

Therapeutic indulgent of Fibromyalgia - A systematic review revealing research crevices

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Article Authorship & Affiliation Details	Abstract
<p>Communication Date: Apr 23, 2015</p> <p>Acceptance Date: May 16, 2015</p> <p>DOI: 10.18376/2016/v12i1/86808</p> <p>Ranganathan, Arunmozhi Associate Professor, Department of Physiotherapy, SBS (P.G.) Institute of Biomedical Sciences and Research, Balawala, Dehradun Uttarakhand. E-mail: rmozhi@gmail.com</p> <p>Arumugam, Narkeesh Prof & Head, Department of Physiotherapy, Punjab University, Patiala-147001, Punjab, India E-mail: narkeesh@yahoo.com</p> <p>Khattri, Sumitt Professor, SGRR Institute, Dehradun E-mail: charas1979@gmail.com</p> <p>Key Words: Cognitive behavioral therapy, Myofascial Release Therapy, Fibromyalgia, Systematic review.</p> <p>To cite this article: Ranganathan, Arunmozhi; Arumugam, Narkeesh & Khattri, Sumitt. Therapeutic indulgent of Fibromyalgia - A systematic review revealing research crevices. [online]. <i>Journal of Exercise Science and Physiotherapy</i>, Vol. 12, No. 1, June 2016: 1-24.</p>	<p>Background: Fibromyalgia (FM) is a common chronic musculoskeletal pain disorder, which has a negative effect on the quality of life. Patient often feel incapable of performing the basic daily life activities as walking, going up stairs, or lifting objects. The literature indicates the overall prevalence rate is about 2-6% worldwide. Patients with fibromyalgia go through various pharmacology and non-pharmacological treatments. The purpose of this systematic review is to provide an overview of research studies focused on the various treatment procedures and to find out the gap in the literature for the future studies in FM condition. Methods: Studies in any language were identified by searching through databases like MEDLINE, Google Scholar, and Science Direct and PEDro. Articles in which some form of treatment methods was used to manage fibromyalgia were included. The PRISMA guidelines for systematic reviews were followed. Results: Several researchers demonstrated the individual effects of their therapeutic techniques; a specific intervention will not work for every patient because each patient has a different constellation of symptoms resulting in different responses to therapeutic interventions. Conclusion: Our results suggested that the combination of soft tissue releases along with psychotherapy and medication is necessary to resolve the overall symptoms of fibromyalgia.</p>

Introduction

Fibromyalgia is a common chronic musculoskeletal pain disorder, which has a negative effect on the quality of life. Patient often feel incapable of performing the basic daily life activities as walking, going up stairs, or lifting objects

(Cymet, 2003; Bennett, 2005; Sarzi-Puttini et al., 2007). The estimated overall prevalence of FM in Europe was 4.7% of chronic widespread pain, and was 2.9% when stronger pain and fatigue criteria were simultaneously used (Branco et al., 2010). It affects 4% of US population,

approximately 6 -10 million Americans (*Wolfe et al., 1995; Lindell et al., 2000; White and Harth., 2001; Lawrence et al., 2008*) with strong female predominance (*Wolfe et al., 1995*) between the ages of 20 and 50 (*Reiffenberg and Amundson, 1996*). The symptoms of FM have been described as reduced pain thresholds to palpation (*Gran, 2003*), joint stiffness, fatigue (*Bigatti, 2008; Bellato et al., 2012*), sleep alterations and a negative effect on the quality of life. Patients often feel incapable of performing basic daily life activities such as walking, going up stairs, or lifting objects (*Cymet, 2003; Bennett, 2005*). According to *Williams and Clauw (2009)* patients with FM often experience a number of other symptoms that include tenderness, stiffness, mood disturbances (e.g. Depression and/or anxiety), cognitive difficulties (e.g. trouble concentrating, forgetfulness and disorganized thinking). Additionally, tension type headache/migraine, interstitial cystitis or painful bladder syndrome, chronic prostatitis or prostodynia, temporomandibular disorder, chronic pelvic pain, and vulvodynia (*Ablin and Clauw, 2009*) have been shown to be associated with FM.

The 2010 American College of Rheumatologists preliminary classification criteria for the diagnoses of fibromyalgia as the sum of the widespread pain index (WPI) and total symptom severity (SS) being more than a certain score, continuing symptoms for more than 3 months, and all three criteria without disease related to symptoms being satisfied (*Wolf et al., 2010*). *Bennett (2005)* described the most effective interventions of FM in descending order by rest, heat modalities, prescription pain medications,

prescription antidepressants, prescription sleep medications, prayer, and massage. Similarly, numerous other studies have documented on the management of FM like Spa therapy, Internet enhanced Management, Repeated intrathecal antidepressant, Transcranial magnetic stimulation, Low level laser therapy, Hydrotherapy, Craniosacral therapy, Diet, Yoga, Exercise, Affective cognitive behavioral treatment, Hypnosis, Guided imagery, Acupuncture, and Myofascial release (*Donaldson et al., 2001; Assefi et al., 2005; Menzies et al., 2006; Matsutani et al., 2007; Grondahl et al., 2008; Perraton et al., 2009; Williams et al., 2010; Castro-Sanchez et al., 2011; Nishiyori et al., 2011; Mataram-Penarrocha et al., 2011; Curtis et al., 2011; Busch et al., 2011; Woolfolk et al., 2012; Tzabazis et al., 2013; Fraioli et al., 2013*). To find out the gap in the literature for the future studies in FM condition a systematic review of randomized controlled trials are considered to provide the best evidence about the interventions. Thus the purpose of this systematic review is to provide an overview of available research studies focused on the various treatment procedures and to find out the gap in the literature for the future studies.

Methods: The search integrated a variety of sources including text books, journals and the computerized searches were generally performed, searching for studies in any language using the MeSH terms like fibromyalgia and fibromyalgia treatment from the databases of MEDLINE, PUBMED Central, Google Scholar, PEDRO (Physiotherapy Evidence Database) and Science Direct. The study was limited from January 2000 to July

2015. Free text articles were collected from each database. Articles in English language were included if they described any form of treatment procedure on FM. We excluded study protocols, pilot studies, case reports, clinical study, studies not related to FM (trigger points, diagnosis and treatment), non-randomized controlled treatment, and article scored below two in

Pedro score and reviews. All the articles were read, and data were extracted from the articles based on treatments. The methodological quality of the included studies was performed according to PRISMA (Preferred Reporting Items for Systematic Review and Meta Analysis) Statement (*Fig. 1*).

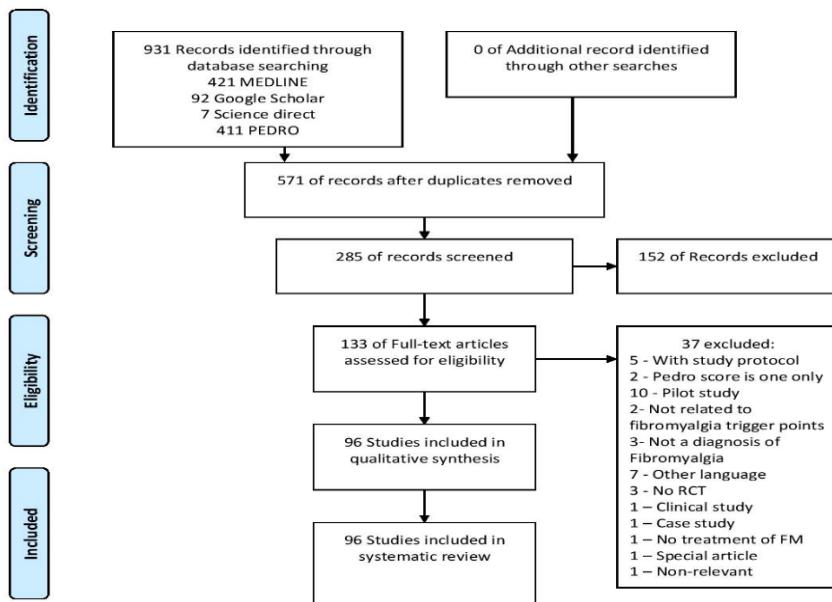


Figure 1: PRISMA Flow Diagram

Results: The study yielded 134 studies, out of these; 97 studies were included in this review, we found 42 randomized controlled trials, 14 double blinded studies; thus these studies had a low risk of

performance bias and low detection bias, 39 single blinded studies; these studies avoid any potential biased reactions or responses. Other studies are clinical and case controlled studies prone to have a

high risk of performance bias or a strong detection bias. For all the studies, the following details were extracted: type of

study, design, number of patients, outcome measures, interventions used and results (Table 1).

Table 1: PEDro scoring system for various Randomized controlled studies

Authors (Year)	Random Alloc.	Cone. Alloc.	Baseline Compar.	Blind Subjects	Blind Therapist	Blind Assessor	Follow Up	Intention to Treat	Between Group Comparison	Points estimates & variability	Total Score
Aldia et al (2011)	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
Almeida et al (2003)	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	6/10
Ang et al (2013)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Ang et al. (2012)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Arcos-Carmona et al (2011)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Arnold et al (2011)	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8/10*
Assefi et al (2005)	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	6/10
Assefi et al (2008)	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8/10
Assis et al (2006)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Babu et al (2007)	Yes	No	No	Yes	No	No	Yes	No	Yes	Yes	5/10
Bement et al (2011)	Yes	No	Yes	No	No	No	No	Yes	No	No	4/10
Bjersing et al (2012)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Bourgault et al (2015)	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5/10
Bressan et al (2008)	Yes	No	No	No	No	No	No	No	No	Yes	2/10
Carleton et al (2011)	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7/10*
Castel et al (2013)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Castro-Sanchez et al (2011)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
Castro-Sanchez et al (2011)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10*
Cedraschi et al (2004)	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5/10
Chappell et al (2008)	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7/10*
Clarke-Jensen et al (2014)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Da Costa et al (2005)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Fioravanti et al (2009)	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5/10
Fontaine et al (2010)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Fontaine et al (2011)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Gamber et al (2002)	Yes	Yes	No	No	No	Yes	Yes	No	No	No	4/10
Garza-Villarreal et al (2014)	No	No	No	No	No	No	Yes	No	Yes	Yes	3/10*
Gavi et al (2014)	No	No	Yes	No	No	Yes	Yes	No	Yes	Yes	4/10
Gowans et al (2001)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Gowans et al (2002)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	No	5/10
Gusi & Tomas-Carus et al (2008)	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	5/10
Gusi et al (2006)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Gusi et al (2010)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Hadianfarid & Parizi (2012)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Hakkinnen et al (2001)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Hammes et al (2012)	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5/10
Harris et al (2005)	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8/10
Harris et al (2009)	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	5/10
Hasson et al (2004)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Hsu et al (2010)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Ide et al (2008)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	7/10
Itoh & Kitakoji (2010)	Yes	No	Yes	No	No	No	No	No	No	Yes	4/10
Jentoft et al (2001)	Yes	No	No	No	No	Yes	No	No	Yes	Yes	4/10
Jones et al (2002)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
Jones et al (2008)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Kaleth et al (2013)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Kashikar-Zuck et al (2012)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Kashikar-Zuck et al (2013)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
Kashikar-Zuck et al (2013)	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5/10
King et al (2002)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6/10
Kingsley et al (2005)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6/10
Koulli et al 2010	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Lenstra & Olszynski (2005)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Letieri et al (2013)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Lofgren et al (2009)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Luciano et al (2014)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10*
Lynch et al (2012)	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6/10
Mannerkorpi et al (2009)	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7/10
Martin et al (2006)	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8/10
Martins et al (2014)	Yes	No	No	No	No	No	Yes	No	Yes	Yes	4/10
Mataran-Penarrocha et al (2011)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Matsutani et al (2007)	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Menga et al (2014)	Yes	No	Yes	No	No	No	No	Yes	Yes	No	4/10*
Menzies et al (2006)	Yes	Yes	Yes	No	No	No	No	No	No	Yes	5/10
Menzies et al (2014)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Munguia-Izquierdo & Legaz- Arres (2008)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Newcomb et al (2011)	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Ramsay et al (2000)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6/10
Redondo et al (2004)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6/10
Reis et al (2014)	No	No	Yes	No	Yes	No	Yes	No	Yes	No	4/10*
Ribeiro et al (2011)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	6/10*
Richards & Scott (2002)	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	5/10
Rooks et al (2007)	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7/10
Sanudo et al (2010)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Sanudo et al (2011)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Sanudo et al (2013)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Schachter et al (2003)	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	5/10

Septon et al (2007)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	5/10
Stephens et al (2008)	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	7/10
Stival et al (2014)	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	6/10
Targino et al (2008)	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	7/10
Thieme et al (2003)	Yes	No	Yes	No	No	No	Yes	No	Yes	5/10
Tomas-Carus et al (2007)	Yes	No	Yes	No	No	No	Yes	No	Yes	5/10
Tomas-Carus et al (2008)	Yes	No	Yes	No	No	No	Yes	No	Yes	6/10
Tomas-Carus et al (2009)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	6/10
Valim et al (2013)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	5/10
Valkeinen et al (2004)	Yes	No	Yes	No	No	No	Yes	No	Yes	5/10
Valkeinen et al (2008)	Yes	No	Yes	No	No	Yes	Yes	No	Yes	6/10
Van Santen et al (2002)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	6/10
Van Santen et al (2002)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	6/10
Wahner-Roedler et al (2011)	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	7/10*
Wang et al (2010)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7/10
Williams et al (2010)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7/10
Woolfolk et al (2012)	Yes	No	Yes	No	No	No	Yes	Yes	Yes	6/10
Younger et al (2009)	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	7/10*
Zijlstra et al (2005)	Yes	Yes	Yes	No	No	No	No	No	Yes	5/10

Random alloc. =Random allocation, Conc. Alloc. = Concealed allocation, Baseline Compar. = Baseline Comparability

*Pedro score rated by the authors.

Diagnosis: Fibromyalgia syndrome (FMS) was diagnosed in 92 studies by the American College of Rheumatology criteria (*Wolfe, 1990*); 3 studies by juvenile fibromyalgia (JFM) criteria based on *Yunus and Masi criteria (1985)* and the remaining 2 studies are diagnosed by *Goldenberg criteria (1987)* and *Smythe and Modofsky (1977)*.

Outcomes Measures: pain was assessed by Visual analogue Scale (VAS) in 39 studies, Fibromyalgia Impact Questionnaire (FIQ) was assessed in 49 studies, Beck Depression Index (BDI) in 16, Brief Pain Inventory (BPI) in 16, SF-36 in 24 for the QOL, six minute walking test in 11, and Hamilton rating scale for depression (HAMD) in 4 studies.

Quality of evidence: The methodological quality for ninety four trials was extracted from PEDRO database and the other eleven trials were evaluated by the authors using Pedro scale. Out of these 97 trials nine studies reported as high quality score (8/10), another twenty one studies obtained 7/10, twenty four studies scored 6/10, twenty five studies were 5/10, fifteen studies were 4/10, one study was 3/10 and the remaining one scored 2/10 (Table 2).studies scored below two were excluded from the study.

Description of included randomized controlled trials (RCTs): This systematic review described different interventions: Exercises, Hydrotherapy, Myofascial release, Guided imagery, Craniosacral therapy, Cognitive behavioral therapy, pharmacology, pregabalin, acupuncture, reiki, whole body vibration, electrotherapy, music therapy thoracic mobilization, tai chi, osteopathic manipulation, hydrokinesiotherapy, complimentary therapy (phytothermotherapy and spa therapy) and Qigong therapy. We categorized the trials into 7 broad spectrums namely Exercises, Psychotherapy, Multidisciplinary programme, Myofascial release therapy, Pharmacology, Acupuncture, and other techniques.

Details of the studies included in the review. Exercises was used in 43 studies (*Matsutani et al., 2007; Hasson et al., 2004; Ang et al., 2011; Gusi and Tomas-Carus, 2008; Mannerkorpi et al., 2009; Redondo et al., 2004; Ramsay et al., 2000; King et al., 2002; Ide et al., 2008; Da Costa et al., 2005; Cedraschi et al., 2004; Fontaine et al., 2010 & 2011; Gavi et al., 2014; Gowans et al., 2001; 2002; Arcos-Carmona et al., 2011; Assis et al., 2006; Bement et al., 2011; Bjersing et al., 2012; Bressan et al., 2008; Gusi et al., 2006;*

Hakkinen et al., 2001; Jentoft et al., 2001; Jones et al., 2002; Jones et al., 2008; Kaleth et al., 2013; Kingsley et al., 2005; Munguia-Izquierdo et al., 2008; Newcomb et al., 2011; Richards and Scott, 2002; Rooks et al., 2007; Sanudo et al., 2010; 2011; Schachter et al., 2003; Stephens et al., 2008; Tomas-Carus et al., 2007; 2008; 2009; Valim et al., 2013; Valkeinen et al., 2004; 2008; Van Santen et al., 2002; Van Santen et al., 2002); Pharmacology was used in another 3 studies (Younger et al., 2009; Arnold et al., 2011; Chappell et al., 2008); cognitive behavioral therapy and other psychotherapy techniques were studied in 15 studies (Kashikar-Zuck et al., 2012; 2013a, 2013b; Hamnes et al., 2012; Woolfolk et al., 2012; Alda et al., 2011; Carleton and Richter, 2011; Koulik et al., 2010; Ang et al., 2013; Hsu et al., 2010; Luciano et al., 2014; Menga et al., 2014; Menzies et al., 2014; Sephton et al., 2007; Thieme et al., 2003); MFR techniques were reported in 2 studies (Castro-Sanchez et al., 2011a & 2011b); Multidisciplinary programme were reported in 5 studies (Castel et al., 2013;

Clarke-Jenssen et al., 2014; Lemstra and Olszynski 2005; Martins et al., 2014; Bourgault et al., 2015), Acupuncture were studied in 7 studies (Itoh and Kitakoji, 2010; Hadianfard and Parizi, 2012; Harris et al., 2005; Harris et al., 2009; Martin et al., 2006; Stival et al., 2014; Targino et al., 2008) and the remaining 21 studies are reported on other treatment techniques like reiki, acupuncture, biofeedback, Qigong therapy, Soy supplement, Transcranial direct current stimulation, Craniosacral therapy, Guided imagery, Internet-enhanced management, whole-body vibration training, and laser (Assefi et al., 2005; Sanudo et al., 2013; Williams et al., 2010; Menzies et al., 2006; Mataram-Penarrocha et al., 2011; Riberto et al., 2011; Wahner-Roedler et al., 2011; Lynch et al., 2012; Babu et al., 2007; Assefi et al., 2008; Sanudo et al., 2013; Gusi et al., 2010; Lofgren et al., 2009; Garza-Villarreal et al., 2014; Reis et al., 2014; Wang et al., 2010; Gamber et al., 2002; Letieri et al., 2013; Fioravanti et al., 2009; Almeida et al., 2003; Zijlstra et al., 2005).

Table 2: Randomized Controlled Studies

Sl. No.	Author (Year)	Design	Pedro Scale	No. Of Patients	Treatment Applied	Outcome Measures	No. Of Session	Follow-Up	Results
1	Alda et al (2011)	RCT	7/10	169	CBT RPT TAU	PCS, HAM-D, HARS, PVAS, FIQ, EuroQOL-5D	5	6 months	CBT more effective than RPT and TAU.
2	Almeida (2003)	RCT (double blinded)	6/10	17	CTPI group SHAM group	VAS, TP, TT, PSG	12	4 week	CTPI group showed subjective improvement of pain, decreased in morning fatigue and in non-refreshing sleep complaint. Objectively, on PSG treatment group showed improvements.
3	Ang et al (2013)	RCT (double blinded)	4/10	58	Combination therapy Milnacipran + education Placebo + CBT	SF-36	8	21 weeks	Compared to milnacipran, combination therapy demonstrated a moderate effect on improving SF-36 physical function and in reducing

								weekly average pain intensity.
4	Ang et al. (2012)	Randomized attention controlled trial	7/10	216	Motivational interviewing group (6 telephone delivered exercise) Attention control group	FIQ-PI, CHAMPS FIQ, BPI, 6-MWT, Accelerometer, PCS, ESE, Decisional balance, Intention-to-exercise, PHQ-8	6	12 weeks <i>MI group is better than AC group in pain reduction and physical functioning</i>
5	Arcos-Carmona et al (2011)	RCT	5/10	53	Intervention group Sham treatment group	STAI PSQI BDI SF-36	20	10 weeks <i>Intervention group showed significant reduction in sleep duration, trait anxiety and QOL.</i>
6	Arnold et al (2011)	RCT (Double blind, Placebo-controlled trial)	6/10*	530	Duloxetine Placebo	MFI, Numerical scale, PGI-I BPI, rating	7	24 weeks <i>Duloxetine showed significant improvement on multiple dimensions of fatigue in patients with fibromyalgia</i>
7	Asseifi et al (2008)	RCT	8/10	93	Direct Reiki Distant Reiki	VAS, SF-36, Medication, Health care	16 session	20 weeks <i>Neither reiki nor touch had any effect of pain or any of the secondary outcomes.</i>
8	Asseifi et al (2005)	RCT	6/10	96	Acupuncture Sham acupuncture	VAS, SF-36	24	6 months <i>Acupuncture did not reduced pain in patients with fibromyalgia</i>
9	Assis et al (2006)	RCT (single blinded)	8/10	52	Deep water running (DWR) Land-based exercises (LBE)	VAS, FIQ, BDI, SF-36, PGART	45	15 <i>DWR could be an exercise option for patients with FM who have problems adapting to LBE or lower limb limitations.</i>
10	Babu et al (2007)	RCT	5/10	30	Electromyography biofeedback Sham biofeedback	FIQ, VAS, 6MWT, number of trigger points	6 sessions	6 days <i>Both groups showed improvement in physical and psychological realms. Also, decrease in pain and number of tender points</i>
11	Bement (2011)	RCT	4/10	15	Decreased pain Increased pain No change in pain	Pain threshold and rating VAS FIQ	4	4 weeks <i>Greatest pain relief for women with fibromyalgia occurred at a young age</i>
12	Bjersing et al (2012)	RCT	4/10	49	Nordic walking (NW) Low intensity walking	6 MWT Algometer Blood tests (IGF-I)	30	30 weeks <i>6 MWT significantly improved in the NW group.</i>
13	Bourgault et al (2015)	RCT	5/10	43	Intervention group Wait-list group	NRS, PGIC, SF-12v2, BDI	9	12 months <i>The intervention had a statistically significant impact on the three PGIC measures. At the end of the PASSAGE Program, the percentages of patients who perceived overall improvement in their pain levels, functioning and quality of life were significantly higher in the INT Group than in the WL Group.</i>
14	Bressan et al (2008)	RCT	2/10	15	Muscle stretching Physical conditioning	FIQ, sleep quality, pain-modulating factors, medications	8	8 weeks <i>Muscle stretching showed statistically significant differences on FIQ (morning tiredness and stiffness)</i>

15	Carleton et al (2011)	RCT (Double blind clinical trial)	5/10*	15	Attentional Modification Paradigm (AMP) Attention control condition	ASI-3, ISI-R, PASS-20, FPQ-SF, STAI, VAS	8	4 weeks	AMP condition reported statistically significant and substantial reductions on several individual difference variables relative to those in the control condition, and a greater proportion experienced clinically significant reductions in pain
16	Castel et al (2013)	RCT (single blinded)	7/10	88	Pharmacology group Multidisciplinary group	FIQ, CSQ, COOP/WONCA, SLEEP scale	24	12 months	Multidisciplinary treatment shown superiority in all variables at posttreatment. The differences were maintained at 12 month follow-up in sleep disturbances, catastrophizing, and psychological distress.
17	Castro-Sanchez et al (2011)	RCT (placebo controlled trial)	6/10	86	Myofascial therapy group Placebo group	Pressure Algometry, MPQ, Postural stability, FIQ, CGI-S	4	1 year	Myofascial release showed a significant reduction in all the outcome measures except postural stability
18	Castro-Sanchez et al (2011)	RCT	4/10*	59	Massage-myofascial release therapy Placebo	VAS, pressure algometry, STAI, BDI, PSQI, SF-36	4	6 months	Massage-myofascial release therapy Showed a significant effect on pain, pain sensitivity, anxiety and sleep duration and no differences in depression scale.
19	Cedraschi et al (2004)	RCT	5/10	129	Multidisciplinary program group Control group	Myalgic pain score, SF-36, PGWB, FIQ, Regional pain score, patient satisfaction measures	12	6 months	Significant improvements in quality of life and functional consequences of FM were seen in the treatment group as compared with the controls and as measured by scores on both the FIQ and PGWB
20	Chappell et al (2008)	RCT (double blind, placebo controlled)	6/10*	204	Duloxetine Placebo	BPI, PGI-I, FIQ, CGI, HAMD	11	27 weeks	Duloxetine showed significant improvement in all the outcome measures Nausea was the most common treatment emergent adverse event in the duloxetine group.
21	Clarke-Jensen et al (2014)	RCT	6/10	129	Rehabilitation program group Control group	TPC, 6MWT, MPQ, FIQ, ASES, SF-36, HADS, LTPA1, Dynamometer	20	12 months	Rehabilitation program for fibromyalgia may have a long term effect on pain, as measured by TPC and pain distribution, and may improve physical function.
22	Da Costa et al (2005)	RCT	8/10	61	Home-based moderate-intensity exercise program	FIQ, VAS, SCL-90-R	12	9 month	Exercise group shown improvements in

					<i>Usual care</i>				<i>upper body pain and no significant group differences on lower body pain and psychological distress</i>
23	Fioravanti <i>et al</i> (2009)	RCT (single blinded)	5/10	56	<i>Phytothermotherapy group</i> <i>Control group</i>	<i>FIQ, Tender point count, HAQ, and AIMS</i>	10	24 weeks	<i>Phytothermotherapy group showed visible and significant improvements in all parameters at the end of the treatment.</i>
24	Fontaine <i>et al</i> (2010)	RCT	5/10	73	<i>LPA group</i> <i>FE group</i>	<i>FIQ, VAS, FSS, CESD, 6 MWT</i>	60-84	12 weeks	<i>LPA group increased their average daily steps; significantly less perceived functional deficits and pain. Also no differences between the groups on the 6MWT, fatigue, depression, body mass index, or tenderness.</i>
25	Fontaine <i>et al</i> (2011)	RCT	4/10	53	<i>Lifestyle physical activity (LPA)</i> <i>Fibromyalgia Education (FE)</i>	<i>6MWT, FIQ, FSS, CES-D</i>	6	12 months	<i>LPA participants reported greater perceived improvements and self reported functioning declined markedly. LPA did not differ from other measures from controls.</i>
26	Gamber <i>et al</i> (2002)	RCT (Single blinded)	4/10	24	<i>Manipulation group</i> <i>Manipulation + teaching group</i> <i>Moist heat group</i> <i>Control group</i>	<i>PPIRS, CPEI, HAQ, Dolorimeter Present pain intensity scale, chronic pain experience inventory</i>	23	23 weeks	<i>Significant findings between the four treatment groups on measures of pain threshold, perceived pain, attitude towards treatment, activities of daily living, and perceived functional ability were found.</i>
27	Garza-Villarreal <i>et al</i> (2014)	Controlled study	3/10*	22	<i>Music group</i> <i>Control group</i>	<i>PCS, STAI, STATE, CES-D, PI, PU, VRS, TUG.</i>	3	Immediate effects	<i>Music as a treatment adjuvant to reduce chronic pain in FM and increases functional mobility thereby reducing the risk of disability.</i>
28	Gavi <i>et al</i> (2014)	RCT (Single blinded)	4/10	66	<i>Strengthening group (STRE)</i> <i>Flexibility (FLEX) group</i>	<i>VAS, HRV, FIQ, IDATE, SF-36, WILLS AND DILLONS BENCH.</i>	32	16	<i>STRE was more effective to strength gain and pain control. FLEX group showed higher improvements in anxiety.</i>
29	Gowans <i>et al</i> (2001)	RCT (Single blinded)	7/10	31	<i>Exercise group</i> <i>Control group</i>	<i>VAS, FIQ, BDI, MHI, point, Strength.</i>	69	23	<i>Exercise can improve the mood and physical function of individuals with fibromyalgia.</i>
30	Gowans <i>et al</i> (2002)	RCT	5/10	50	<i>Exercise group</i> <i>Control group</i>	<i>BDI, CES-D, STAI, MHI, FIQ</i>	69	23 weeks	<i>BDI cognitive and STAI are recommended to measure exercise-induced changes in mood. MHI-5 has acceptable for a</i>

									general measure of mood.
31	Gusi & Tomas-Carus (2008)	RCT	5/10	33	1. Usual care and Water based exercise group 2.Usual care	QALYs	3 times / week	8 months	Water-based programme is a cost effective strategy on QALY in both healthcare and social perspectives.
32	Gusi et al (2006)	RCT	5/10	34	Exercise group Control group	EQ-5D, VAS, Isokinetic strength	36	12 weeks	The strength of the knee extensors in concentric actions increased in both limbs after the training period. HRQOL improved and pain was decreased in the exercise group during the training, but pain returned close to the pretraining level during the subsequent de-training.
33	Gusi et al (2010)	RCT (Single blinded)	7/10	41	Vibration group Control group	Balance platform	36	12 weeks	The dynamic balance of the vibration group improved as compared to control group
34	Hadianfarid & Partizi (2012)	RCT	8/10	30	Acupuncture fluoxetine	VAS, FIQ, number of tender points	5	1 year	Acupuncture group is significantly better than the control group in number of trigger points, fatigue and anxiety
35	Hakkinen et al (2001)	RCT	5/10	21	Strength training (FM _t) group Control (FM _c) group	EMG, HAQ, BDI, Dynamometry	42	21 weeks	The progressive strength training showed immediate benefits on subjectively perceived fatigue, depression, and neck pain of training patients with FM.
36	Hamnes et al (2012)	RCT	5/10	118	Self-management programme (SMP) group Control group	GHQ-20, EC-17, FIQ, ASEs.	7	3 week	There was a significant difference in EC-17 in favor of the treatment group
37	Harris et al (2005)	RCT (Single blinded)	8/10	59	T/S needles placed in traditional sites with manual needle stimulation T/I traditional needles location without stimulation N/S needles inserted in nontraditional location N/I nontraditional needle location without stimulation	NRS, MDI,SF-36	18	15 sessions	Participants received three sessions weekly provided more analgesia than sessions once weekly. Among treatment responders, improvements in pain, fatigue and physical function were highly codependent.
38	Harris et al (2009)	RCT (Single blinded)	5/10	20	Traditional Chinese acupuncture Sham acupuncture	SFMPQ PET scan	8	4 weeks	Acupuncture group provided more analgesic effects

									than sham acupuncture.
39	Hasson <i>et al</i> (2004)	RCT	6/10	117	Massage Mental relaxation	Health Questionnaire Mental energy scale	10	3 months	Massage shown improvement in self rated health, mental energy and muscle pain at 5 th week and no significance in 3 month follow-up
40	Hsu <i>et al</i> (2010)	RCT	7/10	45	Affective awareness Wait-list control	BPI, TPT, SF-36	18	6 months	Intervention group had significantly lower pain severity, higher self reported physical function, and higher tender point threshold.
41	Ide <i>et al</i> (2008)	RCT	7/10	40	Aquatic respiratory exercise-based program Control group	SF-36, FIQ, HAS, PSQI,VAS, Number of tender points	16	4 weeks	Aquatic respiratory exercise-based program , compared with control group showed improvement in all the outcome measures.
42	Itoh & Kitakoji (2010)	RCT	4/10	13	Electroacupuncture Trigger point Acupuncture	VAS, FIQ	3	10 weeks	Acupuncture treatment is effective to relieve pain in terms of QOL and FIQ
43	Jentoft <i>et al</i> (2001)	RCT (Single blinded)	4/10	18	Pool based Exercise program (PE) Land based Exercise program (LE)	FIQ VAS, ASS, Bicycle ergometry, walking time.	40	6 months	Both groups showed significant improvements in CV capacity, walking time and daytime fatigue. Also improvement in grip strength was seen in LE group compared with the PE group.
44	Jones <i>et al</i> (2008)	RCT	4/10	165	Pyridostigmine + exercises Placebo + exercises Pyridostigmine + Diet recall. Placebo+ Diet recall.	VAS FIQ	72	6 months	The combination of PYD and exercise did not improve pain scores. PYD groups showed a significant improvement in sleep and anxiety and QOL improvements in therapeutic regimens.
45	Jones <i>et al</i> (2002)	RCT (single blinded)	6/10	68	Exercise group Control group	TMS, VAS, FIQ, BDI, QOLS, ASES	24	12 weeks	Significant improvements in the strengthening group compared to the stretching group
46	Kaleth <i>et al</i> (2013)	RCT	4/10	170	Moderate vigorous physical activity	FIQ-PI FIQ-total BPI PHQ-8	108 – 144	36 weeks	Performing greater volumes of physical activity is not associated with worsening pain in FM.
47	Kashikar-Zuck <i>et al</i> (2012)	RCT	7/10	114	1.CBT 2.Education	FDI, VAS, PedsQOL, Generic core scale, PedsQL rheumatology module and sleep quality	3	6 months	No significant reduction in pain.
48	Kashikar-Zuck <i>et al</i> (2013)	RCT (Multisite clinical trial)	6/10	100	CBT Fibromyalgia Education	PCQ, FDI, CDI	10 session	6 month	CBT shown greater improvements immediately following treatment up to follow up period. Functional disability or depressive

									symptoms shown no improvements.
49	Kashikar-Zuck et al (2013)	RCT (single blinded)	5/10	68	<i>CBT group</i> <i>Fibromyalgia Education group</i>	<i>Actigraphy monitor</i> <i>Functional disability inventory (FDI)</i> <i>Children depression inventory (CDI)</i>	8	9 week	<i>Self reported functioning improved in the CBT condition compared to FE, no significant changes were seen in either group for activity counts, sedentary, moderate or vigorous activity.</i>
50	King et al (2002)	RCT	6/10	152	<i>Exercise only</i> <i>Education only</i> <i>Exercise + Education Control</i>	<i>Chronic pain self efficacy scale, FIQ, 6MW, tender point count, total survey site score</i>	5	3 months	<i>Exercise -education group showed better sense of control and exercise only group showed improvement in fitness over the FM patients</i>
51	Kingsley et al (2005)	RCT (Single blinded)	6/10	29	<i>Strength training group</i> <i>Waitlisted control group</i>	<i>Strength, functionality, Tender point sensitivity, FIQ</i>	24	12 weeks	<i>The strength group significantly improved upper and lower body strength. Tender point and fibromyalgia impact did not change.</i>
52	Kouil et al 2010	RCT	6/10	136	<i>Treatment condition waiting list control condition</i>	<i>IRGL, FIQ, pain coping inventory</i>	17	6 months	<i>Treatment condition showed Significant effects on all the outcome measures than the wait list control condition</i>
53	Lemstra & Olszynski (2005)	RCT (single blinded)	8/10	71	<i>Intervention group</i> <i>Control group</i>	<i>VAS, BDT, PDI</i>	12	15 months	<i>Intervention group experienced statistical significance in self perceived health status, average pain intensity, pain related disability, depressed mood, days in pain, and hours in pain</i>
54	Letieri et al (2013)	RCT	5/10	64	<i>Hydrokinesiotherapy</i> <i>Control group</i>	<i>VAS, FIQ, BDI</i>	30	15 weeks	<i>Significant improvements in the perception of pain intensity, QOL, and depression symptoms in favor of the hydrotherapy group.</i>
55	Lofgren & Norrbink (2009)	RCT	6/10	32	<i>Superficial warmth</i> <i>TENS group</i>	<i>FIQ Numerical Rating Scale</i>	42	6 weeks	<i>Seventeen of 32 patients preferred warmth therapy and 10 preferred TENS.</i>
56	Luciano et al (2014)	RCT (single blinded)	7/10*	168	<i>CBT</i> <i>RPT</i> <i>TAU</i>	<i>Mini EUROQOL-5D questionnaire</i> <i>CSRI, EQ-5D</i>	V _{so} , 1	6 months	<i>CBT is the most cost-effective treatment for adult FM.</i>
57	Lynch et al (2012)	RCT	6/10	73	<i>Qigong training group</i> <i>Control group</i>	<i>IMMPACT, NRS-PI, FIQ, PSQI, SF-36</i>	3	6 months	<i>Qigong showed significant improvements in pain, impact, sleep, physical function and mental function when compared with control group</i>
58	Mannerkorpi et al (2009)	RCT	7/10	125	<i>Exercise-education group</i> <i>Education only group</i>	<i>FIQ, 6MWT, HADS-D, SF-36, LTPAI, SCI, MFI-20</i>	26 session	11-12 months	<i>The exercise-education programme showed significant, but small improvement in health status in patients with</i>

									<i>fibromyalgia and chronic widespread pain.</i>
59	<i>Martin et al (2006)</i>	<i>RCT (Double blinded)</i>	8/10	50	<i>Acupuncture Simulated group Acupuncture group</i>	<i>FIQ, MPI.</i>	6	7 months	<i>Total fibromyalgia symptoms were significantly improved in the acupuncture group compared to control group. Fatigue and anxiety were the most significantly improved symptoms and there is no change on the physical function level.</i>
60	<i>Martins et al (2014)</i>	<i>RCT</i>	4/10	27	<i>Weekly interdisciplinary program (WIP) group Control group</i>	<i>FIQ, VAS, PSI, SF-12 Post Sleep Protocol</i>	12	12 Weeks	<i>WIP has statistical significance in all outcome measures</i>
61	<i>Mataran-Penarrocha et al (2011)</i>	<i>RCT</i>	4/10	84	<i>1.Craniosacral Therapy group 2.placebo group</i>	<i>VAS, SF-36 Health survey, PSQI, BDI, STAI</i>	4	1 year	<i>Craniosacral therapy improves anxiety and QOL</i>
62	<i>Matsutani et al (2007)</i>	<i>RCT</i>	4/10	20	<i>Laser therapy and stretching Stretching only</i>	<i>VAS, Dolorimeter FIQ, SF-36</i>	10	10	<i>Stretching exercises program is efficient to reduce pain and painful sensibility at tender points, thus enhancing patient QOL.</i>
63	<i>Menga et al (2014)</i>	<i>RCT</i>	4/10*	56	<i>CBT (Moodgym) group Control group</i>	<i>FIQ, Tender assessment point</i>	4	12 weeks	<i>CBT could be beneficial in the treatment of mild to moderate depression and anxiety in patients with FM.</i>
64	<i>Menzies (2006)</i>	<i>RCT</i>	5/10	48	<i>1.Guided Imagery plus Usual care 2.Usual care alone</i>	<i>SF-MPQ, ASES, FIQ</i>	4	10 weeks	<i>FIQ scores decreased overtime in the GI group compared to the usual care group. Self efficacy for managing pain and other symptoms of FM also increased significantly over time in the GI group. Pain as measured by the SF-MPQ did not change over time or by group</i>
65	<i>Menzies et al (2014)</i>	<i>RCT</i>	6/10	64	<i>Usual care + Guided Imagery Usual care</i>	<i>ASES, PSS, BMI, BFI, BPI, CES-D</i>	70	10 weeks	<i>Statistically significant reduction in perceived stress and self efficacy for managing other symptoms.</i>
66	<i>Munguia-Equero & Ligaz-Arrese (2008)</i>	<i>RCT (Single blinded)</i>	7/10	78	<i>Exercise therapy Healthy control group</i>	<i>FIQ Pittsburgh Sleep Quality Index (PSQI) SAI – State anxiety Inventory Paced auditory serial addition task (PASAT)</i>	48	16 weeks	<i>Exercise therapy was effective in decreasing the tender point count and improving sleep quality, cognitive and physical functions.</i>
67	<i>Newcomb et al (2011)</i>	<i>RCT</i>	5/10	21	<i>Preferred exercise intensity Prescribed exercise intensity</i>	<i>Body diagram FIQ, SF-MPQ, POMS, PGIC</i>	2	2 weeks	<i>Pain threshold and pain tolerances increased significantly after exercise.</i>
						<i>VAS, Total myalgic score, Modified</i>	12	48	<i>Exercise class group showed some</i>

68	Ramsay et al (2000)	RCT	6/10	72	Aerobic Exercises + stretching and relaxation techniques Cardiovascular fitness classes + stretching and relaxation techniques	HAQ, HAD, sleep difficulty, sleep duration, resting pulse rate		weeks	significant benefit in psychological well being and slowing of mental deterioration
69	Redondo et al (2004)	RCT	6/10	31	CBT Physical exercise	FIQ, BAI, BDI, CPS, CPC, Aerobic exercise capacity, Physical activity of vertebral column, Upper limb & lower limb.	5/week	12 months	Physical function and general health domains of the SF-36 showed a significant improvement at 6 months and non-significant at one year follow up.
70	Reis et al (2014)	Clinical controlled study	4/10*	20	FM group Control group	Numeric pain scale, Heart rate, RR interval	1	Immediate effects	Mobilization technique did not significantly reduce pain, it was able to improve HRV quantified by an increase in rMSSD and SDI indices, reflecting an improved autonomic profile through increased vagal activity.
71	Riberto et al (2011)	RCT (double blinded, placebo controlled trial)	5/10*	23	1.Transcranial direct current stimulation 2.Sham	VAS, SF - 36	3 times / week	4 months	IDCS significantly reduced SF - 36 pain domain scores and improved FIQ scores
72	Richards and Scot (2002)	RCT (Single blinded)	5/10	132	Active Exercise group Control group	Self-Assessment, TPC, SEMPOQ.	24	12 months	Exercise group had a greater reduction in tender point counts and in scores on the FIQ.
73	Rooks et al (2007)	RCT (Single blinded)	7/10	135	Aerobic + Flexibility Exercise Strength training, aerobic, and Flexibility Exercise Fibromyalgia Self Help course Strength training + Fibromyalgia Self Help Course.	FIQ SF-36 BDI ASES	32	16 weeks	All the measures showed improvements on social function, mental health, fatigue, depression and self efficacy. The beneficial effect on physical function of exercise alone and in combination with education persisted at 6 months.
74	Samudo et al (2010)	RCT	6/10	55	Aerobic exercise (AE) Combined Exercise (CE) Usual care control	FIQ SF-36 BDI 6MWT Dynamometer	48 sessions	24 weeks	Both the exercise groups showed improvements on FIQ, BDI scores and physical functioning.
75	Samudo et al (2011)	RCT (single blinded)	8/10	38	Exercise group Usual care	VAS, FIQ, BDI.	48	24	Long term combination of aerobic exercise, strengthening and flexibility improves psychological health status and HRQOL.
76	Samudo et al (2013)	RCT	7/10	46	Whole body vibration + exercise training group Exercise training group Usual care	BSS T Force system	16	8 weeks	Statistically significant improvements in the medio-lateral stability index and medio-lateral deflection with open eyes were found in the whole body vibration exercise group compared with the control.

									<i>Non-significant effects were found for lower limb physical function.</i>
77	Schachter <i>et al</i> (2003)	RCT	5/10	112	<i>Short Bout exercise</i> <i>Long Bout exercise</i>	<i>FIQ</i> <i>Arthritis Impact Measurement Scale</i> <i>Chronic pain self efficacy scale</i>	48-80	16 weeks	<i>Progressive, home based, low impact aerobics improved physical function and fibromyalgia symptoms minimally who completed atleast two thirds of the recommended exercise.</i>
78	Septon <i>et al</i> (2007)	RCT	5/10	91	<i>Mindfulness-Based Stress Reduction (MBSR).</i> <i>Waiting list control</i>	<i>FIQ,</i> <i>BDI,</i> <i>VAS,SSQ,</i>	8	2 months	<i>Depressive symptoms improved significantly in treatment versus control participants over 3 assessments.</i>
79	Stephens <i>et al</i> (2008)	RCT (Single blinded)	7/10	30	<i>Aerobic group</i> <i>Qigong group</i>	<i>Adherence,</i> <i>FIQ,</i> <i>QOL,</i> <i>C-HAQ,QOML</i> <i>QUALITY OF MY LIFE,</i> <i>PedsQL,</i> <i>FSSQ,</i> <i>CDI, HAES.</i>	36	12 weeks	<i>Better adherence was reported in the aerobics group than in the qigong group. Significant improvements in physical function, functional capacity, QOL, and fatigue were observed in the aerobics group. Aerobic function, tender point count, pain, symptom severity improved similarly in both groups.</i>
80	Stival <i>et al</i> (2014)	RCT (double blinded)	6/10	36	<i>Acupuncture</i> <i>SHAM acupuncture</i>	VAS	1	Immediate	<i>Acupuncture has proven effective in the immediate pain reduction in patients with FM</i>
81	Targino <i>et al</i> (2008)	RCT (Single blinded)	7/10	59	<i>Acupuncture + tricyclic antidepressants + Exercise</i> <i>Tricyclic antidepressants + Exercise</i>	VAS, PPT, SF-36	20	2 years	<i>After one year, acupuncture group showed significance in one subscale of the SF-36; at 2 years there were no significant differences in any outcomes.</i>
82	Thieme <i>et al</i> (2003)	RCT	5/10	61	<i>Operant pain treatment (OTG)</i> <i>Physical therapy group (PTG)</i>	MPI, TBS	35	15 months	<i>OTG patients reported a significant and stable reduction in pain intensity, interference, solicitous behavior of the spouse, medication, pain behaviors, number of doctors visits, and days at a hospital as well as an increase in sleeping time.</i>
83	Tomas-Caruso (2009)	RCT (Single blinded)	6/10	30	<i>Exercise group</i> <i>Control group</i>	<i>Muscle strength,</i> <i>Balance,</i> <i>HRQOL</i>	96	32 weeks	<i>Water exercise therapy showed statistically significant improvements in concentric knee flexors and extensors strength at 60° /s. the treatment led to additional improvements in</i>

									physical function, role physical problems, body pain, general health, vitality, role emotional problems and mental health dimensions of SF-36.
84	Tomas-Caruso et al (2007)	RCT	5/10	34	Exercise group Control group	SF-36 HRQOL FIQ Physical fitness	36	24 weeks	Significant positive effects of aquatic training were found in all the measures. After detraining, only the improvements in body pain and role emotional problems were maintained.
85	Tomas-Caruso et al (2008)	RCT (single blinded)	6/10	33	Exercise group Control group	FIQ, STAI, CAF, Hand Dynamometer	96	8 months	Supervised exercise in warm water was feasible and led to long term improvements in physical and mental health in patients with FM at a similar magnitude to those of shorter therapy programs.
86	Valim et al (2013)	RCT (single blinded)	5/10	22	Aerobic walking Stretching exercises	Serum levels – 5HT 5 HIAA Serotonin	60	20 weeks	Aerobic training increases the SHIAA and 5HT.
87	Valkeinen et al (2003)	RCT	5/10	13	Strength training group Control group	VAS, EMG, HAQ, STRENGTH.	42	21 weeks	Supervised strength training suits elderly FM patients, has positive effects on perceived symptoms and improves functional capacity without complications.
88	Valkeinen et al (2008)	RCT (Single blinded)	6/10	24	Concurrent strength training + Endurance training Control group	Muscle strength, peak oxygen uptake, HAQ, self reported functional capacity.	63	21 weeks	Concurrent strength and endurance training showed improvement in all the measures except in V _O 2 peak.
89	Van Santen et al (2002)	RCT (single blinded)	6/10	143	Fitness training Biofeedback training Control group	VAS, TMS, SCL-90, AIMS, SIP	48	24 Weeks	There is no significant effects between the groups. Thus compared to usual care, the fitness training and biofeedback training had no clear beneficial effects on FM.
90	Van Santen et al (2002)	RCT (single blinded)	6/10	30	High intensity fitness training (HIFT) Low intensity fitness training (LIFT)	VAS, TMS, SCL-90, AIMS, Ergometer	40	20 weeks	The VAS for global well being improved slightly and the physical fitness changed modestly in HIFT compared to LIFT.
91	Wahner-Roedler et al (2011)	Randomized double blind, placebo-controlled trial	7/10*	28	Soy supplement Placebo	FIQ, Center for epidemiologic studies depression scale (CES-D).	2	6 weeks	Dietary soy supplementation is no more beneficial than casein shakes
92	Wang et al (2010)	RCT (Single blinded)	7/10	66	Yang tai chi group Control group	FIQ, SF-36	24	12 weeks	Tai chi group had clinically important improvements in the FIQ total score and QOL. Both the treatment are shown

									effectiveness on SF-36.
93	Williams et al (2010)	RCT	7/10	118	Standard care plus WEB-SM Standard Care	SF-36, BPI, MFI, MOS sleep scale, CES-D, STPI	7	6 months	Standard care plus WEB-SM group demonstrated a statistically significant improvement in Pain and Physical function. But a non-significant results in sleep, fatigue and mood.
94	Woolfolk et al (2012)	RCT	6/10	76	1.Affective-cognitive behavioral therapy+ treatment as usual (TAU) 2.TAU	VAS, MOS-PF, CPSE, BDI, BAI	3	10 weeks	ACBT decreases pain but non-significance in CPSE
95	Younger et al (2009)	RCT (Double blinded, placebo)	6/10*	20	Naltrexone group Placebo group	FIQ, SECS, SHS, PANAS	1	Immediate effects	Significant group effects revealed on opioid withdrawal symptoms, time and positive mood.
96	Zijlstra et al (2005)	RCT	5/10	58	Active treatment group TAU group	RAND-36 health survey, FIQ, MPQ, BDI, Tender point Score, 6 minute walking test	7-8	12 months	A combination of thalassotherapy, exercise and patient education may temporarily improve fibromyalgia symptoms and health-related QOL.

CES-D - Center for Epidemiologic Studies Depression Scale, **TAU** - Treatment As Usual, **FIQ** - Fibromyalgia Impact Questionnaire, **VAS**- Visual Analogue Scale, **MOS-PF** - Medical Outcome Study – Physical Functioning, **CPSE (CPSS)** - Chronic Pain Self Efficacy Scale, **BDI** - Beck Depression Inventory, **BAI**- Beck Anxiety Inventory , **RPT** – Recommended Pharmacological Treatment, **PCS** - Pain Catastrophizing Scale, **HAM-D** – Hamilton Rating Scale for Depression, **HARS** - Hamilton Anxiety Rating Scale, **PVAS** – Pain Visual Analogue Scale, **EuroQOL** - European Quality Of Life Scale, **ASES** - Arthritis Self Efficacy Scale, **SF-MPQ** - Short Form McGill Pain Questionnaire, **MPQ** – McGill Pain Questionnaire, **SF-36** - Short Form 36 Health Survey, **BQ** - Berlin Questionnaire, **ESS** – Epworth Sleepiness Scale, **QALY** – Quality Adjusted Life – years, **PSQI** - Pittsburg Sleep Quality Index , **STAI** – State Trait Anxiety Inventory, **TPI** - Tender Point Index, **HSQ** – Health Status Questionnaire, **GHQ** – General Health Questionnaire, **EC** – Effective Musculoskeletal Consumer Scale, **BPI** – Brief Pain Inventory, **STPI** - State Trait Personality Inventory, **WEB-SM** – Web-Enhanced Behavioral Self Management, **CGISS** – Clinical Global Impression Severity Scale, **MFI**- Multidirectional Fatigue Inventory, **SECS** – Somatization And Emotional Contribution Scale, **SHS** – Sensory Hypersensitivity Scale, **SOWS** – Subjective Opiate Withdrawal Symptoms Scale, **PANAS** – Positive And Negative Affects Scale, **CSRI** – Client Service Receipt Inventory, **LTPAI** – Leisure Time Physical Activity Instrument, **SCI** – Stress And Crisis Inventory, **MFI-20** - Multidirectional Fatigue Inventory, **IRGL** – Impact of Rheumatic Diseases on General Health And Lifestyle Instrument, **SCL-90-R** – Symptom Checklist 90 Revised, **PGWB** – Psychological General Well Being, **ASI-3**- Anxiety Sensitivity Index-3, **ISI-R** – Illness/Injury Sensitivity Index-Revised, **PASS-20** – Pain Anxiety Symptoms Scale-20, **FPQ-SF** – Fear of Pain Questionnaire-Short Form, **AIMS** - Arthritis Impact Measurement Scale, **HRQOL** - Health Related Quality Of Life, **6 MWT** – Six Minute Walking Test, **QOML** – Quality Of My Life, **SIP** – Sickness Impact Profile, **POMS** – Profile of Mood Status, **ASES** – Arthritis Self-Efficacy Scale, **QOLS** – Quality of Life Scores, **TMS** – Total Myalgic Scores, **BAI** - Beck Anxiety Inventory, **PGART** - Patient Global Assessment of Response to Therapy, **TP** – Tender Point, **TT** – Tender Threshold, **PSG** – Polysomnography, **NRS** – Numerical Rating Scale, **HRSD** - Hamilton Rating Scale For Depression, **HRSA**- Hamilton Rating Scale For Anxiety, **BSS** - Body Stability System, **TUG** –Time Up and Go, **PU** - Pain Unpleasantness, **PI** – Pain Intensity, **HR**- Heart Rate, **PPIRS** - Present Pain Intensity Rating Scale, **CPEI** - Chronic Pain Experience Inventory, **FS** - Fatigue Scale, **PGIC** – Patient Global Impression Of Change, **EQ 5D** Questionnaire, **MHI** – Mental Health Inventory, **PHQ-8** Patient Health Questionnaire, **FSS** - Fatigue Severity Scale, **RPE** – Rated Perceived Exertion, **BSI** - Brief Symptom Inventory, **SIP** – Sickness Impact Profile, **SHIAA** – Hydroxindolacetic Acid, **FSHC** – Fibromyalgia Self-Help Course, **MUMQ** – Maastricht Utility Measurement Questionnaire, **VPMI** – Vanderbilt Pain Management Inventory, **PASAT** – Paced Auditory Serial Addition Task, **TPC** – Tender Point Count, **HRV** – Heart Rate Variability, **IDATE** – Idate Trait-State Inventory, **CAF** – Canadian Aerobic Fitness, **MDI** - Multi-Dimensional Fatigue Inventory, **HAQD** – Health Assessment Questionnaire adapted for Dentist, **PSI**- Post-Sleep Protocol, **CSQ** - Coping Strategies Questionnaire, **COOP/WONCA** - COOP/WONCA Functional Health Assessment Charts, **TPT** – Trigger Point Threshold, **TBS** – Tubingen Pain Behavior Scale, **MPI** – Multidimensional Pain Inventory, **FDI** – Functional Disability Inventory, **CDI** – Children Disability Inventory, **BFI** – Brief Fatigue Inventory, **SSQ** – Stanford Sleep Questionnaire, **HSCL** – Hopkins Symptom Check List, **MINI v50** – MINI Neuropsychiatric Interview,

*Pedro score rated by the authors.

Discussion: the principal finding of this review is to document the available treatment approaches on the management of FM and to find out the gap in the literature for the future studies. Based on the currently available data, the systematic review found that most of the RCTs trying to propose exercise and CBT as a mainstay in the management of FM. We found that very few studies which emphasize on manual therapy (Myofascial release and mobilization techniques). All the interventions are try to manage some of the components of FM like pain, Depression, quality of life and the results demonstrate that none of the interventions are superior to others. So, the most urgent requirement for further research is to establish the effective treatment approaches which resolve all the components in FM like pain sensitivity, psychosocial components and quality of life.

Conclusion: there are numerous RCTs on the multimodal treatment approaches but most of the researches demonstrated the individual effects of their treatment techniques; we found no single treatment technique which resolves all the symptoms of FM because every study has its methodological limitations. We found lack in the literature on the combination of CBT with soft tissue releases; CBT with pharmacology; pharmacology with soft tissue releases, CBT with dry needling and mobilization with soft tissue releases. Therefore we suggest that the future studies could emphasize on these topics to resolve the widespread musculoskeletal pain sensitivity and psychosocial milieu and to improve quality of life on patients with FM.

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