60 62 65] In addition, the majority of the studies did not include long-term follow-up assessments. However, as all the studies included in the review fulfilled the inclusion criteria of a randomised, controlled design, they generally meet the minimum standard for methodological quality. Furthermore, according to the criteria of the quality of clinical trials stipulated by Jaded *et al*[71] (eg, randomisation, double-blind conditions, description of withdrawals and dropouts), the studies included in the review had sufficient quality overall except for the double-blind condition, which is unfeasible under active treatment conditions.

The effect sizes of randomised, controlled trials in FM in general show small to moderate effect sizes.[10] The clinical relevance of the studies reviewed is limited, as the overall effects found are rather small and the percentage of patients showing significant clinical improvement is minimal. Moreover, if encouraging effects are reported, a lack of long-term follow-up assessments, small sample sizes and treatments that encompass multiple unspecified CBT techniques limits their possible implications for clinical practice.

Nevertheless, what this review did clarify is that standardised non-pharmacological interventions are inadequate in sufficiently reducing symptoms and psychological distress in patients with FM. To improve treatment outcomes, more evidence is needed from experimental and prospective studies to unravel the specific cognitive behavioural mechanisms responsible for the development and maintenance of chronic pain and disability that function as mediators of treatment effects, such as avoidance behaviour, hypervigilance and pain-related fear. There is also an urgent need to delineate patient and treatment characteristics better to allow subgroups of patients that respond best to a specific treatment to be identified. Several studies on FM have suggested that the limited treatment outcomes are due to the large individual differences in treatment response. It is apparent that not all patients will show the same response to the same treatment, and this disparity is likely to be related to the heterogeneity of the illness and the variability within patients.[8 64] The current problem could be that all patients with FM are treated with the same commonly accepted interventions, resulting in small overall treatment effects and high dropout rates.

In the next section we will elaborate on the potentially predictive features that may help to enhance the efficacy of non-pharmacological treatments for patients with FM separately, and in relation to studies of other chronic pain conditions. We will conclude the review by offering suggestions for more targeted treatments and future research.

FUTURE DIRECTIONS

Early intervention

The significance of early detection and treatment of patients who are at risk of developing persistent pain and related problems is increasingly recognised.[72] Timing is important for several reasons. Firstly, FM is a condition associated with high levels of pain, disabilities in daily life, psychological distress and diminished quality of life. Intervening early in the course of a pain condition may help prevent the vicious cycle of long-term physical and psychological suffering. Secondly, patients who have had FM for an extended period might have ingrained, maladaptive patterns of pain-coping and illness behaviours that are resistant to treatment, making it more difficult for patients to change their behaviour. Finally, early intervention has the potential to reduce or prevent disability in patients with chronic pain, which, in turn, will reduce societal and medical costs. It follows that early intervention is far more likely to be effective than interventions administered in the later stages of the condition. Non-pharmacological treatments that are initiated shortly after a patient has been diagnosed with FM can help prevent long-term dysfunction and chronicity.

There has been preliminary evidence indicating that early intervention is indeed an important factor in improving non-pharmacological treatment outcomes in FM. Keel *et al*[67] showed that a subgroup with a shorter disease duration responded best to treatment. Similar results are also found in other chronic pain conditions. Marhold[73] showed that a cognitive behavioural return-to-work programme proved effective for those patients with chronic pain who were on short-term sick leave but not for patients who had been out of work for longer periods of time. In addition, two interventions for recently diagnosed patients with rheumatoid arthritis (RA) were shown to be effective.[74 75] Other retrospective findings of studies in RA also demonstrated that, patients who were treated shortly after diagnosis responded best to non-pharmacological treatment.[76 77] Collectively, these findings suggest that early intervention can enhance the efficacy of cognitive behavioural therapies, also for FM.

Patient selection

As stated earlier, the limited effects of non-pharmacological interventions for patients with FM have also been attributed to the variability within patients. Gains in treatment outcome could be achieved if subgroups of patients with FM who are most likely to benefit from a specific treatment are identified. Evidence to this effect has already been reported for RA, showing that specific cognitive behavioural factors are disturbed in patients with a high degree of psychological distress, and that this subgroup of patients benefited from CBT addressing these cognitive behavioural factors.[74 78 79] On the basis of psychosocial and behavioural characteristics, specific subgroups can be identified—for example, a dysfunctional group that is characterised by low levels of activity, high levels of pain interference and psychological distress.[80 81] Previous research revealed that treatment gains could indeed be predominantly attributed to the effects found for such a dysfunctional group—that is, the patients in whom the disease had a higher daily-life impact.[82 83] Furthermore, in this

review, dysfunctional subgroups of patients with FM also showed the best outcomes during the course of the treatment in three studies[48 82 83] but not in one.[69] Overall, it seems to imply that patients with FM with a relatively high level of psychological distress and impact of the disease on daily living are likely to benefit most from non-pharmacological interventions.

Tailoring treatment to the patient's risk profile

There is some evidence that targeted non-pharmacological interventions that address the specific needs of a particular subgroup are more effective. In his recent overview, Turk[84] supports the notion that results of treatment in patients with chronic pain can be enhanced if treatment is tailored to the patient characteristics, which, according to Thieme and her team,[85] also applies to patients with FM. Treatment can be tailored in various ways, allowing for, among other factors, the demographic, medical, psychological or psychosocial factors of the patients.[72] In patients with chronic pain, including FM, outcomes of pain, disability and psychological distress tend to be affected by specific cognitive behavioural factors such as passive pain coping and helplessness.[26 86] Only patients with FM who are characterised by these specific cognitive behavioural factors might benefit from interventions that focus on these factors. However, it has to be taken into consideration that in order to improve treatment effects, interventions need to be systematically based on the cognitive behavioural mechanisms proven to be important in FM and chronic pain. More recent CBT interventions that systematically modify key elements of the fear-avoidance model through exposure in vivo, for instance, have yielded promising results in patients with chronic low-back pain.[87–89] Moreover, the factors typical of specific subgroups may need to be taken into account. For example, in chronic pain, including FM, besides patients characterised by disuse syndrome and passive pain coping, there is also a subgroup of patients that have demanding, non-accepting cognitions and possible overuse, and tailored treatments directed at their specific risk factors might be promising.[90] Recent developments of approaches aimed at pain acceptance proved relevant in chronic pain,[91 92] and the subgroup characterised by overuse could particularly benefit from such an approach. Research into other chronic physical symptoms also indicates that treatment tailored to the shared cognitive behavioural factors of subgroups of patients may enhance treatment effects.[93 94] Based on these preliminary but promising findings, we conclude that if patients with FM were to be subdivided consistent with their distinctive cognitive behavioural patterns and if interventions were subsequently modified to match these specific risk profiles, the efficacy of non-pharmacological treatment programmes could be substantially taken forward. Future research needs to explore the cognitive behavioural mechanisms relevant in subgroups of patients and develop tailored treatments accordingly.

CONCLUSION

In summary, in spite of wide theoretical and selective empirical support of the rationale of non-pharmacological treatment programmes for patients diagnosed with FM, the studies that were evaluated in this review show their effects to be limited. Preliminary evidence suggests that treatment outcomes could be improved if tailored interventions are offered early to patients at risk of developing chronic physical and psychological impairments. Future research and the clinical practice should respect the heterogeneity and individual variability in patients with FM and should aim at developing non-pharmacological interventions that best match the needs of the individual patient.

ACKNOWLEDGEMENTS

This study was supported by grants from the Dutch Arthritis Association (''Reumafonds'') and Netherlands Organization for Health Research and Development (''ZON-MW'').

Authors' affiliations

S van Koulil, F W Kraaimaat, A W M Evers, Department of Medical Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
M Effting, Department of Clinical Psychology, University of Amsterdam, Amsterdam, The Netherlands
W van Lankveld, T van Helmond, H Cats, Department of Rheumatology, Sint Maartenskliniek, Nijmegen, The Netherlands
P L C M van Riel, Department of Rheumatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
A J L de Jong, Department of Rheumatology, Rijnstate Hospital, Arnhem, The Netherlands
J F Haverman, Department of Rheumatology, Jeroen Bosch Ziekenhuis, 's Hertogenbosch, The Netherlands

Competing interests: None.

REFERENCES

1 **Wolfe F**, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, *et al.* The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990;**33**:160–72.
2 **Wolfe F**, Ross K, Anderson J, Russel IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995;**38**:19–28.
3 **Forseth KO**, Gran JT. The occurrence of fibromyalgia-like syndromes in a general female population. *Clin Rheumatol* 1993;**12**:23–7.
4 **Burckhardt CS**, Clark SR, Bennett RM. Fibromyalgia and quality of life: a comparative analysis. *J Rheumatol* 1993;**20**:475–9.
5 **Mannerkorpi K**, Burckhardt CS, Bjelle A. Physical performance characteristics of women with fibromyalgia. *Arthritis Care Res* 1994;**7**:123–9.
6 **Martinez JE**, Ferraz MB, Sato EI, Atra E. Fibromyalgia versus rheumatoid arthritis: a longitudinal comparison of the quality of life. *J Rheumatol* 1995;**22**:270–4.
7 **Penrod JR**, Bernatsky S, Adam V, Baron M, Dayan N, Dobkin PL. Health services costs and their determinants in women with fibromyalgia. *J Rheumatol* 2004;**31**:1391–8.
8 **Goldenberg DL**, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA* 2004;**292**:2388–95.
9 **Sandstrom MJ**, Keefe FJ. Self-management of fibromyalgia: the role of formal coping skills training and physical exercise training programs. *Arthritis Care Res* 1998;**11**:432–47.
10 **Rossy LA**, Buckelew SP, Dorr N, Hagglund KJ, Thayer JF, McIntosh MJ, *et al.* A meta-analysis of fibromyalgia treatment interventions. *Ann Behav Med* 1999;**21**:180–91.
11 **McCain GA**. Treatment of the fibromyalgia syndrome. *J Musculoskelet Pain* 1999;**7**:193–208.
12 **Hadhazy VA**, Ezzo J, Creamer P, Berman BM, McCain GA. Mind-body therapies for the treatment of fibromyalgia. A systematic review. *J Rheumatol* 2000;**27**:2911–18.
13 **Sim J**, Adams N. Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia. *Clin J Pain* 2002;**18**:324–36.
14 **Flor H**, Birbaumer N, Turk DC. The psychobiology of chronic pain. *Adv Behav Res and Therapy* 1990;**12**:47–84.
15 **Evers AW**, Kraaimaat FW, van Riel PL, Bijlsma JW. Cognitive, behavioral and physiological reactivity to pain as a predictor of long-term pain in rheumatoid arthritis patients. *Pain* 2001;**93**:139–46.
16 **Turk DC**, Flor H. Chronic pain: a biobehavioral perspective. In: Gatchel RJ, Turk DC, eds. *Psychosocial factors in pain: critical perspectives*. New York: Guilford Press, 1999:18–34.
17 **Lethem J**, Slade PD, Troup JD, Bentley G. Outline of a fear-avoidance model of exaggerated pain perception. I. *Behav Res Ther* 1983;**21**:401–8.
18 **Vlaeyen JW**, Kole-Snijders AM, Boeren RG, van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. *Pain* 1995;**62**:363–72.
19 **Philips HC**. Avoidance behaviour and its role in sustaining chronic pain. *Behav Res Ther* 1987;**25**:273–9.
20 **Sharp TJ**. Chronic pain: a reformulation of the cognitive-behavioural model. *Behav Res Ther* 2001;**39**:787–800.
21 **McCracken LM**, Gross RT. Does anxiety affect coping with chronic pain? *Clin J Pain* 1993;**9**:253–9.
22 **McCracken LM**. "Attention" to pain in persons with chronic pain: A behavioral approach. *Behav Ther* 1997;**28**:271–84.
23 **Bortz WM**. The disuse syndrome. *West J Med* 1984;**141**:691–4.
24 **Norton PJ**, Asmundson GJ. Amending the fear-avoidance model of chronic pain: What is the role of physiological arousal? *Behav Ther* 2003;**34**:17–30.

25 **Vlaeyen JW**, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain* 2000;**85**:317–32.
26 **Nicassio PM**, Schoenfeld Smith K, Radojevic V, Schuman C. Pain coping mechanisms in fibromyalgia: relationship to pain and functional outcomes. *J Rheumatol* 1995;**22**:1552–8.
27 **McDermid AJ**, Rollman GB, McCain GA. Generalized hypervigilance in fibromyalgia: evidence of perceptual amplification. *Pain* 1996;**66**:133–44.
28 **Rollman GB**, Lautenbacher S. Hypervigilance effects in fibromyalgia: pain experience and pain perception. In: Vaeroy H, Merksey H, eds. *Progress in fibromyalgia and myofascial pain*. Amsterdam: Elsevier, 1993:149–59.
29 **Crombez G**, Eccleston C, van den Broeck A, Goubert L, van Houdenhove B. Hypervigilance to pain in fibromyalgia: the mediating role of pain intensity and catastrophic thinking about pain. *Clin J Pain* 2004;**20**:98–102.
30 **Martin MY**, Bradley LA, Alexander RW, Alarcon GS, Triana-Alexander M, Aaron LA, *et al*. Coping strategies predict disability in patients with primary fibromyalgia. *Pain* 1996;**68**:45–53.
31 **Hassett AL**, Cone JD, Patella SJ, Sigal LH. The role of catastrophizing in the pain and depression of women with fibromyalgia syndrome. *Arthritis Rheum* 2000;**43**:2493–500.
32 **de Gier M**, Peters ML, Vlaeyen JW. Fear of pain, physical performance, and attentional processes in patients with fibromyalgia. *Pain* 2003;**104**:121–30.
33 **Turk DC**, Robinson JP, Burwinkle T. Prevalence of fear of pain and activity in patients with fibromyalgia syndrome. *J Pain* 2004;**5**:483–90.
34 **Smeets RJ**, Vlaeyen JW, Kester AD, Knottnerus JA. Reduction of pain catastrophizing mediates the outcome of both physical and cognitive-behavioral treatment in chronic low back pain. *J Pain* 2006;**7**:261–71.
35 **Burns JW**, Kubilus A, Bruehl S, Harden RN, Lofland K. Do changes in cognitive factors influence outcome following multidisciplinary treatment for chronic pain? A cross-lagged panel analysis. *J Consult Clin Psychol* 2003;**71**:81–91.
36 **Spinhoven P**, ter Kuile M, Kole-Snijders AMJ, Mansfeld MH, den Ouden DJ, Vlaeyen JWS. Catastrophizing and internal pain control as mediators of outcome in the multidisciplinary treatment of chronic low back pain. *Eur J Pain* 2004;**8**:211–19.
37 **Williams DA**. Psychological and behavioural therapies in fibromyalgia and related syndromes. *Best Pract Res Clin Rheumatol* 2003;**17**:649–65.
38 **Smythe HA**, Moldofsky H. Two contributions to understanding of the "fibrositis" syndrome. *Bull Rheum Dis* 1977;**28**:928–31.
39 **Burckhardt CS**, Mannerkorpi K, Hedenberg L, Bjelle A. A randomized, controlled clinical trial of education and physical training for women with fibromyalgia. *J Rheumatol* 1994;**21**:714–20.
40 **Vlaeyen JW**, Teeken-Gruben NJ, Goossens ME, Rutten-van Molken MP, Pelt RA, van Eek H, *et al*. Cognitive-educational treatment of fibromyalgia: a randomized clinical trial. I. Clinical effects. *J Rheumatol* 1996;**23**:1237–45.
41 **King SJ**, Wessel J, Bhambhani Y, Sholter D, Maksymowych W. The effects of exercise and education, individually or combined, in women with fibromyalgia. *J Rheumatol* 2002;**29**:2620–7.
42 **Buckelew SP**, Conway R, Parker J, Deuser WE, Read J, Witty TE, *et al*. Biofeedback/relaxation training and exercise interventions for fibromyalgia: a prospective trial. *Arthritis Care Res* 1998;**11**:196–209.
43 **Ferraccioli G**, Ghirelli L, Scita F, Nolli M, Mozzani M, Fontana S, *et al*. EMG-biofeedback training in fibromyalgia syndrome. *J Rheumatol* 1987;**14**:820–5.
44 **van Santen M**, Bolwijn P, Verstappen F, Bakker C, Hidding A, Houben H, *et al*. A randomized clinical trial comparing fitness and biofeedback training versus basic treatment in patients with fibromyalgia. *J Rheumatol* 2002;**29**:575–81.
45 **Nicassio PM**, Radojevic V, Weisman MH, Schuman C, Kim J, Schoenfeld-Smith K, *et al*. A comparison of behavioral and educational interventions for fibromyalgia. *J Rheumatol* 1997;**24**:2000–7.
46 **Wigers SH**, Stiles TC, Vogel PA. Effects of aerobic exercise versus stress management treatment in fibromyalgia. A 4.5 year prospective study. *Scand J Rheumatol* 1996;**25**:77–86.
47 **Williams DA**, Cary MA, Groner KH, Chaplin W, Glazer LJ, Rodriguez AM, *et al*. Improving physical functional status in patients with fibromyalgia: a brief cognitive behavioral intervention. *J Rheumatol* 2002;**29**:1280–6.
48 **Thieme K**, Gromnica-Ihle E, Flor H. Operant behavioral treatment of fibromyalgia: a controlled study. *Arthritis Rheum* 2003;**49**:314–20.
49 **Gowans SE**, deHueck A, Voss S, Silaj A, Abbey SE, Reynolds WJ. Effect of a randomized, controlled trial of exercise on mood and physical function in individuals with fibromyalgia. *Arthritis Rheum* 2001;**45**:519–29.
50 **McCain GA**, Bell DA, Mai FM, Halliday PD. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. *Arthritis Rheum* 1988;**31**:1135–41.
51 **Mengshoel AM**, Komnaes HB, Forre O. The effects of 20 weeks of physical fitness training in female patients with fibromyalgia. *Clin Exp Rheumatol* 1992;**10**:345–9.
52 **Nichols DS**, Glenn TM. Effects of aerobic exercise on pain perception, affect, and level of disability in individuals with fibromyalgia. *Phys Ther* 1994;**74**:327–32.
53 **Schachter CL**, Busch AJ, Peloso PM, Sheppard MS. Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. *Phys Ther* 2003;**83**:340–58.
54 **Norregaard J**, Lykkegaard JJ, Mehlsen J, Danneskiold-Samsoe B. Exercise training in treatment of fibromyalgie. *J Musculoskelet Pain* 1997;**5**:71–9.
55 **Richards SC**, Scott DL. Prescribed exercise in people with fibromyalgia: parallel group randomised controlled trial. *BMJ* 2002;**325**:185–8.
56 **Valim V**, Oliveira L, Suda A, Silva L, de Assis M, Barros Neto T, *et al*. Aerobic fitness effects in fibromyalgia. *J Rheumatol* 2003;**30**:1060–9.
57 **Jones KD**, Burckhardt CS, Clark SR, Bennet RM, Potempa KM. A randomized controlled trial of muscle strengthening versus flexibility training in fibromyalgia. *J Rheumatol* 2002;**29**:1041–8.
58 **Kingsley JD**, Panton LB, Toole T, Sirithientad P, Matis R, McMillan V. The effects of a 12-week strength-training program on strength and functionality in women with fibromyalgia. *Arch Phys Med Rehabil* 2005;**86**:1713–21.
59 **Valkeinen H**, Hakkinen K, Pakarinen A, Hannonen P, Hakkinen A, Airaksinen O, *et al*. Muscle hypertrophy, strength development, and serum hormones during strength training in elderly women with fibromyalgia. *Scand J Rheumatol* 2005;**34**:309–14.
60 **Martin L**, Nutting A, MacIntosh BR, Edworthy SM, Butterwick D, Cook J. An exercise program in the treatment of fibromyalgia. *J Rheumatol* 1996;**23**:1050–3.
61 **Verstappen FTJ**, van Santen-Hoeufft HMS, Bolwijn PH. Effect of a group activity program for fibromyalgie patients on physical fitness and well being. *J Musculoskelet Pain* 1997;**5**:17–28.
62 **Da Costa D**, Abrahamowicz M, Lowensteyn I, Bernatsky S, Dritsa M, Fitzcharles MA, *et al*. A randomized clinical trial of an individualized home-based exercise programme for women with fibromyalgia. *Rheumatology* 2005;**44**:1422–7.
63 **Gowans SE**, deHueck A, Voss S, Richardson M. A randomized, controlled trial of exercise and education for individuals with fibromyalgia. *Arthritis Care Res* 1999;**12**:120–8.
64 **Mannerkorpi K**, Nyberg B, Ahlmen M, Ekdahl C. Pool exercise combined with an education program for patients with fibromyalgia syndrome. A prospective, randomized study. *J Rheumatol* 2000;**27**:2473–81.
65 **Cedraschi C**, Desmeules J, Rapiti E, Baumgartner E, Cohen P, Finckh A, *et al*. Fibromyalgia: a randomised, controlled trial of a treatment programme based on self management. *Ann Rheum Dis* 2004;**63**:290–6.
66 **Zijlstra TR**, van de Laar MA, Bernelot Moens HJ, Taal E, Zakraoui L, Rasker JJ. Spa treatment for primary fibromyalgia syndrome: a combination of thalassotherapy, exercise and patient education improves symptoms and quality of life. *Rheumatology* 2005;**44**:539–46.
67 **Keel PJ**, Bodoky C, Gerhard U, Muller W. Comparison of integrated group therapy and group relaxation training for fibromyalgia. *Clin J Pain* 1998;**14**:232–8.
68 **Lemstra M**, Olszynski WP. The effectiveness of multidisciplinary rehabilitation in the treatment of fibromyalgia: a randomized controlled trial. *Clin J Pain* 2005;**21**:166–74.
69 **King SJ**, Wessel J, Bhambhani Y, Sholter D, Maksymowych W. Predictors of success of intervention programs for persons with fibromyalgia. *J Rheumatol* 2002;**29**:1034–40.
70 **Yates SL**, Morley S, Eccleston C, Williams AC deC. A scale for rating the quality of psychological trials for pain. *Pain* 2005;**117**:314–25.
71 **Jadad AR**, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, *et al*. Assessing the quality of reports of randomized, clinical trials: is blinding necessary? *Control Clin Trials* 1996;**17**:1–12.
72 **Keefe FJ**, Rumble ME, Scipio CD, Giordano LA, Perri LM. Psychological aspects of persistent pain: current state of the science. *J Pain* 2004;**5**:195–211.
73 **Marhold C**, Linton SJ, Melin L. A cognitive-behavioral return-to-work program: effects on pain patients with a history of long-term versus short-term sick leave. *Pain* 2001;**91**:155–63.
74 **Evers AW**, Kraaimaat FW, van Riel PL, de Jong AJ. Tailored cognitive-behavioral therapy in early rheumatoid arthritis for patients at risk: a randomized controlled trial. *Pain* 2002;**100**:141–53.
75 **Sharpe L**, Sensky T, Timberlake N, Ryan B, Brewin CR, Allard S. A blind, randomized, controlled trial of cognitive-behavioural intervention for patients with recent onset rheumatoid arthritis: preventing psychological and physical morbidity. *Pain* 2001;**89**:275–83.
76 **Sinclair VG**, Wallston KA. Predictors of improvement in a cognitive-behavioral intervention for women with rheumatoid arthritis. *Ann Behav Med* 2001;**23**:291–7.
77 **Kraaimaat FW**, Brons MR, Geenen R, Bijlsma JW. The effect of cognitive behavior therapy in patients with rheumatoid arthritis. *Behav Res Ther* 1995;**33**:487–95.
78 **Evers AW**, Kraaimaat FW, Geenen R, Jacobs JW, Bijlsma JW. Pain coping and social support as predictors of long-term functional disability and pain in early rheumatoid arthritis. *Behav Res Ther* 2003;**41**:1295–310.
79 **Evers AW**, Kraaimaat FW, Geenen R, Jacobs JW, Bijlsma JW. Stress-vulnerability factors as long-term predictors of disease activity in early rheumatoid arthritis. *J Psychosom Res* 2003;**55**:293–302.
80 **Kerns RD**, Turk DC, Rudy TE. The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). *Pain* 1985;**23**:345–56.
81 **Turk DC**, Rudy TE. Toward an empirically derived taxonomy of chronic pain patients: integration of psychological assessment data. *J Consult Clin Psychol* 1988;**56**:233–8.
82 **Turk DC**, Okifuji A, Sinclair JD, Starz TW. Differential responses by psychosocial subgroups of fibromyalgia syndrome patients to an interdisciplinary treatment. *Arthritis Care Res* 1998;**11**:397–404.
83 **Turk DC**, Okifuji A, Sinclair JD, Starz TW. Interdisciplinary treatment for fibromyalgia syndrome: clinical and statistical significance. *Arthritis Care Res* 1998;**11**:186–95.
84 **Turk DC**. The potential of treatment matching for subgroups of patients with chronic pain: lumping versus splitting. *Clin J Pain* 2005;**21**:44–55.
85 **Thieme K**, Spies C, Sinha P, Turk DC, Flor H. Predictors of pain behaviors in fibromyalgia syndrome. *Arthritis Rheum* 2005;**53**:343–50.
86 **Evers AW**, Kraaimaat FW, Geenen R, Bijlsma JW. Psychosocial predictors of functional change in recently diagnosed rheumatoid arthritis patients. *Behav Res Ther* 1998;**36**:179–93.
87 **de Jong J**, Vlaeyen JW, Onghena P, Goossens ME, Geilen M, Mulder H. Fear of movement/(re)injury in chronic low back pain: education or exposure in vivo as mediator to fear reduction? *Clin J Pain* 2005;**21**:9–17.

88 **Vlaeyen JW**, de Jong J, Geilen M, Heuts PH, van Breukelen G. The treatment of fear of movement/(re)injury in chronic low back pain: further evidence on the effectiveness of exposure in vivo. *Clin J Pain* 2002;**18**:251–611.
89 **Vlaeyen JW**, de Jong J, Geilen M, Heuts PH, van Breukelen G. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. *Behav Res Ther* 2001;**39**:151–666.
90 **Vlaeyen JW**, Morley S. Active despite pain: the putative role of stop-rules and current mood. *Pain* 2004;**110**:512–16.
91 **McCracken LM**, Vowles KE, Eccleston C. Acceptance-based treatment for persons with complex, long standing chronic pain: a preliminary analysis of treatment outcome in comparison to a waiting phase. *Behav Res Ther* 2005;**43**:1335–466.
92 **Evers AW**, Kraaimaat FW, van Lankveld W, Jongen PJ, Jacobs JW, Bijlsma JW. Beyond unfavorable thinking: the illness cognition questionnaire for chronic diseases. *J Consult Clin Psychol* 2001;**69**:1026–36.
93 **Prins JB**, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL, *et al*. Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. *Lancet* 2001;**357**:841–7.
94 **Bazelmans E**, Prins JB, Bleijenberg G. Cognitive behaviour therapy for relatively active and for passive chronic fatigue syndrome patients. *Cogn Behav Pract* 2006;**13**:157–66.