Review Article

The impact of therapeutic education programs on the quality of life of patients with multiple sclerosis: Protocol of a systematic review

Ilham Raji[1,2], Ibtissam El Harch[3], Mohammed E. A. Ragala[4,5], Mohamed Berraho[3], Mohammed F. Belahsen[1,2]

Abstract:

The quality of life (QOL) of patients with multiple sclerosis (MS) is estimated to be poor compared to the general population. Its management is complex thus requiring openness to non-pharmacological approaches such as therapeutic education (TPE). However, there is an abundance of educational programs with several components and varying degrees of effectiveness. This protocol is developed with the objective to determine the impact of TPE programs on the QOL of MS patients. We will undergo research in PubMed, Web of Science, and Scopus to identify all eligible articles published between January 1st, 2007, and February 2022 evaluating the QOL. We will include any quantitative study design: Randomized Controlled Trials (RCTs), non-randomized controlled trials, non-randomized uncontrolled trials, and observational studies. The quality of these studies will be assessed by recommended tools. Two investigators will independently perform the data extractions and any disagreements will be resolved by other reviewers. A narrative synthesis will report results according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist guidelines to draw conclusions based on the totality of the evidence. These results will be summarized by characteristics of studies and programs and by effects on the QOL. This systematic review will provide practice guidance and evidence to effectively target the features and components of TPE programs, to effectively meet the specific needs of MS patients and thereby improve their QOL, and on the other hand to facilitate the appropriation of these programs by clinicians and researchers to optimize the management of MS.

Systematic review registration: PROSPERO CRD42022338651.

Keywords:

Multiple sclerosis, programs, quality of life, therapeutic education

[1]Laboratory of Epidemiology and Health Sciences Research, Faculty of Medicine, Pharmacy and Dentistry, Sidi Mohammed Ben Abdallah University, Fez, Morocco, [2]Department of Neurology, Hassan II University Hospital Center, Fez, Morocco, [3]Laboratory of Epidemiology, Clinical Research and Community Health, Faculty of Medicine, Pharmacy and Dentistry, Sidi Mohammed Ben Abdallah University, Fez, Morocco, [4]Laboratory of Natural Substances, Pharmacology, Environment, Modeling, Health and Quality of Life, Faculty of Sciences Dhar El Mahraz, Sidi Mohamed Ben Abdellah University, Fez, Morocco, [5]Department of Biology and Geology, Teachers Training College (Ecole Normale Superieure), Sidi Mohamed Ben Abdellah University, Fez, Morocco

Address for correspondence:
Dr. Ilham Raji, Laboratory of Epidemiology and Health Sciences Research, Faculty of Medicine, Pharmacy and Dentistry, Sidi Mohammed Ben Abdallah University, BP 1893, Road of Sidi Hrazem, Fez, 30070, Morocco.
E-mail: ilham.raji@usmba. ac.ma

Received: 09-03-2023
Accepted: 14-04-2023
Published: 31-08-2023

Introduction

According to the Multiple Sclerosis International Federation (MSIF), 2.8 million people worldwide are affected by pathology.[1] With a female, multiple sclerosis (MS) affects young adults, usually between the ages of 20 and 40 challenging the most productive years of their lives.[2,3] It is an autoimmune, chronic, and degenerative disease of the central nervous system that manifests itself by demyelination, multifocal inflammation, and axonal damage.[2] Its etiology remains unknown with a phenotype probably related to interference between genetic parameters considered complex and others environmental.[4,5] It is a disease with a progressive evolutionary character but which remains unpredictable[3,6] traditionally assuming disparate forms, in this case, the relapsing-remitting (RR), primary progressive (PP), and secondary progressive (SP) forms.[4]

Great uncertainty accompanies patients diagnosed with MS in all aspects of their lives.[7] Its most typical physical symptoms include monocular vision loss, sensory loss, ataxia, spasticity, chronic pain, sexual dysfunction, speech impairment, and fatigue.[2,8] At the same time, people with MS exhibit impaired psychological well-being, including an increased prevalence of depressive, anxiety, and mood disorders,[9] often subjectively perceived by patients as even more severe than physical symptoms, with detrimental consequences.[10] They often feel unable to cope with daily tasks and obstacles, leading to increased passivity and impaired social relationships.[11-13] The most common onset of MS in early adulthood means that in addition to personal and psychological problems, the disease also causes an emotional, social, and economic burden for the patient and the family[13-15] expressed needs, individual roles and coping styles are inevitably questioned.[16] Given this, the quality of life (QOL) can only be considered poor compared to the general population.[1,17,18]

Faced with the physical, psychosocial, and economic challenges and the chronic nature of the disease, the management of MS is complex,[19] thus requiring a biopsychosocial aspect,[3,20] where the medicinal approach is fully integrated with new therapeutic approaches to optimize daily activities, the QOL and the psychological well-being of individuals.[11] In this respect, therapeutic patient education (TPE) is emerging as a non-pharmacological intervention[21] and an imperative lever in the care pathway of individuals suffering from chronic pathologies[22,23] including MS.

According to the WHO definition in 1998, TPE is an ongoing process that " helps patients acquire or maintain the skills they need to manage their lives with a chronic pathology as well as possible. It is an integral and ongoing part of patient care. It includes organized activities, with psychosocial support, designed to make them aware of and informed aboutthedisease, thecare, the organization, the hospital procedures, and the behaviors related to health and the pathology".[22] Indeed, TPE programs improve understanding and decrease the occurrence of certain preventable complications and symptoms,[22] which can reduce the impact of MS on the patient's personal and/or social life.[24] In this sense, studies have shown an improvement in the QOL of MS patients after educational programs[25,26] thanks to good management of the disease. These patients certainly develop their sense of autonomy and self-efficacy.[24,27,28]

Indeed, TPE programs for MS patients have been widely offered for many years in a variety of formats and content. What is missing is the proper clarification of the key elements that frame these educational programs enabling these patients to acquire coping and self-management skills in their daily lives to optimize QOL. This is mainly due to the presence of complex programs[29] that are characterized by the absence of a standardized conceptual framework that can describe strategies for the promotion of educational management of MS patients[24] in order to positively change their behaviors.[30] Therefore, the effectiveness of these programs on QOL and MS symptoms is particularly debatable showing different effects and outcomes, and clinicians or researchers find difficulties in the appropriation of educational programs. This observation raises a great need for a precise description of the different dimensions that can influence and accompany the fluctuation of effectiveness from one TPE program to another to effectively meet the needs of patients.

To our knowledge, this systematic review is the first study to determine the impact of TPE programs specifically on the QOL of MS patients by identifying effectiveness factors associated with the characteristics and components of these programs that are important for future research.

The guiding question of this review is: Do TPE programs have an impact on the QOL of patients with MS?

Materials and Methods

This protocol is based on the PRISMA- P (Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols) checklist.[31] It has been submitted for registration to the PROSPERO International Prospective Registry of Systematic Reviews (PROSPERO) under the registration number: CRD42022338651

We will perform and report the results of this systematic review according to PRISMA guidelines.[32]

Eligibility criteria
The studies included in this review must meet all the inclusion criteria set out in the PICOS model (Patients, Intervention, Comparison, Outcome, and Study design type). All studies that meet the eligibility criteria will be selected for further review and synthesis. A summary of the eligibility criteria is reported in Table 1.

Population
This review will examine studies including patients who are older than 18 years old with a confirmed diagnosis of definite MS by a neurologist according to the revised McDonald criteria[33] regardless of the type of the pathology (relapsing-remitting (RR), secondary progressive (SP), primary progressive (PP)).[4]

Intervention
Although the literature expresses a great conceptual diversity in the definitions related to health education

Table 1: Summary of eligibility criteria for systematic review under the PICOS model

	Inclusion criteria	Exclusion criteria
Population	Studies including patients >18 years old with a diagnosis of definite MS	Studies including patients <18 years old
Intervention	TPE programs will be defined as any intervention that provides patients with either (a) information about disease-related symptoms and consequences and (b) learning and education about self-management strategies leading to behavior change	-Any intervention that does not meet the definition of a TPE program -Not TPE intervention
Comparison	Studies that compared QOL before and after a TPE program with or without the presence of a control group.	
Outcomes	-Articles that assessed QOL as either a primary or secondary outcome and assessed by a valid instrument -Assessment of QOL at two or more time points	Studies evaluating outcome measures other than QOL
Type of Studies	Any quantitative study design: Randomized Controlled Trials (RCTs), non-randomized controlled trials, non-randomized uncontrolled trials and observational studies. -Papers published between the January 1st, 2007 and February 2022	Pilot and feasibility studies, abstracts, systematic reviews, protocols or dissertations

programs such as self-management, self-management education, health education, and TPE. These concepts all lead to the same goal, which is the acquisition or maintenance of skills that ensure an optimized and healthy QOL where the patient takes effective ownership of their own disease.[22,34] Thus, in this systematic review, TPE programs will be defined as any structured intervention that allows patients to receive (a) information on disease-related symptoms and their consequences and (b) learning and education on self-management strategies[34] leading to a behavior change.[35] The goal remains the development or maintenance of cognitive, sensorimotor, and psycho-affective skills[36] through the active participation of the MS patient. These programs can be delivered individually, in groups, by telephone or online, in any setting or session length, and by any provider.

Comparison

We will include studies that compared the QOL before and after a TPE program with or without the presence of a control group.

Outcomes

We will include articles that assessed the QOL as a primary or secondary outcome. Only studies that consider this assessment at two or more time points (baseline, postintervention, follow-up) will be selected. The QOL of MS patients should be assessed by a valid instrument such as the Multiple sclerosis quality of life scale (MSQOL-54).[37]

Type of studies

Eligible articles must meet the following inclusion criteria: (a) any quantitative study design: Randomized Controlled Trials (RCTs), non-randomized controlled trials, non-randomized uncontrolled trials, and observational studies,(b) articles published between January 1st, 2007 and February 2022 determining the effect of TPE programs on the QOL of MS patients, (c) no restrictions on the language of publication of articles

will be made, (d) pilot and feasibility studies, abstracts, systematic reviews, protocols or dissertations will not be considered.

Information sources and search strategy

A systematic literature search will be performed in PubMed, Web of Science, and Scopus to identify all eligible articles. Combinations of MESH (Medical Subject Headings) terms and keywords will be used and combined with appropriate Boolean operators ("AND" and "OR") and truncations to search the three databases mentioned above. The following keywords will be maintained and extended with synonyms:

-"Multiple Sclerosis", "MS, "Chronic Progressive Multiple Sclerosis", "Relapsing Remitting Chronic", "Secondary-progressive multiple sclerosis", "Primary Progressive Multiple Sclerosis", "Relapsing-Remitting Multiple Sclerosis";

-Therapeutic Education", "Self-Management", "Patient Education", "Self-Care", "Therapeutic Patient Education", "Patient Therapy", "Education of the Patient", "Health Education", "Counselling/Methods", "Patient Information", "Patient Care Planning", "Self-Management", "Self-care", "Self-management Program";

-Quality of Life", "HRQL", "QOL", "Health-Related Quality of Life", "Quality of Life", "QOL tools", "SF-36", "WHOQOL", "DQOL", "well-being", "psychological well-being", "emotional well-being.

An initial search strategy in PubMed was developed: (("Multiple Sclerosis" [Mesh]) AND ("Self-Management" [Mesh] OR "Patient Education as Topic" [MeSH] OR "Self-Care" [Mesh]) AND "Quality of Life" [Mesh]. Then, the strategy will be adapted and modified according to the specific syntax of the other databases [Additional file N°1]. In parallel, additional searches will be performed manually in the reference

lists of the included primary studies and systematic reviews for a selection of other potentially relevant articles missing from the databases.

Selection process

All identified studies will be exported to an Excel spreadsheet to identify and remove duplicates. First of all, initial database searches will be performed by two research team members (IR) and (IE) to independently review the titles/abstracts of research articles obtained according to the eligibility criteria framed by the PICOS model. Afterward, the full texts will be selected and evaluated in contribution with another member (MER) to verify the accuracy of the data and lead to a comprehensive and thorough review of the articles. The final decision will be discussed within the group and the remaining discrepancies will be resolved by consensus. The reasons for exclusion will be reported and a PRISMA[32] flowchart will be produced based on the results of the selection process.

Data extraction and management

To document and organize the data of the eligible articles a data extraction form will be developed first on Microsoft Office Excel sheets and will be pilot tested by both reviewers (IR) and (IE). A final template will be established, and for each study, the following information will be extracted separately and grouped into tables:

Article characteristics (author, year, country), sample characteristics (size, age, gender, type of MS, EDSS: Expanded Disability Status Scale[38]), study characteristics (study design, tools for measuring the QOL, number of measures, total follow-up and summary of results).

We will use the systemic approach of TPE to frame and structure the content of educational programs in terms of four successive steps:[34,36]

1) Educational diagnosis which identifies the patient's needs, 2) personalized program which consists of negotiating with the patient the skills to be acquired either cognitive, sensorimotor, or psycho-affective skills,[36] 3) implementation of the program with subcategories: type of intervention, underlying approach/model/theory, pedagogical methods and tools and 4) the last step is the evaluation of the targeted skills/program course.

We will also report the description of the program delivery: aspect, duration, and frequency of sessions, provider/educator, and support sessions. Again, to optimize data consistency any disagreements will be resolved by discussion and consensus and if necessary two counselors (MER) and (MB) will be consulted.

Quality assessment

Critical assessment of the methodological quality and relevance of included studies to the research question will be systematically assessed by tools that are considered more appropriate for different types of studies[39] [Additional file N°2].

The Cochrane RoB 2.0 tool will be used to assess the risk of bias in RCTs.[40] It consists of five domains: 1) bias arising from the randomization process, 2) bias due to deviations from planned interventions, 3) bias due to lack of outcome data, 4) bias in outcome measurement, and 5) bias in the selection of reported outcomes. Possible judgments of risk of bias are Low risk, High risk, and some concerns.

For non-randomized controlled trials, the Risk of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool[41] will be used. The seven bais related to this tool are confounding, participant selection, intervention classification, intervention deviations, missing data, outcome measurement, and selection of reported outcome. The judgment of risk of bias assigned will be either "Low risk", "Moderate risk", "Serious risk" or "Critical risk".

For non-randomized, non-controlled studies, it is preferable to use[39] the National Institutes of Health (NIH) quality assessment tool for the before-after (Pre-Post) studies with no control group.[42] It includes 12 questions with a rating assigned to judge the quality of each study: Good/Fair/Poor.

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist[43] will be deployed for observational studies. The answers will vary between "Yes", "No", "Unclear" and "Not applicable". The number of positive answers by "YES" will be added to grant the studies either: "Low risk of bias", "Moderate risk of bias" or "High risk of bias".

Two reviewers (IR) and (IL) will independently assess the risk of bias and the methodological quality of each included study. Any disagreement will be resolved by discussion, and by consultation with an advisor (MB) if necessary.

Data synthesis

The summary tables produced will facilitate the comparison of the results obtained. On the basis of these results, a narrative and qualitative synthesis will be made to describe in a structured way: a) the characteristics of the studies, b) the characteristics of the different TPE programs, and c) their effects on the QOL of MS patients. We will also report the results of the quality assessment of the studies.

Discussion

Conclusions will be drawn from the results of the evaluation of the body of evidence from the comprehensive review of studies. In effect, we will analyze the components of the educational programs in relation to the outcomes of the QOL dimensions. The discussion will be related to the educational content and delivery modalities using a rigorous systems approach to TPE. The aim is to show the key points of these programs that will contribute to improve the QOL. The place of caregivers in the programs as well as the educational reinforcement sessions will also be shown.

Conclusion

This systematic review will provide practice guidance and evidence to effectively target the features and components of TPE programs, to effectively meet the specific needs of MS patients and thereby improve their QOL, and on the other hand to facilitate the appropriation of these programs by clinicians and researchers to optimize the management of MS.

Abbreviations
MS: Multiple Sclerosis- TPE: Therapeutic Education- QOL: Quality of Life- RCT: Randomized Control Trial- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses- CASP: The Critical Appraisal Skills Programme- JBI: The Joanna Briggs Institute - ROBINS-I: Risk of Bias In Non-randomized Studies - of Interventions- NIH: the National Institutes of Health - EDSS: Expanded Disability Status Scale- PRISMA- P: Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols- MESH: Medical Subject Headings.

Conflicts of interest
There are no conflicts of interest.

References

1. International Federation MS. Atlas of MS 3rd edition, PART 1: Mapping multiple sclerosis around the world key epidemiology findings. 2020. Available from: https://scleroseenplaques. ca/ressources/nouvelles/article/latlas-de-la-sp-presente-les-principaux-facteurs-faisant-obstacle-a-une-prise-en-charge-clinique-efficace-de-la-sclerose-en-plaques-dans-le-monde. [Last accessed on 2022 Apr 19].
2. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med 2000;343:938-52.
3. Pagnini F, Bosma CM, Phillips D, Langer E. Symptom changes in multiple sclerosis following psychological interventions: A systematic review. BMC Neurol 2014;14:222.
4. Comabella M, Khoury SJ. Immunopathogenesis of multiple sclerosis. Clin Immunol 2012;142:2-8.
5. Compston A, Coles A. Multiple sclerosis. Lancet 2008;372:1502-17.
6. Thomas PW, Thomas S, Hillier C, Galvin K, Baker R. Psychological interventions for multiple sclerosis. Cochrane Database Syst Rev 2006;2006:CD004431. doi: 10.1002/14651858. CD004431.pub2.
7. Simmons RD. Life issues in multiple sclerosis. Nat Rev Neurol 2010;6:603-10.
8. Reich DS, Lucchinetti CF, Calabresi PA. Multiple sclerosis. N Engl J Med 2018;378:169-80.
9. Boeschoten RE, Braamse AMJ, Beekman ATF, Cuijpers P, van Oppen P, Dekker J, *et al*. Prevalence of depression and anxiety in multiple sclerosis: A systematic review and meta-analysis. J Neurol Sci 2017;372:331-41.
10. Văcăraș V, Văcăraș V, Nistor C, Văcăraș D, Opre AN, Blaga P, *et al*. The influence of depression and anxiety on neurological disability in multiple sclerosis patients. Behav Neurol 2020; 2020:e6738645. doi: 10.1155/2020/6738645.
11. Strober LB. Quality of life and psychological well-being in the early stages of multiple sclerosis (MS): Importance of adopting a biopsychosocial model. Disabil Health J 2018;11:555-61.
12. Stoeckel K, Kasser SL. Spousal support underlying self-determined physical activity in adults with multiple sclerosis. Disabil Rehabil 2022;44:1091-7.
13. Masuccio FG, Gamberini G, Calabrese M, Solaro C. Imaging and depression in multiple sclerosis: A historical perspective. Neurol Sci 2021;42:835-45.
14. von Wyl V, Décard BF, Benkert P, Lorscheider J, Hänni P, Lienert C, *et al*. Influence of age at disease onset on future relapses and disability progression in patients with multiple sclerosis on immunomodulatory treatment. Eur J Neurol 2020;27:1066-75.
15. Kalb le DR, Rosalind C. Kalb P. Multiple Sclerosis: A Guide for Families. 3rd ed. New York: Demos Health; 2005.
16. Kouzoupis AB, Paparrigopoulos T, Soldatos M, Papadimitriou GN. The family of the multiple sclerosis patient: A psychosocial perspective. Int Rev Psychiatry 2010;22:83-9.
17. Peters S, Wilkinson A, Mulligan H. Views of healthcare professionals on training for and delivery of a fatigue self-management program for persons with multiple sclerosis. Disabil Rehabil 2019;41:2792-8.
18. Benedict RHB, Wahlig E, Bakshi R, Fishman I, Munschauer F, Zivadinov R, *et al*. Predicting quality of life in multiple sclerosis: Accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change. J Neurol Sci 2005;231:29-34.
19. Landtblom A-M, Lang C, Flensner G. The study circle as a tool in multiple sclerosis patient education in Sweden. Patient Prefer Adherence 2008;2:225-32.
20. Wagner EH, Bennett SM, Austin BT, Greene SM, Schaefer JK, Vonkorff M. Finding common ground: Patient-centeredness and evidence-based chronic illness care. J Altern Complement Med 2005;11(Suppl 1):S7-15.
21. Amatya B, Young J, Khan F. Non-pharmacological interventions for chronic pain in multiple sclerosis. Cochrane Database Syst Rev 2018;2018:CD012622. doi: 10.1002/14651858.CD012622.pub2.
22. World Health Organization. Therapeutic patient education: Continuing education programmes for health care providers in the field of prevention of chronic diseases: Report of a WHO working group, regional office for Europe, Copenhague. 1998. Available from: https://apps.who.int/iris/handle/10665/108151. [Last accessed on 2022 May 05].
23. D'Ivernois JF, Albano MG. Therapeutic patient education: A new deal for medical education? Med Teach 2010;32:945-6.

24. Demaille-Wlodyka S, Donze C, Givron P, Gallien P, ETP Sofmer Group. Self care programs and multiple sclerosis: Physical therapeutics treatment-literature review. Ann Phys Rehabil Med 2011;54:109-28.

25. Mathiowetz VG, Finlayson ML, Matuska KM, Chen HY, Luo P. Randomized controlled trial of an energy conservation course for persons with multiple sclerosis. Mult Scler 2005;11:592-601.

26. Mathiowetz V, Matuska KM, Murphy ME. Efficacy of an energy conservation course for persons with multiple sclerosis. Arch Phys Med Rehabil 2001;82:449-56.

27. Sabouri M, Shakibazadeh E, Mohebbi B, Tol A, Yaseri M, Babaee S. Effectiveness of an educational intervention using theory of planned behavior on health care empowerment among married reproductive-age women: A randomized controlled trial. J Educ Health Promot 2020;9:293.

28. Karimi N, Saadat-Gharin S, Tol A, Sadeghi R, Yaseri M, Mohebbi B. A problem-based learning health literacy intervention program on improving health-promoting behaviors among girl students. J Educ Health Promot 2019;8:251.

29. Kidd T, Carey N, Mold F, Westwood S, Miklaucich M, Konstantara E, *et al*. A systematic review of the effectiveness of self-management interventions in people with multiple sclerosis at improving depression, anxiety and quality of life. PLoS One 2017;12:e0185931. doi: 10.1371/journal.pone. 0185931.

30. Plow MA, Finlayson M, Rezac M. A scoping review of self-management interventions for adults with multiple sclerosis. PM R 2011;3:251-62.

31. PRISMA-P Group, Moher D, Shamseer L, Ghersi D, Liberati A, Petticrew M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1. doi: 10.1186/2046-4053-4-1.

32. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Open Med 2009;3:e123-30.

33. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, *et al*. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. Ann Neurol 2011;69:292-302.

34. Haute Autorité de Santé. Éducation thérapeutique du patient Définition, finalités et organisation. Haute Autorité de Santé. 2007. Available from: https://www.has-sante.fr/jcms/c_1241714/fr/education-therapeutique-du-patient-etp. [Last accessed on 2022 May 05].

35. Whitehead D. Health promotion and health education: Advancing the concepts. J Adv Nur 2004;47:311-20.

36. d'Ivernois J-F, Gagnayre R. Apprendre à Eduquer le Patient-Approche Pédagogique. 3éme éd. Paris-France: Editions Maloine; 2008.

37. Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. Qual Life Res 1995;4:187-206.

38. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). Neurology 1983;33:1444-52.

39. Ma LL, Wang YY, Yang ZH, Huang D, Weng H, Zeng XT. Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: What are they and which is better? Mil Med Res 2020;7:7.

40. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al*. RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ 2019;l4898. doi: 10.1136/bmj.l4898.

41. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, *et al*. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919. doi: 10.1136/bmj.i4919.

42. NIH. Study Quality Assessment Tools | NHLBI, NIH Before-After (Pre-Post) Studies With No Control Group. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. [Last accessed on 2022 May 23].

43. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, *et al*. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. JBI; 2020. doi: 10.46658/JBIMES-20-08.