



The Effectiveness of Cognitive-Behavioral, Mindfulness and Acceptance and Commitment Therapies to Improving the Psychological Symptoms of Patients with Multiple Sclerosis in Iran: Systematic Review and Meta-analysis

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Received 2022 May 10; Revised 2022 September 08; Accepted 2022 October 06.

Abstract

Context: Multiple sclerosis (MS) is a neurological disease in which the myelin lining the central nervous system is damaged and often occurs between the ages of 20 and 40. In addition to loss of motor, sensory, and cognitive function, patients with MS also experience related symptoms such as depression, anxiety, stress, fatigue, and pain.

Objectives: The aim of this study was to systematically and meta-analyze the effectiveness of cognitive-behavioral, mindfulness and acceptance and commitment (CMAC) therapies to improving the psychological symptoms of patients with multiple sclerosis in Iran.

Methods: The study was conducted using preferred reporting items for systematic reviews and meta-analysis. This study examined articles published from the beginning until November 20, 2021 in Persian and English on cognitive and behavioral interventions performed in Iran, in order to influence psychological symptoms for people with multiple sclerosis. Articles relevant to research were screened in external (Google Scholar, PubMed, Scopus, Science Direct, Web of Science) and internal databases (Sid, Magiran, Ganj, Irandoc, Civilica). The quality of the included RCTs was assessed using the Cochrane guideline risk of bias tool. The results were expressed in terms of mean difference (MD) and the corresponding 95% confidence interval. Data analyses were performed by RevMan5.4.

Results: In the first stage of the search, 792 articles were obtained. After reviewing the titles of the articles, 701 articles were discarded due to irrelevance and duplication and 91 articles remained. Finally, 21 studies were selected by reviewing the abstracts and considering the inclusion criteria. Compared with the control group, the standardized mean difference (SMD) estimate depression was 1.60 (2.27, 0.93), for anxiety 0.49 (0.80, 0.19), for stress 0.97 (1.70, 0.23) and for fatigue 0.19 (2.75, 1.25) had a positive effect; But no significant effect on pain reduction equal to 0.49 (2.21, 1.23) was not found.

Conclusions: The meta-analysis in the posttest showed that the effects of CMAC were considerable on reducing depression, anxiety, stress, and fatigue, but the effects were not notable for pain mitigation. Future high quality studies with follow-up evaluations are needed to support the effects of CMAC on reducing symptoms in people with multiple sclerosis and to evaluate the interventional features that enhance and maintain the effects.

Keywords: Acceptance and Commitment Therapy, Cognitive-Behavioral Therapy, Meta-analysis, Mindfulness, Multiple Sclerosis, Systematic Review

1. Context

Multiple sclerosis (MS) is a neurological disease in which the CNS-covering myelin is damaged. Based on the data obtained from the Iranian MS Association, around 50,000 patients, i.e. 60 to 70 patients per every 100,000 people in Iran's population have this disease (1).

Persons with MS (PwMS) in addition to losing motor, sensory, and cognitive functions, also experience associated symptoms including depression, anxiety, stress, fatigue, and pain (2,3). Thus, PwMS confront numerous physical, mental, and emotional problems on a daily basis (4). Although in the initial stages of the disease, the physical

problems are usually limited, patients experience anxiety and psychological distress (5, 6). Based on different studies, 48% of patients experience stress, anxiety, and depression within the first year following diagnosis (7, 8). Depression with prevalence of 50% is another common comorbid disease among PwMS (9). Fatigue is another common symptom of this disease (10) which is experienced by around 80% of patients in its early stages (11). In a large epidemiological study based on a semi-structured interview, it was reported that 43% of PwMS experience at least one type of pain (12). The symptoms can be controlled to some extent by pharmacotherapy, though considering the problems and side effects resulting from drugs, use of nonpharmacological methods that can mitigate the negative symptoms seems logical. In recent years, nonpharmacological methods such as cognitive behavioral therapy, mindfulness, as well as acceptance and commitment (ACT) therapy have gained the interest of patients including PwMS, and are known as complementary treatment. These treatments have a holistic nature which are used for enhancing the psychological and physical welfare of patients.

Cognitive behavioral therapy (CBT) is used for management of symptoms and increase of psychosocial consequences for individuals suffering from chronic diseases (13, 14). The goal of CBT is to correct wrong interpretations, giving a sense of control over life, increasing positive as well as constructive self-talks, and improving coping strategies (15). There is evidence suggesting that CBT may be useful in mitigating depression, anxiety, fatigue, disability, problems related to cognition, in addition to improving the quality of life of PwMS (13, 16). Meanwhile, other therapies of this field which are called third wave therapies are mindfulness plus acceptance and commitment therapy. Mindfulness refers to "attention to a special targeted method at the present with no judgment" (17). Studies have shown that training mindfulness is associated with decreased anxiety, depression, stress, pain, as well as enhanced positive psychological functions (17, 18). Acceptance and commitment therapy (ACT) refers to improving psychological flexibility and is defined as the ability of facing challenging experiences in an open and informed way as well as changing the individual behaviors for participation in valuable activities (19). In acceptance-based therapies, unlike many other treatments, no special value or lifestyle is imposed to the person; rather in these treatments the clients make decisions about change based on their own system of values (20). The effectiveness of ACT has been confirmed for mitigating the depression, anxiety, stress, fatigue, and pain in PwMS (21-23). Previous meta-analyses for PwMS have been performed with a limited range of mindfulness-based interventions (24), which have not covered different forms of interventions including CBT, mindfulness-based stress

mitigation approach, ACT, or a wide range of symptoms. Meanwhile, this meta-analysis is only specific to the interventions performed for PwMS in Iraq and so far no systematic review covering meta-analyses has been performed on PwMS in Iran.

2. Objectives

The aim of this study is to summarize, evaluate, and quantify the findings of controlled clinical trials on psychological interventions that are based on CBT, mindfulness, and ACT for the symptoms of PwMS in Iran.

3. Methods

3.1. Sources of Information and Search Methods

This is a meta-analysis of randomized trials involving the effectiveness of cognitive-behavioral, mindfulness and acceptance and commitment (CMAC) on psychological syndrome of pwMS in Iran. In order to find the relevant published studies, search was performed from the beginning of 20 November 2021 across both Iranian databases (Sid, Magiran, Irandoc, Civilica, Iranmedex) and foreign ones (Web of Sciences, PubMed Cochrane Library Scopus, Google Scholar). The key search terms associated with interventions and the population (MS) were combined to identify the relevant literature. The search was done through both Persian and English keywords including cognitive behavioral therapy, acceptance and commitment therapy, mindfulness, dialectical behavioral therapy, clinical trial, multiple sclerosis, MS, anxiety, depression, stress, pain, fatigue, and systematic review. Search and investigation of the eligible studies were performed by two independent researchers in terms of the inclusion criteria along with methodological quality assessment of the chosen studies.

3.2. The Selection Criteria of Studies

Initially, the abstract of papers was examined. Then, based on the inclusion criteria, the full text of the papers was inspected. The papers with these features were chosen for this meta-analysis: (1) the study should have been a randomized clinical trial (RCT) with pretest and posttest with control group; (2) the participants in the study should have had MS regardless of age, gender, types, and intensity of symptoms; (3) the study should have had reported pretest and posttest results in symptoms including depression, anxiety, stress, fatigue, or pain among PwMS; (4) the outcomes should have been evaluated using criteria with tested or reported psychometric features; (5) the study should have been done in Iran and published in a credible journal.

3.3. Measuring the Effect

The reported mean, standard deviation (SD), and sample size of the intervention plus control groups in studies were introduced in an Excel file and then inputted into RevMan 5.4.1 software for meta-analysis. The standardized mean difference (SMD) with confidence interval of 95% was used as a summary statistic for measuring the effect of intervention to calculate the outcomes measured by various assessment tools (25). In order to incorporate the heterogeneity of studies resulting from the variety in participants and interventions, weighting of studies was done based on the sample size and experimental errors, random effects model with inverse variance method (26).

4. Results

Overall, 792 papers were identified across databases (Figure 1). The search results of different databases were merged using EndNote software and similar studies were removed. After eliminating 701 irrelevant studies, 91 papers were screened based on the title and abstract. After reading the full text, other papers were excluded because of the reasons mentioned in Figure 1. Eventually, 21 papers fulfilling the inclusion criteria were chosen for the present review.

4.1. The Characteristics of Included Studies

The main characteristics of 21 eligible RCTs are summarized in Table 1. The included interventions were as follows: mindfulness-based stress reduction (MBSR) four studies (27-30), ACT five studies (22, 23, 31-33), CBT eight studies (31, 34-38), MBSR and CBT four studies (39-44). Out of 21 studies, in 20 of them the sessions had been held as in person (21-23, 27-41, 43), and in one study it had been done using Telegram application (42). Fifteen studies had been done as 8-session, four as 10-session, and three as 9-session studies. The minimum sample size was 20 and maximum was 70 with the mean of 36.72. Four studies had been conducted in Tehran (33, 35, 42, 43), four in Isfahan (22, 23, 36, 45), and others in different cities of Iran. Out of the studies, in seven of them, the gender of patients was unspecified (22, 27, 30, 34, 35, 40, 41). In six studies, the age of patients had not been mentioned (32, 34, 36, 40, 42, 44), and in other studies the mean age of the patients was 35.06 years. The type of MS had not been mentioned in any of the studies.

4.2. The Results of Risk of Bias (ROB) Assessment

Two authors separately evaluated the risk of bias based on Cochrane guideline. Assignment concealment and bias of reporting were evaluated as low risk in 70% of studies, and unknown bias in 30%. In all studies out of seven

domains, the domain related to blinding of participants and personnel in about 90% of the included clinical trials was evaluated as unknown risk of bias (RoB), as these studies had not reported sufficient information for judgment about blinding of participants and personnel. The bias of random sequence generation was evaluated as low risk in 20% of studies (23, 29, 31, 33, 44), and as unknown risk in 75% of studies (Figures 1 and 2).

4.3. The Results of Meta-analysis of Effects

4.3.1. Effects of CMAC on Depression

The first meta-analysis in which 10 clinical trials (181 participants) was investigated, SMD using the random effects model was 1.60 with confidence interval 95% (0.93, 2.27). Since the confidence interval did not cover zero, it suggests strong evidence of the positive effect of the therapy. I^2 which is a criterion of heterogeneity representing the percentage of variance across studies (25) was 86%, indicating that 86% variance in estimating the effect of therapy was due to real differences of studies (heterogeneity) and only 14% was because of chance (Figure 3).

4.3.2. Effects of CMAC on Anxiety

The meta-analysis on 12 studies and the largest sample size (187 participants) showed the effect of CMAC on anxiety reducing in the posttest in comparison to control groups (SMD = 0.49, 95% CI = [0.19, 0.80]) (Figure 4).

4.3.3. Effects of CMAC on Stress

The meta-analysis on six clinical trials (125 participants) indicated that the overall effect of CMAC on stress reducing in the posttest (SMD = 0.97, 95% CI = [0.23, 1.70]) was statistically significant in comparison to the control groups (Figure 5).

4.3.4. Effects of CMAC on Fatigue

The effects of CMAC on reducing the fatigue symptoms were examined in seven studies (177 participants). This meta-analysis revealed the effect of CMAC on reducing fatigue in the posttest in comparison to the control groups (SMD = 0.19, 95% CI = [1.25, 2.57]) (Figure 6).

4.3.5. The Effects of CMAC on Pain

The meta-analysis on four clinical trials (75 participants) showed that the total effect of CMAC on pain reducing was not statistically significant in the posttest (SMD = 0.49, 95% CI = [1.23, 2.21]) compared to the control groups (Figure 7).

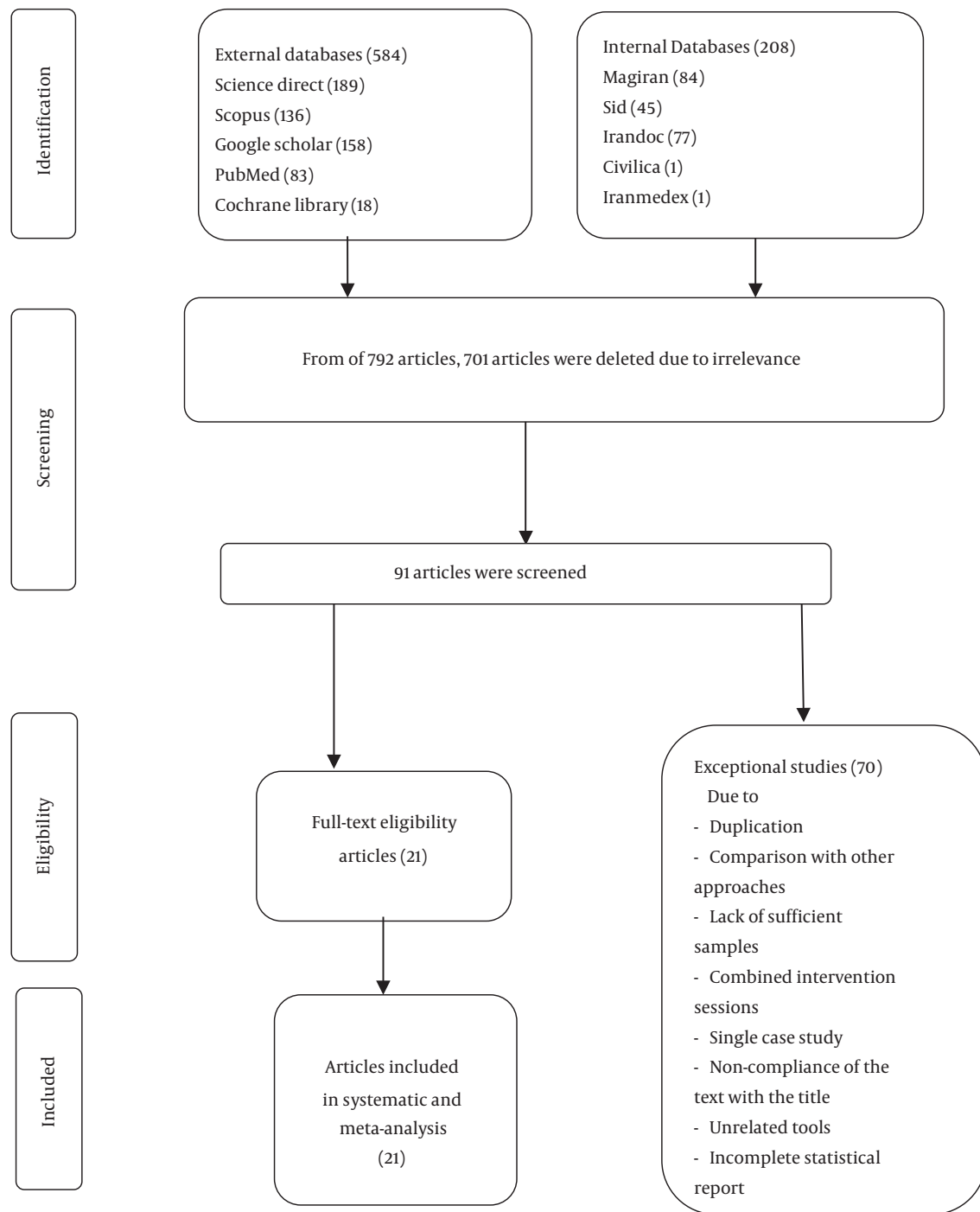


Figure 1. Levels of search and selection of articles (flow diagram)

5. Discussion

This systematic review and meta-analysis evaluated 21 clinical trials evaluating the effects of CMAC on depres-

sion, anxiety, stress, fatigue, and pain of PwMS. The meta-analysis in the posttest showed that the effects of CMAC were considerable on reducing depression, anxiety, stress,

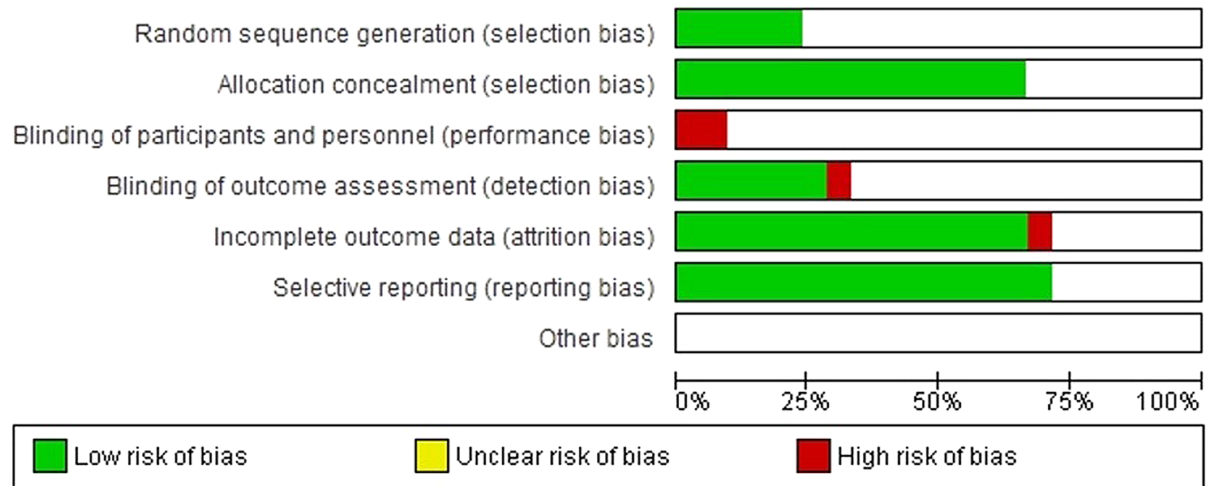


Figure 2. The diagram of risk of bias

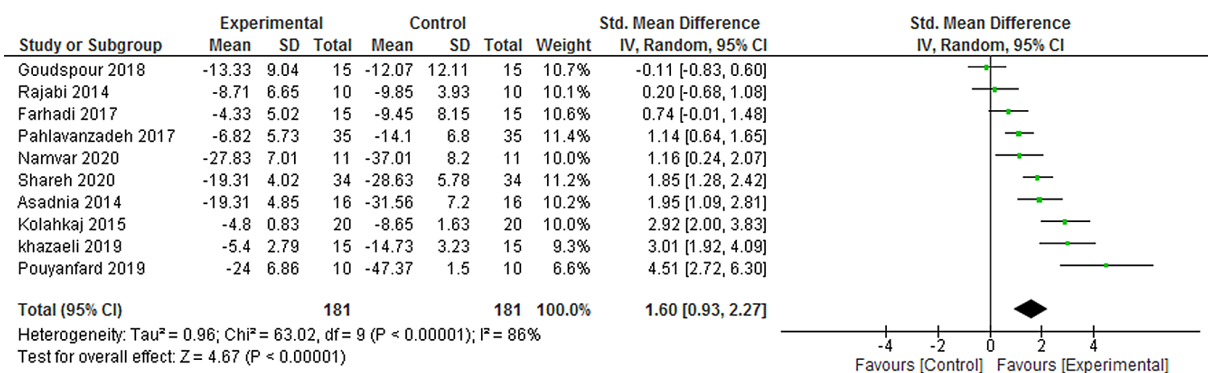


Figure 3. Forest plot of effects of CMAC on depression

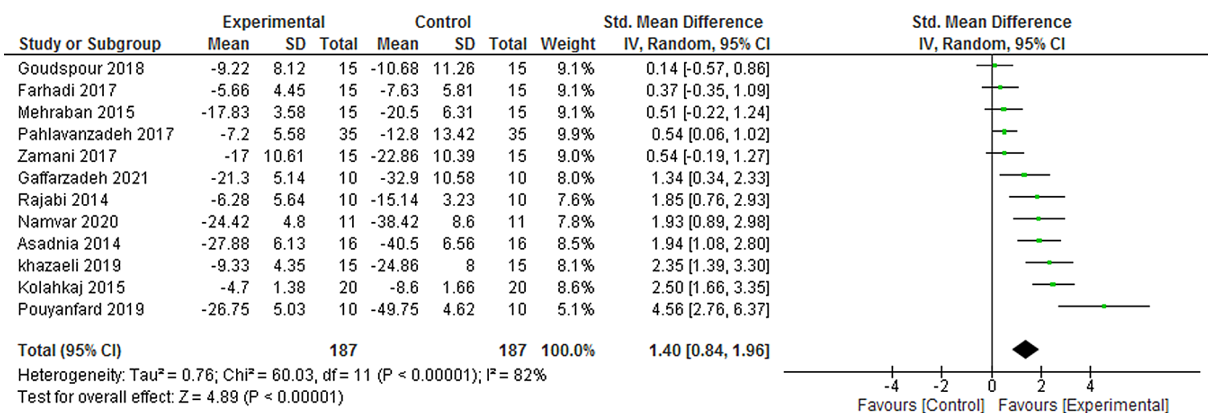


Figure 4. Forest plot of effects of CMAC on anxiety

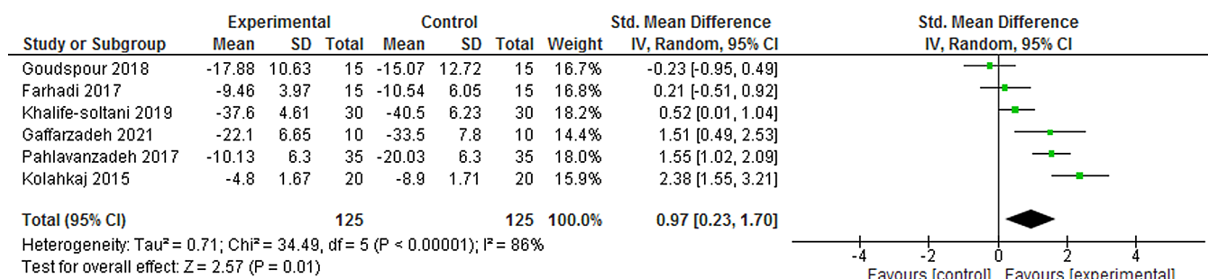


Figure 5. Forest plot of effects of CMAC on stress

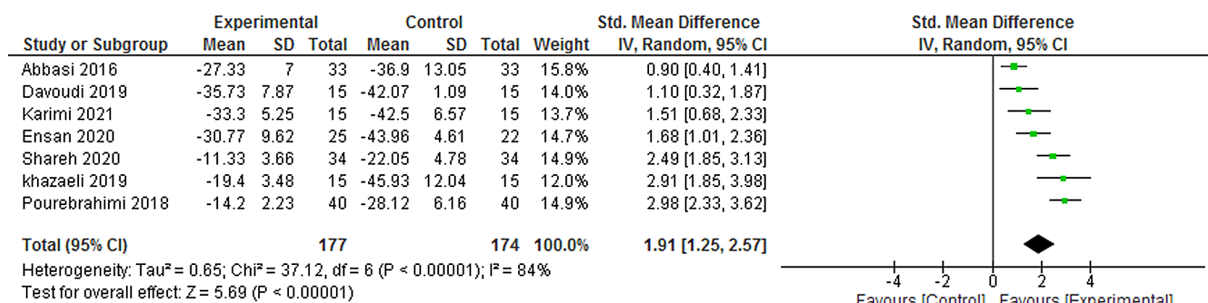


Figure 6. Forest plot of effects of CMAC on fatigue

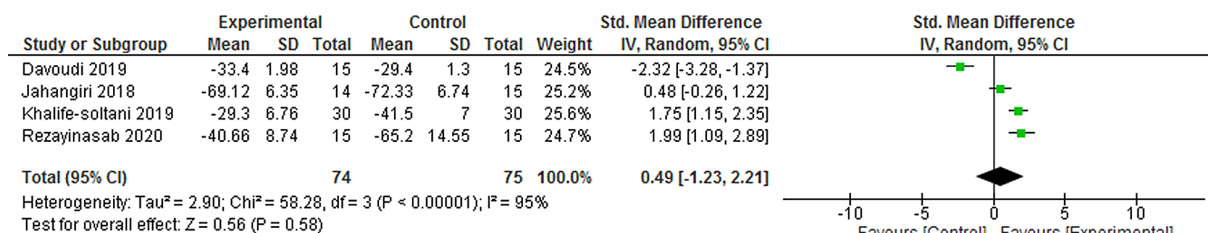


Figure 7. Forest plot of effects of CMAC on pain

and fatigue, but the effects were not notable for pain mitigation. The findings of this meta-analysis have been in line with previous meta-analysis findings for other populations, as they also reported the effects of CMAC on alleviating the symptoms of depression, anxiety, stress, fatigue, and pain. A meta-analysis on seven clinical trials showed considerable effect of CBT on mitigating the depression symptoms of PwMS posttest (46). Van Kessel et al. (47) compared CBT and relaxation therapies, and found that CBT lead to more significant improvement in the extent of fatigue, depression, anxiety, and stress of PwMS.

In interpreting the effectiveness of CBT, it can be stated that with increasing the awareness of patients about negative thoughts, cognitive errors, and with emphasis on ac-

tive coping strategies such as attempts for doing tasks, in spite of presence of symptoms and ignoring them, the severity of psychological symptoms would diminish. This approach by correcting cognitive errors of the patient allows them to liberate themselves from do's and don'ts as well as idealistic thoughts. Further, existence of behavioral strategies which are a step for activating the patient helps them not to drown in patient role and get engaged with daily activities as much as possible (48).

Studies performed over the past two decades have provided massive data on supporting the usefulness and efficiency of mindfulness-based therapies on mitigating stress, depression symptoms, improving cognitive executive functioning of PwMS brains, and even other physical

diseases such as chronic pain and cancer (49).

Han (24) in a meta-analysis by investigating 23 clinical trials reported the effects of mindfulness and acceptance-based therapies as significant on mitigating the symptoms of depression, anxiety, stress, and fatigue, but the effects for pain mitigation were not significant. Simpson et al. (50) observed the effect of mindfulness-based intervention on mitigating the symptoms of depression and anxiety from eight clinical trials, moderate effect on reducing stress from six clinical trials, and small effect on alleviating fatigue from seven clinical trials.

Carletto et al. (51) included 10 controlled clinical trials in meta-analyses, and found moderate effects of mindfulness-based interventions on mitigating the symptoms of depression and anxiety. In immediate posttest (nine studies for depression symptoms and eight studies for anxiety) as well as follow-up (seven studies for depression symptoms and six studies for anxiety), they observed large effects on stress mitigation in immediate posttest (five studies) and follow-up (four studies) as well as moderate effect on mitigating fatigue in the immediate posttest (eight studies) which diminished in the follow-up (six studies).

Training mindfulness is helpful in reducing mental preoccupations of individuals with negative self-assessment which leads to increased negative symptoms of patients. This technique trains patients to steer away from their self-critical cognitions, and observe them only with awareness with no judgment, without any need to separate from them, they would attach to them, and modify or control them (52).

Similar to and in line with the results of meta-analysis of efficacy of ACT on improving the PwMS symptoms, meta-analysis of Li et al. (53) also found that ACT had moderate to considerable effects on mitigating anxiety, depression, and stress, as well as improving hope in patients with cancer. Hughes et al. (54) also reported the effectiveness of ACT therapy on pain as trivial. ACT therapy is a therapeutic method in which individuals are trained to instead of mental and practical avoidance from disturbing thoughts and situations, have active and effective coping with thoughts and emotions, refrain from avoidance, and by establishing accessible goals and commitment to them, they cope with the condition (55). In explaining the findings of the present meta-analysis regarding the effectiveness of ACT therapy on mitigating the symptoms of PwMS, it can be stated that implementation of these therapeutic approach leads to development of psychological flexibility in PwMS, and this brings about changes in the suffering and mood of patients.

The studies included in the present meta-analysis were similar to previous studies of meta-analysis about CMAC

for other populations in terms of types, duration, and form of CMAC intervention (24, 47, 53, 54). Similar to the studies incorporated in the present paper, CMAC was presented mostly in group and in eight weekly sessions in the previous meta-analysis papers. However, the difference of this meta-analysis with previous meta-analysis was in assessment of CBT, ACT, and MBSR for reducing the symptoms of PwMS; in previous studies, only one of the mentioned therapies had been examined but in our review involved more studies compared with previous meta-analyses for individuals with MS. Another difference of this study with previous meta-analysis was in the region of conducting the included studies. These studies had been performed in Iran. Generally, no larger effects were found in the current study.

5.1. Strengths and Limitations

Nevertheless, several strengths and limitations have taken into account in this review. The strong point of this study was that it has been the first meta-analysis on the effectiveness of CMAC on mitigating the symptoms of PwMS in Iran. One limitation was use of available sampling, small sample size, and not having follow-up test in the assessed studies, which would affect its generalizability. Another limitation was that the studies were only limited to Iran. None of the studies had specified the type of MS. In this study, the effectiveness of three therapeutic methods was evaluated, which can impair data collection because of considerable scattering. A meta-analysis (24) on four clinical trials also showed that MBSR therapy for mitigating the pain symptoms in PwMS was not significant in comparison to the control group. The reason of this similarity can be small sample size and limited studies. Most of the studies chosen for the meta-analysis had no follow-up stage. The available studies include different types of MBSR, ACT, and CBT. It is suggested that future studies deal with examining the effects of DBT as well.

5.2. Implications for Clinical Practice and Future Research

This review found evidence for the effects of CMAC on the mood of patients with multiple sclerosis. It is recommended that these treatments be applied to improve the quality of life of pwMS. We recommended to investigate the effectiveness of each treatment approach separately in future meta-analysis studies. Also Future studies should ensure that rigorous of methodology, mainly adequate randomization, allocation concealment, intention-to-treat analysis, and blinding of at least outcome assessors.

5.3. Conclusions

Current evidence suggests that CMAC showed efficacious on depression, anxiety, stress and fatigue in pwMS,

however, no significant effect was found in the meta-analysis for effectiveness in reducing pain. Given the high prevalence and often associated mood symptoms in pwMS, the low cost of CMAC makes it a self-management option for reducing mood symptoms in pwMS. Future high-quality studies with follow-up evaluations are needed to support effects of CMAC on reducing symptoms common to pwMS and to examine intervention features that increase and maintain intervention effects.

Footnotes

Authors' Contribution: SH. M. and B. B. designed the study, analyzed the data, and wrote the manuscript. M. KH. participated in the design, analysis, interpretation of the data, and revision of the manuscript. M. A. was involved in the revision of the manuscript, including the clinical component of the study and data collection. MO. A. participated in the statistical analysis, interpretation of the data, and was involved in writing the manuscript. All authors had access to the data and participated in writing the manuscript. All authors read and approved the final version of the manuscript.

Conflict of Interests: The second and fourth authors of the article are the reviewer of the journal.

Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after its publication.

Funding/Support: This paper had not received any funding from any institute or organizations.

References

1. Etemadifar M, Sajjadi S, Nasr Z, Firoozeei TS, Abtahi SH, Akbari M, et al. Epidemiology of multiple sclerosis in Iran: a systematic review. *Eur Neurol*. 2013;**70**(5-6):356-63. [PubMed ID: 24192707]. <https://doi.org/10.1159/000355140>.
2. Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, Taylor BV, et al. Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. *Neurology*. 2014;**83**(11):1022-4. [PubMed ID: 25200713]. [PubMed Central ID: PMC4162299]. <https://doi.org/10.1212/WNL.0000000000000768>.
3. Marck CH, De Livera AM, Weiland TJ, Jelinek PL, Neate SL, Brown CR, et al. Pain in People with Multiple Sclerosis: Associations with Modifiable Lifestyle Factors, Fatigue, Depression, Anxiety, and Mental Health Quality of Life. *Front Neurol*. 2017;**8**:461. [PubMed ID: 28928713]. [PubMed Central ID: PMC5591834]. <https://doi.org/10.3389/fneur.2017.00461>.
4. Rae-Grant AD, Turner AP, Sloan A, Miller D, Hunziker J, Haselkorn JK. Self-management in neurological disorders: systematic review of the literature and potential interventions in multiple sclerosis care. *J Rehabil Res Dev*. 2011;**48**(9):1087-100. [PubMed ID: 22234713]. <https://doi.org/10.1682/jrrd.2010.08.0159>.
5. Giordano A, Granella F, Lugaesi A, Martinelli V, Trojano M, Confalonieri P, et al. Anxiety and depression in multiple sclerosis patients around diagnosis. *J Neurol Sci*. 2011;**307**(1-2):86-91. [PubMed ID: 21621796]. <https://doi.org/10.1016/j.jns.2011.05.008>.
6. Tan-Kristanto S, Kiropoulos LA. Resilience, self-efficacy, coping styles and depressive and anxiety symptoms in those newly diagnosed with multiple sclerosis. *Psychol Health Med*. 2015;**20**(6):635-45. [PubMed ID: 25588098]. <https://doi.org/10.1080/13548506.2014.999810>.
7. Jones KH, Ford DV, Jones PA, John A, Middleton RM, Lockhart-Jones H, et al. A large-scale study of anxiety and depression in people with Multiple Sclerosis: a survey via the web portal of the UK MS Register. *PLoS One*. 2012;**7**(7): e41910. [PubMed ID: 22860028]. [PubMed Central ID: PMC3408498]. <https://doi.org/10.1371/journal.pone.0041910>.
8. Nagaraj K, Taly AB, Gupta A, Prasad C, Christopher R. Prevalence of fatigue in patients with multiple sclerosis and its effect on the quality of life. *J Neurosci Rural Pract*. 2013;**4**(3):278-82. [PubMed ID: 24250159]. [PubMed Central ID: PMC3821412]. <https://doi.org/10.4103/0976-3147.118774>.
9. Feinstein A. Multiple sclerosis and depression. *Mult Scler*. 2011;**17**(11):1276-81. [PubMed ID: 22058085]. <https://doi.org/10.1177/1352458511417835>.
10. Krupp LB, Serafini DJ, Christodoulou C. Multiple sclerosis-associated fatigue. *Expert Rev Neurother*. 2010;**10**(9):1437-47. [PubMed ID: 20819014]. <https://doi.org/10.1586/ern.10.99>.
11. Fox RJ, Bacon TE, Chamot E, Salter AR, Cutter GR, Kalina JT, et al. Prevalence of multiple sclerosis symptoms across lifespan: data from the NARCOMS Registry. *Neurodegener Dis Manag*. 2015;**5**(6 Suppl):3-10. [PubMed ID: 26611264]. <https://doi.org/10.2217/nmt.15.55>.
12. Solaro C, Brichetto G, Amato MP, Cocco E, Colombo B, D'Aleo G, et al. The prevalence of pain in multiple sclerosis: a multicenter cross-sectional study. *Neurology*. 2004;**63**(5):919-21. [PubMed ID: 15365151]. <https://doi.org/10.1212/01.wnl.0000137047.85868.d6>.
13. Moss-Morris R, Dennison L, Landau S, Yardley L, Silber E, Chalder T. A randomized controlled trial of cognitive behavioral therapy (CBT) for adjusting to multiple sclerosis (the saMS trial): does CBT work and for whom does it work? *J Consult Clin Psychol*. 2013;**81**(2):251-62. [PubMed ID: 22730954]. <https://doi.org/10.1037/a0029132>.
14. Skokou M, Soubasi E, Gourzis P. Depression in multiple sclerosis: a review of assessment and treatment approaches in adult and pediatric populations. *ISRN Neurol*. 2012;**2012**:427102. [PubMed ID: 23097716]. [PubMed Central ID: PMC3477767]. <https://doi.org/10.5402/2012/427102>.
15. Wenzel A. Basic Strategies of Cognitive Behavioral Therapy. *Psychiatr Clin North Am*. 2017;**40**(4):597-609. [PubMed ID: 29080588]. <https://doi.org/10.1016/j.psc.2017.07.001>.
16. Dennison L, Moss-Morris R. Cognitive-behavioral therapy: what benefits can it offer people with multiple sclerosis? *Expert Rev Neurother*. 2010;**10**(9):1383-90. [PubMed ID: 20819010]. <https://doi.org/10.1586/ern.10.111>.
17. Kabat-Zinn J. Mindfulness-based stress reduction (MBSR). *Constr Hum Sci*. 2003;**8**(2):73-107.
18. Maxwell L, Duff E. Mindfulness: An Effective Prescription for Depression and Anxiety. *J Nurse Pract*. 2016;**12**(6):403-9. <https://doi.org/10.1016/j.nurpra.2016.02.009>.
19. Hayes SC, Pistorello J, Levin ME. Acceptance and Commitment Therapy as a Unified Model of Behavior Change. *Couns Psychol*. 2012;**40**(7):976-1002. <https://doi.org/10.1177/0011000012460836>.
20. Eifert GH, Forsyth JP, Arch J, Espejo E, Keller M, Langer D. Acceptance and Commitment Therapy for Anxiety Disorders: Three Case Studies Exemplifying a Unified Treatment Protocol. *Cogn Behav Pract*. 2009;**16**(4):368-85. <https://doi.org/10.1016/j.cbpra.2009.06.001>.
21. Davoodi M, Shamel L, Hadianfard H. The Effectiveness of Acceptance and Commitment Therapy on Chronic Fatigue Syndrome and Pain Perception in People With Multiple Sclerosis. *Iran J Psychiatry Clin Psychol*. 2019;**25**(3):250-65. <https://doi.org/10.32598/ijpcp.25.3.250>.
22. Khalifeh-Soltani FAS, Borhani M. The Effectiveness of Acceptance and Commitment Therapy on Pain Severity, Perceived Stress, and Aggression in Patients with Multiple Sclerosis in Isfahan, Iran. *Int J Body Mind Cult*. 2019;**6**(1):35-41. <https://doi.org/10.22122/ijbmc.v6i1.148>.

23. Rajabi S, Yazdkhasti F. [The Effectiveness of Acceptance and Commitment Group Therapy on Anxiety and Depression in Women with MS Who Were Referred to the MS Association]. *J Clin Psychol*. 2014;6(1):29–38. Perian. <https://doi.org/10.22075/jcp.2017.2152>.
24. Han A. Mindfulness- and Acceptance-Based Interventions for Symptom Reduction in Individuals With Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil*. 2021;102(10):2022–20310000. [PubMed ID: 33812883]. <https://doi.org/10.1016/j.apmr.2021.03.011>.
25. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. London: The Cochrane Collaboration; 2011, [updated March 2011]. Available from: <https://handbook-5-1.cochrane.org/>.
26. Haidich AB. Meta-analysis in medical research. *Hippokratia*. 2010;14(Suppl 1):29–37. [PubMed ID: 21487488]. [PubMed Central ID: PMC3049418].
27. Ensan N, Rahimian Boogar I, Talepasand S, Estilae F. The effectiveness of mindfulness-based stress reduction in fatigue severity among patients with multiple sclerosis. *Stud Med Sci*. 2020;31(2):137–45. Persian. <https://doi.org/10.32598/JAMS.22.5.56>.
28. Farhadi M, Pasandideh MM. [Mindfulness based cognitive therapy in reducing stress, anxiety, depression and increase self-efficacy in female patients with multiple sclerosis (MS)]. *Clin Psychol Personal*. 2020;15(2):7–15. Persian. <https://doi.org/10.22070/cpap.2020.2812>.
29. Kolahkaj B, Zargar F. Effect of Mindfulness-Based Stress Reduction on Anxiety, Depression and Stress in Women With Multiple Sclerosis. *Nurs Midwifery Stud*. 2015;4(4). e29655. [PubMed ID: 26835467]. [PubMed Central ID: PMC4733502]. <https://doi.org/10.17795/nmsjournal29655>.
30. Namvar M, Khorrami M, Noorollahi A, Pournemat M. [Effectiveness of Mindfulness-Based Stress Reduction (MBSR) Therapy on Anxiety and Depression Symptoms in Patients with Multiple Sclerosis (MS), Bojnurd, Iran]. *Psychol Except Individ*. 2020;10(39):179–200. Persian. <https://doi.org/10.22054/jpe.2021.45321.2037>.
31. Shareh H, Robati Z. [Effect of Cognitive-Behavioral Group Therapy on Pain Self-efficacy, Fatigue, Life Expectancy and Depression in Patients With Multiple Sclerosis: A Randomized Controlled Clinical Trial]. *Iran J Psychiatry Clin Psychol*. 2021;26(4):418–31. Persian. <https://doi.org/10.32598/jjpcp.26.3.225.11>.
32. Mami S, Tahmasebian H, Jahangiri MM. [The Effectiveness of Acceptance and Commitment Therapy on Reducing Intensity Pain in Patients with Multiple Sclerosis]. *Res Clin Psychol Couns*. 2022;8(2):116–27. Persian.
33. Zamani E, Moatamed A, Bakhtiar M. The Effectiveness of Acceptance and Commitment Therapy on Depression in Multiple Sclerosis. *New Trends Issues Proc Humanit Soc Sci*. 2017;3(2):53–8. <https://doi.org/10.18844/gjhss.v3i2.1599>.
34. Ghaffarzadeh M, Aghdasi A. Cognitive-behavioral therapy on the anxiety, stress and despair of MS patients. *Iran J Health Psychol*. 2021;4(3):67–76. <https://doi.org/10.30473/ijohp.2021.53953.1100>.
35. Karimi M, Qaderi Bagajan K, Naghsh Z, Ghazaghi T, Malekzadeh L. [Comparison of the effectiveness of acceptance and commitment therapy and cognitive behavior therapy on fatigue in multiple sclerosis (MS) patients]. *Sci J Kurdistan Univ Med Sci*. 2021;26(4):117–31. Persian. <https://doi.org/10.52547/sjku.26.4.117>.
36. Pahlavanzadeh S, Abbasi S, Alimohammadi N. The Effect of Group Cognitive Behavioral Therapy on Stress, Anxiety, and Depression of Women with Multiple Sclerosis. *Iran J Nurs Midwifery Res*. 2017;22(4):271–5. [PubMed ID: 28904538]. [PubMed Central ID: PMC5590355]. <https://doi.org/10.4103/1735-9066.212987>.
37. Rezaeinasab F, Borjali A, Taghdisi M. [The Effectiveness of Cognitive-Behavioral Group Therapy on Pain Perception in Women with Multiple Sclerosis (MS)]. *Women Stud*. 2020;11(31):65–82. Persian. <https://doi.org/10.30465/ws.2020.5175>.
38. Purbahrami N, Ahangarzadeh Rezaei S, Khalkhali H. [The effect of cognitive-behavioral interventions for fatigue severity in people with multiple sclerosis]. *Nurs Midwifery J*. 2019;17(1):41–51. Persian.
39. Abbasi S, Pahlavanzadeh S, Alimohammadi N. [The effect of cognitive behavioral therapy on the severity of fatigue in women with multiple sclerosis: a Randomized Controlled Trial study]. *J Clin Nurs Midwifery*. 2016;5(2):40–51. Persian.
40. Asadnia S, Mosarrezaii Aghdam A, Saadatmand S, Sepehrian Azar F, Torabzadeh N. [Examining the effectiveness of cognitive – behaviour therapy on improving depression and decreasing anxiety symptoms of multiple sclerosis patients (ms)]. *Stud Med Sci*. 2015;25(11):1023–32. Persian.
41. Ghodspour Z, Najafi M, Rahimian Boogar I. Effectiveness of Mindfulness-Based Cognitive Therapy on Psychological Aspects of Quality of Life, Depression, Anxiety, and Stress Among Patients With Multiple Sclerosis. *Pract Clin Psychol*. 2018;6(4):215–22. <https://doi.org/10.32598/jpcp.6.4.215>.
42. Khazaeili M, Zargham Hajebi M, Mohamadkhani P, Mirzahosseini H. The Effectiveness of Mindfulness-Based Internet Intervention on the Anxiety, Depression, and Fatigue of the Patients With Multiple Sclerosis. *Pract Clin Psychol*. 2019;7(42):137–46. <https://doi.org/10.32598/jpcp.7.2.137>.
43. Mehraban S, Bahmani B, Azimian M, Rezasoltani P. The Effectiveness of Cognitive-Behavioral-Based Stress Management Training on Anxiety in Female MS Patients. *Iran Rehabil J*. 2015;13(3):49–53.
44. Pouyanfard S, Mohammadpour M, ParviziFard AA, Sadeghi K. Effectiveness of mindfulness-integrated cognitive behavior therapy on anxiety, depression and hope in multiple sclerosis patients: a randomized clinical trial. *Trends Psychiatry Psychother*. 2020;42(1):55–63. [PubMed ID: 32321085]. <https://doi.org/10.1590/2237-6089-2018-0105>.
45. Abasii S, Bagheri Panah M, Amirfakhraei A, Khoroshi M, Bidaghi F. [The Effectiveness of Mindfulness-Based Cognitive Therapy on Depression and Emotion Regulation Strategies in Patients with Multiple Sclerosis]. *Iran J Rehabil Res Nurs*. 2019;6(2):90–9. Persian.
46. Hind D, Cotter J, Thake A, Bradburn M, Cooper C, Isaac C, et al. Cognitive behavioural therapy for the treatment of depression in people with multiple sclerosis: a systematic review and meta-analysis. *BMC Psychiatry*. 2014;14:5. [PubMed ID: 24406031]. [PubMed Central ID: PMC3890565]. <https://doi.org/10.1186/1471-244X-14-5>.
47. van Kessel K, Moss-Morris R, Willoughby E, Chalder T, Johnson MH, Robinson E. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Psychosom Med*. 2008;70(2):205–13. [PubMed ID: 18256342]. <https://doi.org/10.1097/PSY.0b013e3181643065>.
48. Leahy RL, Holland SJ, McGinn LK. *Treatment plans and interventions for depression and anxiety disorders*. New York: Guilford Press; 2011.
49. Nejati V, Amini R, Zabihzadeh A, Masoumi M, Maleki G, Shoaie F. [Mindfulness as effective factor in quality of life of blind veterans]. *Iran J War Public Health*. 2011;3(3):1–7. Persian.
50. Simpson R, Simpson S, Ramparsad N, Lawrence M, Booth J, Mercer SW. Mindfulness-based interventions for mental well-being among people with multiple sclerosis: a systematic review and meta-analysis of randomised controlled trials. *J Neurol Neurosurg Psychiatry*. 2019;90(9):1051–8. [PubMed ID: 3196913]. <https://doi.org/10.1136/jnnp-2018-320165>.
51. Carletto S, Cavallera C, Sadowski I, Rovaris M, Borghi M, Khoury B, et al. Mindfulness-Based Interventions for the Improvement of Well-Being in People With Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Psychosom Med*. 2020;82(6):600–13. [PubMed ID: 32541543]. <https://doi.org/10.1097/PSY.0000000000000819>.
52. Koszycki D, Bengner M, Shlik J, Bradwejn J. Randomized trial of a meditation-based stress reduction program and cognitive behavior therapy in generalized social anxiety disorder. *Behav Res Ther*. 2007;45(10):2518–26. [PubMed ID: 17572382]. <https://doi.org/10.1016/j.brat.2007.04.011>.
53. Li H, Wu J, Ni Q, Zhang J, Wang Y, He G. Systematic Review and Meta-Analysis of Effectiveness of Acceptance and Commitment Therapy in Patients With Breast Cancer. *Nurs Res*. 2021;70(4):E152–60. [PubMed ID:

- 33492055], <https://doi.org/10.1097/NNR.0000000000000499>.
54. Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and Commitment Therapy (ACT) for Chronic Pain: A Systematic Review and Meta-Analyses. *Clin J Pain*. 2017;**33**(6):552-68. [PubMed ID: 27479642]. <https://doi.org/10.1097/AJP.0000000000000425>.
55. Ristevska-Dimitrovska G, Filov I, Rajchanovska D, Stefanovski P, Dejanova B. Resilience and Quality of Life in Breast Cancer Patients. *Open Access Maced J Med Sci*. 2015;**3**(4):727-31. [PubMed ID: 27275317]. [PubMed Central ID: PMC4877917]. <https://doi.org/10.3889/oamjms.2015.128>.

Table 1. Characteristics of the Included Studies

Authors (City)	Study Design	Study Period	Sample Size; Mean Age; Female (%); MS Types	Intervention/Treatment	Outcomes	Result
Pouyanfar, et al. (Kerman) (44)	Semi-experimental research with pretest posttest design and control group	Two-hour 8 sessions	20; NR; 60%; NR	Mindfulness-integrated cognitive behavior (MICBT)	Anxiety and depression	MICBT significantly decreased depression and anxiety
Farhadi and Pasandideh (Rasht) (28)	Semi-experimental research with pretest posttest design and control group	Two-hour 8 sessions	30; NR; 100%; NR	Mindfulness-based stress reduction (MBSR)	Depression, anxiety and stress	MBSR significantly decreased depression, anxiety and stress
Khalifeh-Soltani and Borhani (Isfahan) (22)	Semi-experimental research with pretest posttest design and control group	8 sessions	60; 53.40; NR; NR	Acceptance and commitment therapy (ACT)	Pain and stress	ACT significantly reduction pain and stress
Ensan et al. (Neyshabur) (27)	Semi-experimental research with pretest posttest design and control group	8 sessions	47; 38.8; NR; NR	Mindfulness-based stress reduction (MBSR)	Fatigue	MBSR significantly improved fatigue
Mehraban et al. (Tehran) (43)	Semi-experimental research with pretest posttest design and control group	10 sessions (1 session per week, each 120 minute)	30; 29.20; 100%; NR	Cognitive-behavioral-based stress management	Anxiety	Cognitive-behavioral-based stress management training effective anxiety reduction
Zamani et al. (Tehran) (33)	Quasi-experimental research with pretest posttest design and control group	8 sessions (twice a week)	30; 31.36; 83%; NR	ACT	Anxiety	ACT significantly reduction anxiety
Mami et al. (Arak) (32)	Semi-experimental research with pretest posttest design and control group	8 sessions	29; NR; 62%; NR	ACT	Pain	ACT significantly reduction Pain
Ghodspour et al. (Semnan) (41)	Quasi-experimental research with pretest-postes and control group	8 two-hour sessions	3036; NR; NR	Mindfulness-based cognitive therapy (MBCT)	Depression, anxiety, and stress	MBCT significantly decreased depression, anxiety and stress
Rajabi and Yazdkhasti (Isfahan) (23)	Quasi-experimental with pre-test, post-test and control group	Two-hour 8 sessions	20; 34; 100%; NR	ACT	Anxiety and depression	ACT significantly reduction anxiety and depression
Karimi et al. (Tehran) (35)	Semi-experimental research with pretest posttest design and control group	10 sessions	30; NR; 100%; NR	CBT	Fatigue	CBT had effect on reducing the severity of fatigue
Kolahkaj and Zargar (Ahvaz) (29)	Semi-experimental research with pretest posttest design and control group	Two-hour 8 sessions	48; 25.3; 100%; NR	MBSR	Anxiety, depression and stress	MBSR significantly reduction anxiety, depression and stress
Pahlavanzadeh et al. (Isfahan) (36)	Quasi-experimental research with pretest-postes and control group	8 90-minute group sessions (a session per week)	70; NR; 100%; NR	CBT	Stress, Anxiety, and depression	CBT significantly reduction stress and anxiety, depression
Purbahrami et al. (Urmia) (38)	Quasi-experimental research with pretest-postes and control group	Nine sessions of one and a half hours	30; 30; 72%; NR	CBT	Stress, anxiety, and depression	CBT decreased stress, anxiety, and depression

Khazaieili et al. (Tehran and Qom) (42)	Quasi-experimental with pre-test, post-test and control group	Eight 2-h sessions	30; NR; 100%; NR	Mindfulness based internet intervention (MBI)	Anxiety, depression, and fatigue	MBI reducing anxiety, depression, and fatigue
Shareh and Robati (Kazavi Khorasan) (31)	Quasi-experimental with pre-test, post-test and control group	Ten 2-hour sessions	68; 35.22; 32%; NR	CBT	Fatigue, and depression	CBT reducing fatigue and depression
Rezaeinasab et al. (Kara) (37)	Semi-experimental research with pretest posttest design and control group	8 sessions of one and a half hours	30; 40; 100%; NR	CBT	Pain	CBT significantly reduction pain
Namvar et al. (Bojnourd) (30)	Semi-experimental research with pretest posttest design and control group	Eight 2-hour sessions	22; 39.5; NR; NR	MBSR	Anxiety, depression	MBSR significantly reduction anxiety, depression
Davoodi et al. (Ahvaz) (21)	Quasi-experimental with pre-test, post-test and control group	Eight 2-hour sessions	30; 34.95; 66%; NR	ACT	Fatigue and Pain	ACT significantly reduction fatigue and pain
Ghaifarzadeh and Aghdasi (Tehran) (34)	Quasi-experimental with pre-test, post-test and control group	10 sessions	20; NR; NR; NR	CBT	Stress and anxiety	CBT decreased stress and anxiety
Asadnia et al. (Urmia) (40)	Quasi-experimental with pre-test, post-test and control group	Fourteen 60-minute weekly sessions	32; NR; NR; NR	CBT	Anxiety and depression	CBT decreased anxiety and depression
Abbasi et al. (Isfahan) (39)	Semi-experimental research with pretest posttest design and control group	Eight 90-minute sessions	66; 33.47; 100%; NR	CBT	Fatigue	CBT decreased fatigue