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Psychological therapies for chronic widespread pain and fibromyalgia syndrome

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ABSTRACT

Psychological factors such as adverse childhood experiences, traumatic life events, interpersonal conflicts and psychological distress play an important role in the predisposition, onset and severity of chronic widespread pain (CWP) and fibromyalgia syndrome (FMS). Therefore, psychological therapies might have the potential to reduce disability as well as symptom and economic burden in patients with CWP and FMS. Recent interdisciplinary guidelines have suggested different strengths of recommendation for psychological therapies for FMS. The aims of this narrative review are to summarise:
• Mechanisms of actions.
• Evidence on efficacy, tolerability and safety.
• Knowledge gaps and needs for future research
of psychological therapies for CWP and FMS for non-mental health professionals.

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Background

Chronic widespread pain (CWP) is one defining feature of fibromyalgia syndrome (FMS) [1]. Within the continuum of biopsychosocial distress, patients with FMS are characterised by a higher somatic and

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psychological symptom burden and disability than the ones with CWP [2,3]. Both are prevalent conditions in the general population. Recent systematic reviews found that prevalence rates of CWP range from 1.4% to 20.44% [4,5]. The mean prevalence rate of FMS in a review was 2.7% (range 0.4%–8.8%) [6]. The wide range of prevalence rates can be explained by different study settings, diagnostic criteria for CWP and FMS used and different methods of assessment. Patients with CWP experience excess mortality, which can be mostly explained by low levels of physical activity, high body mass index, poor-quality diet and smoking [7]. Two retrospective population-based studies conducted in Denmark and the USA did not find an increased mortality but increased suicide rates compared to controls [8,9]. However, most patients in clinical settings report a reduced health-related quality of life and of daily functioning [10]. The global economic burden of FMS is substantial [11] and higher than that in CWP without FMS [3].

Psychological factors such as adverse childhood experiences, traumatic life events, interpersonal conflicts and psychological distress play an important role in the predisposition, onset and severity of CWP and FMS [12–15]. Therefore, psychological therapies might have the potential to reduce disability as well as symptom and economic burden in patients with CWP and FMS. Recent interdisciplinary guidelines have suggested different strengths of recommendation for psychological therapies for FMS. The European League Against Rheumatism revised recommendations for the management of FMS suggested a weak recommendation for cognitive behavioural therapies (CBTs) and for mindfulness-based stress reduction (MBSR) and a weak recommendation against biofeedback and hypnotherapy [16]. The updated German guideline provided a strong recommendation for CBTs, an open recommendation for hypnotherapy and biofeedback and a weak recommendation against MBSR (if used as single therapy) [17]. The divergent recommendations can be explained by different inclusion criteria, outcome measures used, grading of recommendations used and composition of the review panels [18].

The aims of this narrative review are to summarise:

- Mechanisms of actions
- Evidence on efficacy, tolerability and safety
- Knowledge gaps and needs for future research of psychological therapies for CWP and FMS for non-mental health professionals.

The review is based on the guidelines mentioned above and a selective search of the literature for systematic reviews on psychological therapies for CWP and FMS.

Practice points

Chronic widespread pain (CWP) and fibromyalgia syndrome (FMS) are prevalent conditions in the general population.
The importance of psychological therapies in the management of CWP and FMS needs to be defined more precisely.

Psychological therapies for CWP

There are no systematic reviews, and indeed, there are few randomised controlled trials (RCTs) of psychological therapies for CWP. Most studies have focused on FMS (summarised below), chronic pain, in general, or specific chronic pain, most commonly low back pain. For many of these therapies, there is no explicit rationale why they might be effective in one pain condition but not in another, and the focus is likely to be based – at least in part – on the size of the patient population.

Although there is a paucity of trials of _biofeedback_ in CWP, it may be possible to draw some parallels from chronic low back pain, for which there is some evidence, summarised in a Cochrane Review, demonstrating short-term effectiveness [19]. Although based on three small low-quality studies, with a

total of 64 participants, the authors concluded that electromyography (EMG) biofeedback is modestly effective in terms of short-term pain relief compared to waiting list controls. However, others have shown, also in low back pain, no additional benefit of EMG biofeedback when added to CBT [20].

Most trials of *CBTs* in pain populations have focused on specific pain conditions — commonly low back pain — or on FMS, with a single high-quality, large-scale trial of CBT among patients with CWP. McBeth et al. studied 442 patients with CWP, as defined in the American College of Rheumatology 1990 classification criteria for FMS [21]. They were randomised, evenly, to telephone-delivered CBT, exercise, both or treatment as usual. The CBT treatment was delivered across eight sessions, all approximately 45 min of duration, with a booster session at three and six months. There was no difference between the groups randomised to CBT alone or CBT plus exercise. Adherence was good, with over two-thirds of participants completing at least six sessions. Participants who received CBT alone were five times more likely to report that they felt 'much better or very much better" immediately after treatment (six months post-randomisation) than those who received treatment as usual (odds ratio: 5.2; 95% CI: 2.1 to 12.8), an effect that was sustained three months subsequently (odds ratio: 5.4; 95% CI: 2.3 to 12.8). Some benefit was found with pain severity (Chronic Pain Grade), and no significant improvement was found in terms of function (SF-36 Physical Component Score). Of note, although exercise was also found to be beneficial, there was no additional benefit of receiving both treatments. A subsequent long-term follow-up of the same study revealed that the beneficial effect was sustained at 2 years post-treatment. No adverse events were reported [22].

Veehof et al. conducted a systematic review and meta-analysis of acceptance-based interventions for chronic pain, which included nine RCTs of medium or high quality. Pooled data from two trials suggested a modest and statistically not significant improvement in pain associated with acceptance and commitment therapy (SMD: 0.29; 95% CI: −0.35 to 0.94). It is important to note, however, that neither trial was conducted in a CWP population. A significant effect was observed with MBSR across eight trials (SMD: 0.37; 95% CI: 0.20 to 0.54), although, again, none focussed on CWP specifically. The authors noted no significant difference of effect between ACT and MBSR, although the meta-analysis was not specifically powered to examine this and one must be cautious in not interpreting this as lack of inferiority [23].

Hypnosis has been seldom studied in CWP populations. Grøndahl Rosvold reports the results of a small pilot trial of patients with CWP, with duration between 3 and 60 months. Sixteen patients were randomised to receive hypnosis once a week for 10 weeks or control treatment (about which no details are given). Five of the eight participants in the latter also received hypnosis after the 10-week control period. Participants receiving hypnotherapy reported an improvement in pain. However, treatment groups were clearly imbalanced at the start of the study with regard to pain (average scores: 62.53 and 37.18, out of 100), and it is therefore not possible to draw any robust conclusion [24].

Practice point

Currently, there is insufficient evidence on the role of psychological therapies for CWP available.

Psychological therapies for FMS (alphabetical order; for summary of results see Tables 1 and 2)

Biofeedback

Biofeedback (BFB) is a procedure in which patients' bodily responses such as muscle tension, heart rate or skin temperature are monitored and reported to the patient through an auditory or visual modality. In EMG-FB, patients learn to control and alleviate their muscle tension. Biofeedback is often called a 'psychophysiological intervention', although the mechanisms are more psychological than

physiological: it has been demonstrated that the effectiveness of EMG biofeedback is mediated by cognitive changes such as increases in self-efficacy and coping strategies induced through biofeedback training, rather than primarily by learned physiological control. Electroencephalographic feedback (EEG-FB) is often referred to as 'neurofeedback' or 'EEG biofeedback'. EEG-FB records and reports back EEG waves. Patients are able to learn to influence evoked potentials, event-related potentials, slow cortical potentials and EEG frequency components [25].

After a literature search of articles published until October 2012, a systematic review included seven studies with 321 patients on EEG- and EMG-Biofeedback. Patients received sessions in the range of 6–22. All studies were conducted in an outpatient setting. Most studies included patients with depressive and anxiety disorder. The Cochrane risk of bias was unclear to high for each study. The authors of the review did not use GRADE (Grading of Recommendations Assessment, Development and Evaluation) to rate the quality of evidence of the studies analysed [26]. As compared to control, with all groups combined (sham-BFB, treatment as usual; escitalopram), biofeedback (BFB) showed a clinically relevant reduction in pain intensity. BFB did not show a statistically significant reduction in depression and fatigue as compared to controls. The dropout rate in the BFB groups was not significantly higher than that in the control groups. Three studies reported on adverse events. One study mentioned that no adverse events occurred. Two other studies reported 'stress' due to EMG-BFB, and one study reported a variety of side effects such as headache, fatigue and sleep problems due to EEG-BFB [25]. At follow-up (4–24 months), no statistically significant differences were found between BFB and controls for pain intensity, depressed mood and fatigue.

An RCT, which was published after the search of systematic reviews, did not find any superiority of EMG-BFB on pain, depressed mood and disability at the end of therapy and at 3-month follow-up [27].

Emotional Awareness and expression therapy

Rates of lifetime psychosocial adversities, traumas, interpersonal difficulties and emotional conflicts are substantially elevated in patients with FMS compared to healthy controls and patients with inflammatory rheumatic diseases without FMS. The sensitisation and augmentation of CNS circuits that modulate both emotions and pain are likely prominently involved. The failure to adaptively process and resolve conflicts and trauma appears to drive both somatic and psychological symptoms. Emotional Awareness and Expression Therapy (EAET) integrates techniques from several trauma- and emotion-focused therapies. EAET is designed to help patients attribute their pain and other symptoms to emotionally activated CNS mechanisms and become aware of, experience and adaptively express their emotions stemming from adversity, trauma or conflict. Patients are helped to identify and express avoided emotions by engaging in role-playing and empty chair techniques while activating their bodies and voices to directly express avoided or missing feelings (e.g. anger, guilt or love). Patients are encouraged to communicate honestly with significant people in their lives outside of sessions. Secondary topics are the expression of avoided forgiveness, gratitude, sexuality and developing a new identity [28].

In a cluster-randomised trial, 230 adults with FMS were randomised to EAET, traditional CBT or education and were given eight 90-min sessions. The study was conducted in an outpatient tertiary care setting. The Cochrane risk of bias of the study was low. GRADE ratings of the quality of evidence are not available.

At the end of treatment, EAET did not differ from FMS education in ≥50% pain relief and in reduction of fatigue and disability. EAET showed a clinically relevant benefit compared to education for ≥30% pain relief (30.5% vs 16.6%: NNTB 8) and for reducing mean pain intensity and depressed mood. Attrition did not differ between treatments. No adverse events were reported for CBT or FMS education. During EAET, brief symptom exacerbation (e.g. increased pain or sleep problems) was occasionally reported; however, in only one case, it lasted longer than a few days.

At 6-month follow-up, EAET showed a clinically relevant benefit compared to education for disability and depression but not for pain intensity and fatigue. EAET showed a clinically relevant benefit compared to CBT for > 50% pain relief (22.4% vs. 8.3%: NNTB 7) and for reducing widespread pain, but no statistically significant difference for depression, disability, and fatigue.

Table 1
Results of systematic reviews on psychological therapies for fibromyalgia syndrome at the end of treatment.

Reference	Type of psychological therapy	Number of RCTs and patients	Pain relief Outcome measure with 95% CI	Negative mood Outcome measure with 95% CI	Disability Outcome measure with 95% CI	Fatigue Outcome measure with 95% CI	Acceptability Outcome measure with 95% CI	Safety Outcome measure with 95% CI
[25]	Biofeedback	7/321	SMD −0.79 (−0.22 to −1.36).	n.s.	Not assessed	n.s.	n.s.	Some minor adverse events
[28]	Emotional Awareness and Expression therapy	1/230	n.s.	SMD −0.29 (95% CI not reported)	n.s.	n.s.	n.s.	One short symptom exacerbation in psychological therapy group
[29]	Face-to-face cognitive behavioural therapies	29/2509	50% or more RD 0.05 (0.02−0.07	SMD −0.43 (−0.24 to 0.62)	SMD −0.30 ([−0.08 to −0.52])	SMD −0.27 [−0.03 to −0.50)	n.s.	n.s.
[32]	Guided imagery/ hypnosis	7/387	50% and more RD 0.24 (0.06−0.42)	SMD −0.40 (−0.70 to −0.11)	n.s.	SMD −0.46 (−0.91 to 0.00)	n.s.	Not assessed
[30]	Internet-based cognitive behavioural therapies	6/493	n.s.	SMD −0.51 (−0.87 to −0.15]	SMD −0.56 (−1.00 to −0.13)	n.s	n.s.	In one study, two of 70 participants reported increased pain at 6- and 12-months follow up
[33]	Mindfulness-based stress reduction	6/674	SMD −0.23 (−0.46 to −0.01)	n.s.	Not assessed	Only one study assessed this outcome	Not assessed	Not assessed
[35]	Psycho-dynamic therapy	1/46	n.s.	n.s.	n.s.	n.s.	Not assessed	Not assessed

Abbreviations: CI = Confidence interval; n. s. = not statistically significant; RD = Risk reduction; RCT = Randomised controlled trial; SMD = Standardised mean difference.

Table 2
Results of systematic reviews on psychological therapies for fibromyalgia syndrome at follow-up.

Reference	Type of psychological therapy	Number of RCTs and patients	Mean duration of follow-up	Pain relief Outcome measure with 95% CI	Negative mood Outcome measure with 95% CI	Disability Outcome measure with 95% CI	Fatigue Outcome measure with 95% CI
[25]	Biofeedback	2/86	4–24 months	n.s	n.s.	Not assessed	Not assessed
[28]	Emotional awareness and expression therapy	1/230	6 months	n.s.	SMD −0.34 (95% CI not reported)	SMD 0.31 (95% CI not reported)	n.s.
[29]	Face-to-face cognitive behavioural therapies	15/1159	6 months	50% or more pain relief (RD 0.07 (0.04−0.10)	SMD −0.48 (−0.20 to −0.77)	SMD −0.53 (−0.26 to −0.80)	SMD −0.42 (−0.18 to −0.65)
[32]	Hypnosis	2/99	3 months	50% or more RD 0.05 (−0.05 to 0.16) 30% and more RD 0.18 (0.02−0.35)	n.s.	n.s.	n.s.
[30]	Internet-based cognitive behavioural therapies	No data	No data	No data	No data	No data	No data
[33]	Mindfulness-based stress reduction	6/674	4–15 months	n.s.	n.s.	Not assessed	Not assessed
[35]	Psychodynamic therapy	1/46	12 months	n.s.	n.s.	n.s.	Not assessed

Abbreviations: CI = Confidence interval; n.s. = not statistically significant; RD = Risk reduction; RCT = Randomised controlled trial; SMD = Standardised mean difference.

Cognitive behavioural therapies (CBTs)

Face-to-face cognitive behavioural therapies (CBTs)

There is a broad variety of psychological therapy techniques labelled to be behavioural and cognitive behavioural. A recent systematic review [29] made a distinction between.

(1) Operant therapy, which requires techniques to increase activity, the inclusion of significant others to reduce reinforcement of pain behaviours and the reduction in pain-contingent medication.
(2) Traditional CBT, which requires monitoring of one's own thoughts, feelings and behaviours with regard to the target symptom (e.g. by a symptom diary) and the promotion of alternative ways of coping with the target symptom (also labelled as problem-solving techniques, self-management or coping skills) through methods such as activity participation and skill building or practice opportunities.
(3) Self-management education programmes, which require information of the clinical picture of FMS, cognitive and behavioural skills mastery to manage pain and limitations of daily activities, and modelling as supplied by the facilitators to target cognitive, behavioural and emotional changes.
(4) Acceptance-based CBTs, which include acceptance and commitment therapy, or contextual CBT or mindfulness-based cognitive therapy. All these therapies use acceptance techniques (e.g. mindfulness meditation training) to facilitate a separation between 'self' and one's thoughts, feelings and pain experience and encourage patients to base their actions on their most important values as opposed to their immediate feelings, thoughts and pain.

After a literature search of articles published until May 2017, a systematic review included 29 RCTs with 2509 subjects. All studies but one were carried out in outpatient settings of primary, secondary and tertiary care. Most studies included patients with depressive and anxiety disorders. The median duration of all CBTs was 10 (3–54) weeks. The median number of sessions was 10 (6–60).

GRADE quality of evidence was high for most comparisons. At the end of treatment, CBTs were statistically significantly superior to controls (waiting list, attention control, treatment as usual and other active non-pharmacological therapies) in pain relief of $\geq$50%. However, there was no clinically relevant benefit with an NNTB of 20. There was a clinically relevant benefit of CBTs in reducing negative mood, disability and fatigue. There were no statistically significant differences between CBTs and controls in acceptability and safety.

At long-term follow-up, CBT was statistically significant superior to controls in pain relief of $\geq$50%. However, there was no clinically relevant benefit with an NNTB of 14. There was a clinically relevant benefit of CBTs in reducing negative mood, disability and fatigue.

Subgroup analyses of the different types of CBTs did not find clinically relevant differences in the primary outcomes.

Two studies found no statistically significant differences between CBTs and recommended pharmacological therapy (pregabalin and − in case of depressive disorder − duloxetine) for 50% or more pain relief, improvement in HRQOL of 20% or greater, negative mood and acceptability at the end of treatment and at 6-month follow up. One study offered acceptance-based and one study delivered traditional CBT for a total of 216 patients [29].

Internet-based CBTs

Internet-based treatments can be distinguished depending on whether the Internet is used to communicate and/or to deliver information as follows [30]:

(a) Web-based self-help programmes using the Internet as a delivery medium without any contact with a mental health care specialist (MHCS) (unguided);
(b) Internet-based guided self-help approaches, in which the presentation of a Web-based self-help programme is combined with regular contact with an MHCS (guided); and

(c) Internet-based therapies such as e-mail, chat or videoconference-based therapies, in which the Internet is only used for communication purposes with an MHCS (online or e-therapy).

After a literature search of articles published until January 2018, a systematic review included six RCTs using different types of Internet-based CBTs [ICBTs] (acceptance-based; exposure-based; traditional) with 493 patients. Most studies included patients with depressive and anxiety disorders. The study duration ranged between 6 and 12 weeks. GRADE quality of evidence was moderate for all outcomes.

At the end of treatment, ICBTs showed a clinically relevant superiority over controls (waiting list, attention control, treatment as usual) in reducing negative mood and disability. There were no statistically significant differences between ICBTs and controls in pain relief of 50% or more and acceptability. No data on any efficacy outcomes at long-term follow-up compared to controls were found. The data available did not allow statistical comparisons between unguided and guided ICBTs and between ICBTs and traditional face-to-face therapies [30].

An RCT, which was published after literature search of systematic reviews with 67 patients with FMS, found a clinically relevant superiority of an eight-week online acceptance and commitment online intervention plus treatment as usual compared to treatment as usual alone for reduction in pain and depression at the end of treatment [31].

Guided imagery/hypnosis (GI/H)

A hypnotic induction is a procedure designed to induce hypnosis. Hypnosis is defined as a state of consciousness involving focused attention and reduced peripheral awareness characterised by an enhanced capacity for response to suggestion. The suggestions can be direct (traditional hypnosis) or permissive (Ericksonian hypnosis). Imagery is defined as a dynamic, psychophysiological process in which a person imagines and experiences an internal reality in the absence of external stimuli. These images can be initiated by the patient or guided by a therapist (guided imagery). Both techniques aim to promote changes in subjective experience alterations in perception, sensation, emotion, thought or behaviour by suggestion and/or imagination [32].

The authors of a systematic review searched the literature until February 2016. Seven RCTs with 387 subjects were included for a comparison of GI/H versus controls. The study duration ranged between 4 and 10 weeks. All studies were outpatient based and were delivered in settings of primary and secondary care. It remains unclear whether patients with anxiety or depressive disorders were excluded. The Cochrane risk of bias in the studies ranged from high to moderate. The quality of evidence for all comparisons was low according to GRADE.

There was a clinically relevant benefit of GI/H compared to controls (treatment as usual; waiting list control, other active therapies) on ≥50% pain relief, psychological distress and fatigue at the end of therapy. GI/H did not show statistically significant difference from controls in reducing disability and acceptability at the end of treatment. Adverse events were not assessed.

At 3-month follow-up, there was a clinically relevant benefit of hypnosis: A greater proportion of patients in the hypnosis group achieved ≥30% pain relief than that in the control group. However, there was no difference between groups in the proportion achieving ≥50% pain relief [32].

Mindfulness-based stress reduction

The original curriculum of MBSR applies a structured 8-week group programme of 2.5 h weekly and an additional all-day silent retreat with the overarching aim of cultivating mindfulness, a special way of paying attention often described as moment-to-moment non-judgemental awareness. Key components of MBSR include different formal mindfulness practices (sitting meditation, walking meditation, body scan and yoga exercises), daily homework and informal mindfulness practice with an aim to increase awareness during routine activities in everyday life [33].

After a literature search of articles published until September 2013, a systematic review included six RCTs with 674 patients. The studies were conducted in all types of settings (primary to tertiary care)

and mostly included patients with depressive and anxiety disorders. The study duration ranged between 8 and 12 weeks.

GRADE quality of evidence was judged to be low for all outcomes. Except for a clinically relevant benefit of MBSR over waiting list and usual care controls in reducing pain intensity at the end of treatment, no statistically significant differences could be demonstrated for depression and fatigue at the end of treatment and at follow-up and for pain reduction at follow-up. There were no statistically significant differences. For all of these outcomes, there were no statistically significant differences between MBSR and other active therapies (education with and without the support group) [33].

An RCT with 91 female patients with FMS, which was published after the review, did not find statistically significant differences between MBSR and waiting list controls for reduction of pain, fatigue and disability at the end of treatment and a follow-up [34].

Psychodynamic therapy

In a subgroup of patients with FMS, inter- and intrapersonal conflict and problems in self- and affect recognition due to developmental deficits might result in heightened stress and pain vulnerability. In a psychodynamic approach, during the initial phase, the focus is on establishing a trustful and supportive relationship. Patients give an account on their medical history including their own view concerning the causes of their symptoms and their often disappointing experiences within the health care system. Issues of pain behaviour and dysfunctional coping are addressed. In the second phase, the focus is shifting gradually towards interpersonal problems linking adverse psychosocial experiences and intrapsychic conflict with bodily complaints and emotions. During this phase, issues of self-management, self- and bodily awareness and affect regulation are in the foreground. Difficulties in these areas are linked to attachment history including experiences of emotional deprivation, loss and trauma. The final phase aims to stabilise changes and concentrates on termination issues. This includes the planning of additional psychotherapeutic or pharmacological interventions for target symptoms and a review of the accomplishment of initial treatment goals [35].

Forty-six female patients with FMS and diagnosis of a comorbid depression or anxiety disorder were recruited in a hospital setting. Participants were randomised to receive either psychodynamic therapy (25 sessions, 1 session/week) or treatment as usual by an experienced therapist (4 consultations/6 months). At the end of treatment and at 12-month follow-up, no statistically significant differences were found for pain intensity, psychological distress, disability and dropout rates for any reason between the two treatments. Data on safety (adverse events) were not reported [35].

Importance of psychological therapies in the management of CWP and FMS

There is only a high-quality evidence for the short- and long-term efficacy of face-to-face CBTs (traditional, operant, acceptance-based approaches) to reduce FMS symptoms and disability. EAET and Internet-based CBTs hold promise. Low-quality methodology of most studies limits the validity of study results with biofeedback and guided imagery/hypnosis. The data on the efficacy of MBSR are inconclusive for FMS.

Even for conventional CBT, for which the evidence on FMS is greatest, there is still very little evidence in terms of CWP. Researchers, instead, have focused on specific pain conditions or chronic pain generally. In many circumstances, unless there is a rational and theoretical basis to the contrary, it is likely that the data from FMS may be translatable to non-FMS CWP. However, practitioners should be aware that this is a largely untested assumption. The statements on the efficacy of CBTs are based on comparisons with the frequently used comparators of psychological therapies such as waiting list, attention control and treatment as usual. If CBTs are compared to a 'fair' non-pharmacological control group, which receives the same amount of therapy by experienced therapists, such as aerobic exercise, no statistically significant differences can be found [36]. This gives rise to questions about the active ingredient of many psychological therapies — whether it is the therapy per se or 'contact time' with a therapist. There is also uncertainty about the dosage of psychological therapy, not only what dose is given but also what dose is appropriate. If one assumes that any psychological therapy has some form of active ingredient, the number of sessions or cumulative therapy duration is not necessarily a precise

estimate of treatment 'dose'. They may be the best proxy and commonly (although not always) reported in randomised trials, which does aid the replication of therapy in the clinical setting to a certain extent. However, knowledge of therapy content is likely to be more important than replication of therapy duration, which is subject to numerous other contextual factors.

There is also uncertainty about superiority of one therapy versus another due to missing head-to-head trials. Between-therapy differences are likely to be small, and any trial powered to detect a difference would require being large. With novel drugs, there is the interest of the pharmaceutical industry. However, with non-pharmacological therapies, there is no appetite or resource for these studies to be conducted.

Two RCTs [summarised in 29] and a network meta-analysis did not find statistically significant differences in efficacy, tolerability and safety of CBTs compared to established drug therapies in FMS [37]. However, in contrast to the RCTs with drugs, study samples of psychological therapies in FMS are more representative because the exclusion criteria for somatic diseases and mental disorders were less strict. In addition, the positive effects of drugs disappear after the cessation of therapy [38]. In contrast, positive effects of face-to-face CBTs for FMS symptoms could be demonstrated at follow-up after the end of therapy [29].

Knowledge gaps and need for future research

New trials should address the following issues:

- The definition of subgroups (e.g. patients with FMS with and without major depression or post-traumatic stress disorder, pain persistence and pain avoidance behaviour) with development of more tailored therapies to these subgroups [39];
- The development of graduated treatment approaches (e.g. education, non-guided ICBTs, guided CBTs; multicomponent therapies) depending on the severity of FMS [40];
- The identification of predictors of a favourable outcome [29];
- The development of booster sessions to maintain the positive effects of psychological therapies;
- The assessment and prevention of (serious) adverse events such as mental health episodes (e.g. suicide attempts, mental health—related hospital admissions) during or immediately after therapy, clinically relevant deterioration at the end of treatment and very negative experience of the therapy by the patient [41];
- The comparison of face-to-face versus telephone or Internet-based therapies in terms of efficacy, acceptability and costs;
- The comparison of combined therapies (e.g. CBTs plus a drug) and single therapy (e.g. CBTs or drug alone) in terms of efficacy, safety and costs;
- The application of new study designs beyond the 'gold standard' of RCTs, e.g. clinical effectiveness trials [29,30].

Specific tasks for Internet-delivered psychological therapies are as follows [30]:

- How much qualification of the e-coach is needed (student; licensed psychotherapist with and without specialised postgraduate training)?
- How much personal contact with an MHCP is needed and is it cost effective?
- How can therapeutic rapport be built over the Internet?
- How can privacy protection be ensured?
- How do respond on crisis, e.g. suicidal ideation?
- How can ICBTs be disseminated and implemented in routine clinical care?

Summary

There is only a high-quality evidence for the short- and long-term efficacy of face-to-face cognitive-behavioural therapies (CBTs) (traditional, operant, acceptance-based approaches) to reduce

fibromyalgia syndrome (FMS)-symptoms and disability. Emotional Awareness and Expression Therapy and Internet-based CBTs hold promise. Low-quality methodology of most studies limits the validity of study results with biofeedback and guided imagery/hypnosis. The data on the efficacy of MBSR are inconclusive for FMS. Even for conventional CBT, there is still very little evidence in terms of chronic widespread pain (CWP). If CBTs are compared to a 'fair' non-pharmacological control group, which receives the same amount of therapy by experienced therapists, such as aerobic exercise, no statistically significant differences can be found. The development of tailored therapies to FMS subgroups could improve the efficacy of psychological therapies.

The development of graduated treatment approaches depending on the severity of FMS is needed in the view of limited economic resources and availability of health care professionals. Some problems of Internet-delivered psychological therapies such as privacy protection and management of crisis need to be resolved before further implementation in routine clinical care.

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Conflicts of interest

The authors declare that they have non-financial conflicts of interest related to the paper.

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