Developing an Adapted EMDR Therapy for Major Depressive Disorder and Assessing its Efficacy through Online and Face-to-Face Modalities: A Protocol for Mixed Method Randomized Controlled Trial

Anwar Khan, Amalia bt Madihie, Salah Uddin Khan, Sajjad Haider, Maqsood Haider

Submitted to: JMIR Research Protocols
on: August 05, 2024

Table of Contents

Developing an Adapted EMDR Therapy for Major Depressive Disorder and Assessing its Efficacy through Online and Face-to-Face Modalities: A Protocol for Mixed Method Randomized Controlled Trial

Anwar Khan[1*] PhD; Amalia bt Madihie[2*] PhD; Salah Uddin Khan[3*] PhD; Sajjad Haider[3*] PhD; Maqsood Haider[4*] PhD

[1]Postgraduate Scholar, Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia. Kota Samarahan MY
[2]Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia Kota Samarahan MY
[3]King Salman Center for Disability Research, Riyadh 11614, Saudi Arabia Riyadh SA
[4]Department of Management Sciences, FATA University, Dara Adam Khel, Frontier region Kohat, Khyber Pakhtunkhwa, Pakistan Kohat PK
[*]these authors contributed equally

Corresponding Author:
Anwar Khan PhD
Postgraduate Scholar, Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia.
Postgraduate Scholar, Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia.
Kota Samarahan
MY

Abstract

Background: Major Depressive Disorder (MDD) is a psychiatric condition that globally ranks as the 24th leading cause of Disability-adjusted Life Years. Pakistan, a developing nation, grapples with poverty, resource inequality, population growth, and political instability, which may probable cause MDD among general population. Resultantly high prevalence of MDD in Pakistan in evident from the existing literature. Currently, evidence-based psychotherapies such as Eye Movement Desensitization and Reprocessing(EMDR) are widely available. However, EMDR originated in the United States, it might not be consistent with requirements of non-western countries, so it may require cross-cultural and methodological adaptations. Moreover, therapists have long practiced face-to-face EMDR, but recently, online EMDR modalities have emerged. Nonetheless, it is surprising that there is a dearth of research on both the adaptations of EMDR in Pakistan and its clinical efficacy, particularly its online modes have never been scientifically validated in Pakistan.

Objective: Considering lack of research on adaptations and clinical efficacy EMDR in Pakistan, the present study aims to develop a culturally and methodologically adapted EMDR therapy protocol for MDD in Pakistan, determine its treatment fidelity, and then clinically test its efficacy by administering it through the face-to-face and online modalities of EMDR therapy.

Methods: This study adopted a mixed-mode exploratory sequential Randomized Controlled Trial design in two phases. In the first phase, qualitative exploratory data will be collected, followed by quantitative data, to accomplish the adaptation process of the EMDR therapy protocol. In the second phase, a consecutive sample of 80 patients will be randomly allocated in a 1:1 ratio to face-to-face and online groups to determine the clinical efficacy of the adapted EMDR therapy protocol in both modalities. Symptoms related data will be collected through clinician administered scales during start, mid, end and follow-up stages of therapy. Data will be analyzed using a variety of qualitative and quantitative statistical techniques.

Results: This study has been approved by the Ethics Review Committees of Khushal Khan Khattak University Karak, Pakistan, and University Malaysia Sarawak, Malaysia. It is registered at ClinicalTrials.gov. The process of adapting the DeprEnd-EMDR Depression Protocol has already begun. Recruitment of patients for psychotherapy sessions will start in September 2024.

Conclusions: In conclusion, this study addresses significant research gaps concerning the adaptation and clinical efficacy of EMDR therapy in the Asian region, with a particular focus on its online modalities. By employing a rigorous research methodology, the results are likely to make substantial contributions by providing insights into both the adaptation and clinical

efficacy of EMDR therapy. This study will extend our understanding of the comparative effectiveness of EMDR therapy in the Asian region, offering valuable information on its applicability and impact in diverse, particularly non-Western, settings. Clinical Trial: ClinicalTrials.gov ID NCT06439043

(JMIR Preprints 05/08/2024:65098)
DOI: https://doi.org/10.2196/preprints.65098

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?
Please make my preprint PDF available to anyone at any time (recommended).
✓ **Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all u**
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?
✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Developing an Adapted EMDR Therapy for Major Depressive Disorder and Assessing its Efficacy through Online and Face-to-Face Modalities: A Protocol for Mixed Method Randomized Controlled Trial

Anwar Khan[1],[2]*, Amalia bt Madihie[3], Salah Uddin Khan[4,5], Sajjad Haider[5,6], Maqsood Haider[7]

Abstract

Background: Major Depressive Disorder (MDD) is a psychiatric condition that globally ranks as the 24th leading cause of Disability-adjusted Life Years. Pakistan, a developing nation, grapples with poverty, resource inequality, population growth, and political instability, which may probable cause MDD among general population. Resultantly high prevalence of MDD in Pakistan in evident from the existing literature. Currently, evidence-based psychotherapies such as Eye Movement Desensitization and Reprocessing(EMDR) are widely available. However, EMDR originated in the United States, it might not be consistent with requirements of non-western countries, so it may require cross-cultural and methodological adaptations. Moreover, therapists have long practiced face-to-face EMDR, but recently, online EMDR modalities have emerged. Nonetheless, it is surprising that there is a dearth of research on both the adaptations of EMDR in Pakistan and its clinical efficacy, particularly its online modes have never been scientifically validated in Pakistan. *Objective*: Considering lack of research on adaptations and clinical efficacy EMDR in Pakistan, the present study aims to develop a culturally and methodologically adapted EMDR therapy protocol for MDD in Pakistan, determine its treatment fidelity, and then clinically test its efficacy by administering it through the face-to-face and online modalities of EMDR therapy.

Methods: This study adopted a mixed-mode exploratory sequential Randomized Controlled Trial design in two phases. In the first phase, qualitative exploratory data will be collected, followed by quantitative data, to accomplish the adaptation process of the EMDR therapy protocol. In the second

[1]**Corresponding Author:**
* Postgraduate Scholar, Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia.
[2] Assistant Professor, Department of Management Sciences and Psychology, Khushal Khan Khattak University Karak, Pakistan. Email: akpashtoon1981@gmail.com
[3] Dean, Faculty of Cognitive Sciences and Human Development, Universtiti Malaysia Sarawak, Kota Samarahan, Sarawak, Malaysia.
[4] Energy Technologies Center, College of Engineering, King Saud University, P.O.Box 800, Riyadh 11421, Saudi Arabia.
[5] King Salman Center for Disability Research, Riyadh 11614, Saudi Arabia
[6] Chemical Engineering Department, College of Engineering, King Saud University, P.O.Box 800, Riyadh 11421, Saudi Arabia.
[7] Assistant Professor, Department of Management Sciences, FATA University, Dara Adam Khel, Frontier region Kohat, Khyber Pakhtunkhwa

phase, a consecutive sample of 80 patients will be randomly allocated in a 1:1 ratio to face-to-face and online groups to determine the clinical efficacy of the adapted EMDR therapy protocol in both modalities. Symptoms related data will be collected through clinician administered scales during start, mid, end and follow-up stages of therapy. Data will be analyzed using a variety of qualitative and quantitative statistical techniques.

Results: This study has been approved by the Ethics Review Committees of Khushal Khan Khattak University Karak, Pakistan, and University Malaysia Sarawak, Malaysia. It is registered at ClinicalTrials.gov. The process of adapting the DeprEnd-EMDR Depression Protocol has already begun. Recruitment of patients for psychotherapy sessions will start in September 2024.

Conclusion: In conclusion, this study addresses significant research gaps concerning the adaptation and clinical efficacy of EMDR therapy in the Asian region, with a particular focus on its online modalities. By employing a rigorous research methodology, the results are likely to make substantial contributions by providing insights into both the adaptation and clinical efficacy of EMDR therapy. This study will extend our understanding of the comparative effectiveness of EMDR therapy in the Asian region, offering valuable information on its applicability and impact in diverse, particularly non-Western, settings.

Trial Registration: ClinicalTrials.gov ID NCT06439043.

KEYWORDS: Eye Movement Desensitization and Reprocessing, Major Depressive Disorder, Online Psychotherapy, Cultural and Methodological Adaptations, Fidelity Analysis, Non-inferiority Analysis, Pakistan.

Introduction

Depression as a Disease of Modernity

By the end of the 20th century, scientists speculated that modern environments could lead to a global epidemic of mental health [1]. Recent figures published in the Lancet are alarming. During the year 2019, total 279.60 million (95% CI 251.60–310.30) prevalent cases of depressive disorders were globally recorded [2] with an addition of 53.2 million during COVID-19 pandemic (95% CI 44.80-62.90)[3]. Such an abrupt increase in the global prevalence of depressive symptoms can be attributed to several factors. Scientists call it a “disease of modernity” [4], since modern humans are socially isolated, sleep deprived, and working mechanically day and night [5].The global prevalence of depressive disorders has severely impacted people's lives and it has become a leading cause of disability by accounting for 37.30% of global Disability-adjusted Life Years during 2019, ranking it as the 24th largest cause of global Disability-adjusted Life Years[2]. The long-term effects can be

dire, both for individuals and society at large. Thus, there is an increased global need for various treatment approaches for curing depressive disorders. In the context of Pakistan, a pertinent question comes up: "Are compatible treatment options available in Pakistan for MDD?"

Mental Healthcare System in Pakistan

In Pakistan, the average person's mental health is compromised, and it is influenced by a number of challenges, including a rapidly growing population, inadequate infrastructure, political and economic crises, illiteracy, and uneven distribution of resources [6]. In this context, the most recent statistics revealed that around 24 million individuals in Pakistan require mental health treatment [7]. Unfortunately, Pakistan does not have a well-developed mental healthcare system. The existing literature documents various research studies on the high prevalence of depressive disorders in Pakistan. For example, in a recent study by Ullah et al [8] reported that out of the total 1047 individuals 39.90% had depressive symptoms in Pakistan. Similarly another recent survey in Pakistan revealed that 60.80% people were suffering with depression [9]. Especially, Peshawar[3] is historically known for the high prevalence of depressive disorders mainly due to terrorist acts, natural disasters (floods), community & domestic violence, poverty, and lack of employment. Recent research studies, like for example by Noor, Zahid, & Jamil [10] found that 58.50% population suffered from depression. Similarly, Khattak et al [11] revealed that 67.40% of 356 medical students in the twin cities of Islamabad and Rawalpindi suffered from depression symptoms. Existing research findings on the high prevalence of depression among Pakistanis provide helpful insights into the epidemiology of MDD in the region. It also encourages local researchers to work on the exploring modern evidence-based treatments for MDD in Pakistan.

Treatment of Major Depressive Disorder

Recently various treatment options have been available for MDD. Scientists recommend either psychotherapy or pharmacotherapy. However, findings of recent systematic reviews revealed that psychotherapy is more efficacious, particularly in the long-term treatment of MDD [12-13]. Furthermore, medications have varying negative side effects [14] , and withdrawal effects [15]. Consequently, research studies by Prescott & White [16] and Malhi et al [17] suggested that medication option should be chosen judicially.

Popular evidence-based psychotherapies include EMDR [18] and CBT [19]. Each have their own development and testing histories. The CBT became available in Pakistan in the early 1990s. This form of therapy gained popularity when the Pakistan Association for Cognitive Therapists was established in 2009 [20]. On the other hand, EMDR therapy is relatively new in Pakistan. It was first

[3] This study will be conducted in the capital cities of Peshawar, Rawalpindi, and Islamabad.

introduced in Pakistan by the EMDR Europe HAP Project following the famous 2005 earthquake in northern areas of Pakistan [21]. This indicates that EMDR therapy is relatively new in Pakistan, and as a result, it may have undergone fewer modifications and updates. Therefore, conducting further research on EMDR therapy presents a promising opportunity for future studies in Pakistan.

The Necessity of Developing and Testing An Adapted EMDR Therapy For Pakistan

Readers might ponder certain important questions:"What requires the development of culturally and methodologically adapted EMDR Therapy protocol in Pakistan?" Furthermore, “Should the effectiveness of the adapted protocol be assessed through face-to-face and online modalities of EMDR Therapy?” Answering these queries involves a thorough examination of the existing research on EMDR Therapy, particularly within the context of Pakistan.

Mahatma Gandhi once remarked, “We are unable to bring the clothing of the West and provide them to our own people to wear: they are of a different size and manner”[22]. This analogy highlights the challenges of adopting foreign ideologies. It suggests that rather than forcing oneself to fit unfamiliar systems, one should adapt them to his own context. Similarly, this philosophy calls for modifying EMDR Therapy protocols to make them relevant for Pakistan. EMDR therapy was developed by Dr. Francine Shapiro in the United States. Since its inception, it has been tested and upgraded for its efficacy mostly in the developed western countries mostly in advanced countries such as the United States [23], United Kingdom [24], Canada [25], Australia & New Zealand [26], Italy [27], and Germany [28]. EMDR therapy has also been tested in Turkey [29], Japan [30], and China [31], In Pakistan, relatively few studies have been undertaken on testing efficacy of EMDR therapy, such as by Qayyum, Malik, & Siddique [32] , Muhammad Sami, Mowadat Hussain, Safi Ullah, & Rashid [33] and Khan, Khan, & Shah [34]. The reason for this is that since EMDR is still relatively new in Pakistan, truly little research has been done there, leaving a sizable research gap for future investigation in Pakistan. Therefore, there are several reasons behind the development of a culturally and methodologically adapted EMDR protocol for MDD in Pakistan, as well as its clinical testing to confirm that it has been adapted according to local needs of Pakistan. Given the aforementioned facts, the following research gaps have been identified:

Empirical Research Gaps

Scientists in the west have been empirically investigating the Aetiology, Epidemiology, and therapeutic aspects of depressive disorders, but there is an astonishing dearth of empirical research notably in Asian countries like Pakistan [35]. The existing literature contains just a few published empirical studies on the clinical efficacy of EMDR Therapy in Pakistan. This indicates a serious empirical gap. For instance, studies conducted by Ali & Rana [36] , Bilal & Rana [37] and Bilal,

Hussain, Khan, & Qayyum [38] on efficacy of EMDR Therapy. Another study by Farrell, Keenan, Knibbs, & Hicks [39] recommended that the EMDR practitioners in Pakistan must be culturally sensitive and future researchers should work on cultural adaptation in EMDR Therapy. Recently, Khan, Khan, & Shah [34] tested the comparative efficacy of EMDR Therapy. Previous empirical studies in Pakistan have predominantly focused on the efficacy of EMDR Therapy, with limited focus on the cultural and methodological adaptations of EMDR Therapy, indicating a significant empirical research vacuum.

Technical Research Gaps

Earlier research on the linguistic modification of treatment protocols was carried out in Cambodia [40] and Iran [41]. In similar vein, modifications in structure of therapy was done in Syria [42] and Germany [43]. While recently adaptations such as using of culturally suitable symbols, metaphors, words and avoiding eye winking and personal touching were made in African countries [44]. However, to our knowledge, no studies on the cultural adaptation of the EMDR Therapy protocol for treating depression have been conducted in Pakistan. This indicates a serious literature gap. Apart from the cultural adaptations, relatively few technical adaptations have been made in the EMDR Therapy to date. For example Laliotis et al [45] suggested combining a range of procedures, such as adding new resources during the desensitization stage of therapy. Studies by Cope et al [46] and Strelchuk et al [47], suggested using a combination of qualitative and quantitative techniques to ascertain treatment fidelity and non-inferiority. But, recently, very few studies for example by Marich, Dekker, Riley, & O'Brien [48] have employed such methodologies, indicating serious literature gap. Furthermore, EMDR Therapy has mostly been used for treating PTSD, so only EMDR protocols for PTSD, for example, those by Tripp [49] have historically undergone technical modifications, but protocols for depression have received less attention, indicating serious literature gap. Other technical adaptations include using fragrance to trigger the sense of compassionateness [50]; integration of Positive Psychology principles to EMDR Therapy [45]; and incorporation of Somatic Psychology principles into the EMDR Therapy [51]. Remarkably, though, there have not yet been any large-scale experimental studies conducted on these technological integrations in EMDR Therapy, pointing to a significant research gap. Lastly, there are research gaps related to the use of online modes of EMDR Therapy. Studies such as Yurtsever, Bakalim, Karaman, & Konuk [52] only documented the implementation of trauma-focused EMDR protocols in the online delivery of EMDR Therapy. On the contrary, there is a lack of research focusing on depressive symptoms protocols. Hence, it is unclear if recently developed online EMDR systems like Bilateralbase [53] are safe and usable for treatment of depressive symptoms in Pakistan.

Methodological Research Gaps

Certain methodological gaps continue to persist. For example, pilot studies by Yaşar et al [54] and Farrell et al [55] have employed conventional pilot study methodology instead of adopting newly developed standards such as SPIRIT [56]. Furthermore, Matthijssen et al [57] in their study on future recommendations for EMDR Therapy pointed out that most research studies had employed masked diagnostic assessments with intent-to-treat analyses, and one sided fidelity reviews. Such methodological errors may lead to problems with result generalizability, ethical issues, and treatment effect underestimation. It is surprising that the existing literature lacks mixed mode randomized controlled trail studies on EMDR Therapy that have used both qualitative and quantitative methods for investigating multiple aspects simultaneously. The lack of methodologically rigorous research studies highlights a significant methodological gap since the ultimate effectiveness of EMDR Therapy may not be ascertained.

Theoretical Research Gaps

The theoretical underpinnings of EMDR Therapy have been less evaluated, primarily because the existing theories continue to be subject to scientific investigation [58]. The majority of previous studies have employed Functional Magnetic Resonance Imaging data to examine changes in the brain areas for testing the Adaptive Information Processing Theory of EMDR Therapy [59]. There is, however, a lack of evidence on the adaptation and upgradation of theories of EMDR Therapy. Upgradation can be done through the integration of religious, social, and cultural practices, as well as principles from other psychotherapies. Future research directions about EMDR Therapy as given by Rydberg & Machado [60] and Laliotis et al [46] encourages integrating a variety of procedures into the theories of EMDR Therapy. Moreover, the assumptions of EMDR theories have been primarily tested through face-to-face sessions of EMDR Therapy, while less research has been done on testing EMDR theories through online EMDR Therapy. In this context, only two studies—those by Yaşar et al [54] and Farrell et al [55] —have been identified to assess the effectiveness of the Adaptive Information Processing Model in an online setting. However, further research evidence is required to determine whether the assumptions EMDR theories provide comparable results when applied in online, especially among Pakistani population.

Study Objectives

This study will work on the following objectives:

1. To explore relevant cultural and methodological factors for integration into the DeprEnd-EMDR Depression Protocol to enhance its effectiveness in the treatment of Major Depressive

Disorder in Pakistan.

2. To assess the suitability, functionality, safety, usability, and theoretical validity of Bilateralbase EMDR platform for delivering online EMDR sessions in treating Major Depressive Disorder in Pakistan.
3. To investigate whether Treatment Fidelity requirements are met during the online and face-to-face implementation of the adapted DeprEnd-EMDR depression protocol in Pakistan.
4. To track temporal changes in Major Depressive Disorder symptoms over time following implementing of the adapted DeprEnd-EMDR depression protocol in Pakistan both through online and face-to-face modalities.
5. To investigate reciprocal linkages between symptoms of Major Depressive Disorder and Anxiety by assessing whether these reciprocal linkages are moderated by treatment conditions.

Methods

Study Design and Setting

The present study will be a multi-center, two arms (online EMDR vs face-to-face EMDR) and single-blind between-subjects mixed mode Randomized Controlled Trial design. This design is an updated version of the standard randomized controlled trial [61]. The This study consists of two phases. In the first phase, qualitative exploratory data will be obtained, followed by quantitative data, to accomplish the adaptation process of the EMDR protocol. In the second phase, the clinical efficacy of adapted EMDR protocol will be determined by randomly assigning patients to either online or face-to-face modalities of EMDR. Furthermore, the Consolidated Standards of Reporting Trials Flow-Chart [62] will be employed to report this study.

Phase One (Exploratory Qualitative Part of Study)

Procedure for Adaptation of EMDR Protocol

To carry out the cultural and methodological adaptation process, this study will employ the steps recommended by previous research, such as Seponski [41]; Chowdhary et al [63] ; Wiltsey Stirman, Gamarra, & Bartlett [64] ; Naeem, Phiri, Rathod, & Ayub [65]; and Mbazzi et al [45]. These steps include the following:

1. The first stage entails selecting a therapy protocol. In this regard, the DeprEnd EMDR Therapy Protocol will be selected.
2. In the second stage, a comprehensive narrative review of the existing literature will be conducted to understand the present state of knowledge on EMDR therapy (in general) and the DeprEnd EMDR therapy protocol (in specific). Furthermore, the cultural or

methodological challenges and barriers in the implementation of EMDR Therapy will be investigated, and factors impacting its acceptance will be discovered.

3. In the third stage, discussion themes will be generated. These themes will be shared with four pre-selected EMDR therapy professionals, who will be asked to provide their expert opinions.
4. In the next stage, the four EMDR therapy professionals will be asked to complete a self-reported questionnaire based on themes from the literature review and focus group discussions and rated on a five-point scale.
5. In the fourth stage, information obtained from the secondary data analysis, expert opinions and self-rated questionnaires will be integrated into the DeprEnd EMDR Therapy Protocol and its adapted version will be created.
6. Following the development of the adapted DeprEnd EMDR therapy protocol, it will undergo pilot testing prior to full-scale implementation. The protocol will first be tested with twenty randomly selected patients. This approach aligns with established practices in the literature, including previous pilot studies on culturally adapted psychotherapies [66].

Phase Two (Quantitative Confirmatory Part of Study)

In this phase, the efficacy of the adapted DeprEnd EMDR therapy protocol will be evaluated.

Selection of Patients for Study

The population includes all persons suffering from MDD in Pakistan. However, since it is not practically possible to study every individual suffering from MDD in Pakistan, therefore only geographically accessible individuals residing in big cities of Rawalpindi, Islamabad and Peshawar will be included in this study. It is because recent literature cite various studies such as by Ishtiaq, Afridi, & Khan [67], Noor, Zahid, & Jamil [10] and Umar, Tahir, & Nizami [68] on high prevalence of depressive disorders in these three cities of Pakistan. Furthermore, the total number of MDD patients in the three capital cities is unknown, making conventional sampling techniques involving power calculations impractical. Instead, a multi-stage, more individualized patient selection process has been employed. According to this procedure, the patients will be selected in following sequence:

1. Three rehabilitation centers located in the selected cities will be randomly picked for recruiting patients. The centers will not be chosen fully at random; rather, the characteristics of the vicinity and patient flow into centers will be considered.
2. Within each selected center patients will be recruited through sequential sampling technique with rolling strategy. This approach entails selecting every patient who meets the inclusion criterion till the required sample size is obtained [69].

3. Each subsequent consecutive indoor or outdoor patient in the selected centers will be interviewed through Structured Diagnostic Interview for Screening DSM-5 (TR) Disorders [70] for initial diagnosis of MDD. Moreover, patients will be verified for inclusion by applying the inclusion criteria listed below:
    a. The patient should exhibit symptoms of MDD.
    b. Male and female patients will be chosen equally.
    c. Patients between the ages of 20 and 50 will be selected.
    d. patients should preferable be "treatment-naive," meaning they have no recent

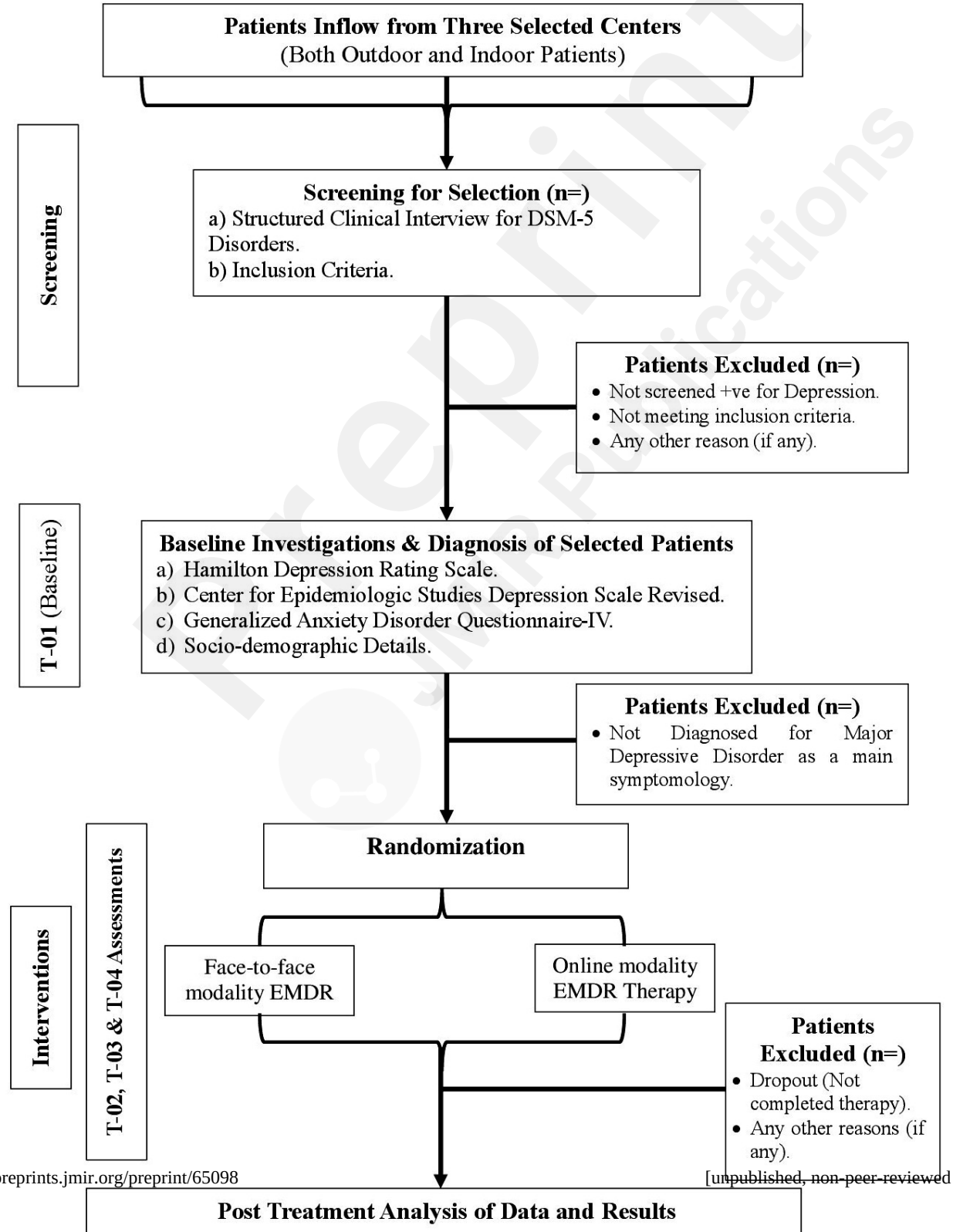

Fig. 1. CONSORT Flow Chart of Randomization

Psychotherapeutic Interventions

Treatment Protocol

This study will utilize the recently developed DeprEnd EMDR therapy protocol for depressive disorders [75]. The DeprEnd EMDR protocol adjusts to the standard EMDR therapy procedure for depressive disorders by adapting in the History Taking, Preparation, and Installation phases.

Platform for Online Delivery of EMDR Therapy

EMDR therapy will be delivered online through the Bilateral Base platform (https://www.bilateralbase.com), developed by British scientists led by Dr. Katherine Elizabeth, an esteemed EMDR therapist and researcher in the UK [76].

Selection and Training of Therapists

EMDR therapy will be provided by a team of three EMDR-certified therapists, each working with three patients simultaneously. The chosen therapists will complete a one-week training program to become familiar with the Bilateral Base online platform.

Data Collection Procedures

Data on Symptomology (Outcome Variables)

The symptoms of Major Depressive Disorder will be assessed using Hamilton Depression Rating Scale-17, with a score of ≥20 indicating depression [77] and Center for Epidemiologic Studies

Depression Scale Revised-20 with a score of ≥20 also indicating depression [78], whereas comorbid Generalized Anxiety Disorder will be assessed with Generalized Anxiety Disorder Questionnaire-IV, with a score of ≥5.7 indicating Anxiety Disorder [79]. Data on symptoms will be collected at four time points: baseline (T01), mid-treatment (T02), end-of-treatment (T03), and follow-up (T04). This approach will facilitate the identification of longitudinal changes in symptoms resulting from the administration of EMDR therapy.

Data on Effectiveness of EMDR Therapy

Previous research on the efficacy of EMDR therapy have proposed the following assessments:

i. Changes in the Subjective Distress & Emotionality will be measured by an 11-point Likert scale known as Subjective Units of Distress Scale [80] during the start, mid and end of EMDR therapy.
ii. The vividness of intrusive and disturbing memories will be measured on an 11-point Likert scale with ratings ranging from (0-not at all vivid) to (10-extremely vivid) [81] during the start, mid and end of EMDR therapy.

Data on Practicability of Online EMDR Therapy

Practicability related data will be collected in following ways:

1. The System Usability Scale [82] regarding usability of online EMDR therapy.
2. The therapist acceptance of online EMDR therapy will be measured through 17-items of Therapist Acceptance Scale [83].
3. Safety of the online EMDR therapy will be measured by 05-items provided by the American Committee on the Patient Safety and Health Information Technology, Institute of Medicine [84].

Methodology for Determining Treatment Fidelity

Treatment fidelity will be established both qualitatively and quantitatively by adhering to the recommendations outlined by Dorsey, Sedlar, & Jungbluth [85].

1. The psychotherapy sessions will be video recorded and reviewed by two EMDR therapy experts through Delphi technique to collect "Expert Opinion" to determine the adherence of the treatment process.
2. Moreover, quantitative ratings of recorded sessions will be done by using predefined rating scales such as the EMDR Fidelity Rating Scale [86].
3. The therapist competence will be assessed by self-reported rating scales such as Instrument for Assessing Therapist Competence in Global Mental Health [87].
4. Finally, patient’s satisfaction and perception about EMDR therapy will be assessed by

Scale for Patient Experience of Online EMDR therapy [88] and Satisfaction With Therapy Scale [89].

Procedures for Analysis of Data

Methodology for Establishing Non-inferiority

In the present study, the decision about declaring online mode of EMDR therapy to be non-inferior to the in-person mode will be based on whether the mean differences (Δ) in the scores or ratings of assessment tools among the patients in two treatment groups (face-to-face and online EMDR therapy) are greater than or equal to (≥) the non-inferiority margins. The non-inferiority margin for the symptoms of MDD and Anxiety will be decided by examining the reduction in the mean scores differences (Δ). This decision will be based on whether a decrease of ≥ 50% in total scores is observed in the scores of selected symptoms assessment tools from the baseline (T-01) point till end of treatment (T-04).

Methodology for Examining Reduction in Symptoms Over Time

Examining Group Differences

Adhering to the procedure given by George & Mallery [90], a series of General Linear Model Repeated Measures of ANOVA will be run to know the effects of time on MDD and its comorbid symptoms. This effect will be determined by examining the group differences (between face-to-face and online). Additionally, planned post-hoc analyses should also be performed with Bonferroni Correction [91]. The post-hoc analyses will help in understanding differences in MDD symptoms from baseline (T-01) to end of treatment (T-04) stages. To verify the ultimate accuracy of post-hoc analyses, a series of paired t-tests will be conducted on MDD symptom scores, comparing the scores from the baseline (T-01) to the end of the treatment (T-04) stages.

Examining Longitudinal Changes in Symptoms

To examine the longitudinal changes in symptoms, following procedures will be employed:

1. A series of Hierarchical Linear Modelling (Multi-level Mixed both direct and reciprocal) with Maximum Likelihood Estimation will be run according to the guidelines provided by David Garson [92]. The longitudinal data will be grouped into two levels: the level-1 will consist of repeated measures (over time) of symptoms. The variable of time will be represented by the “number of treatment sessions from baseline to follow-up stage”. Time will be coded as points of measurement (1, 2, 3, 4, 5…). To improve the accuracy of measurement model, predictor variables will be included in the model as covariates throughout the analytic process.
2. The effects of covariates on the outcome variable will be examined both as fixed effects and

random effects**.** The fixed effects will reflect the overall average effect of the predictor variable on the outcome variable. Random effects will explain the variability between random factors, existing within the groups as predictor variables. The random effects will help in understanding the correlation and covariance (or variance) between the parameter estimates of predictor variables [93].

3. The model fit will be determined by statistical tests such as Likelihood Ratio Test [94], Akaike Information Criterion & Bayesian Information Criterion [92] and Intraclass Correlations [95].
4. Since MDD frequently coexists with anxiety symptoms [96], this relationship will be investigated by employing the Hierarchical Linear Modelling with Reciprocal Association Methodology [92] and 1-1-1 level mediation modelling approach [97]. This approach measures independent (X), mediator (M), and dependent (Y) variables all at the lower level. According to the Reciprocal Association Methodology, the reciprocal effects involve observing the mediational changes by using criterion as proposed by Baron & Kenny [98] and Kenny, Korchmaros, & Bolger [99].

Results

This study has been approved by the Ethics Review Committees of Khushal Khan Khattak University, Karak, Pakistan, and the University Malaysia Sarawak, Malaysia. It is registered on ClinicalTrials.gov. The adaptation process of the DeprEnd-EMDR Depression Protocol has already begun. A narrative literature review has been conducted, and the focus group discussions will commence soon. Recruitment of patients for psychotherapy sessions to test the adapted protocol will begin by mid-September 2024.

Discussion

Through the review of existing literature, it is widely recognized that MDD is a significant mental health issue in the Asian region, particularly in Pakistan. The unfortunate shortage of adequate mental health treatment facilities underscores the importance of providing treatments specifically designed to meet the needs of local patients and therapists. This study aims to develop a culturally and methodologically adapted EMDR therapy protocol for depression, assess its integrity, and evaluate its therapeutic effectiveness in Pakistan through both in-person and online modalities.

This study, in particular, will play a crucial role in advancing mental healthcare system in Pakistan and addressing the availability and accessibility challenges associated with mental health treatments in the country. The study will fill a gap in the literature regarding adapted psychotherapeutic interventions for depressive disorder in the Asian region. It will also have practical implications for

mental health professionals working in the field of psychotherapy research. Overall, this study is expected to make significant advances in the field of psychotherapy research by providing insights into the adaptation process of EMDR therapy. Additionally, it will enhance our understanding of the comparative effectiveness of adapted EMDR therapy in treating MDD both in face-to-face and online clinical settings.

Strengths and Limitations

The primary contribution of this study is the development of a culturally and methodologically adapted EMDR therapy protocol for treating MDD in Pakistan. This study will employ a rigorous, multi-phase methodology with procedures to adapt the protocol and then assess its feasibility, practicability, and fidelity. Additionally, this study will evaluate the clinical efficacy of adapted treatment protocol through non-inferiority and longitudinal trend analyses. By combining methodologies from medical science and psychotherapy, this study will pave the way for transdisciplinary research in psychotherapy in Pakistan.

The present study has certain limitations. First, a larger sample size (more than 100) has not been chosen due to time and resource constraints, so the findings might not be broadly generalizable to all regions of Pakistan. Second, it may be nearly impossible to account for every potential confounding factor, such as comorbidities. Only generalized anxiety disorder will be examined to see if it coexists with MDD, which could impact the effectiveness of the adapted EMDR therapy. Third, adapting the EMDR therapy while considering all methodological and cultural factors is challenging. Consequently, certain methodological or cultural aspects might be omitted, potentially affecting the therapy's effectiveness. Finally, the two-month follow-up period might not be sufficient to determine the adapted EMDR therapy's effectiveness in cases with severe symptoms or resistance to treatment.

Conclusion

In conclusion, the development and scientific validation of an adapted EMDR therapy protocol emerge as imperative endeavors for addressing the escalating mental health needs of the local population in the Asian region, particularly in Pakistan. This is especially crucial given the mental health issues currently affecting the area, which stem from the various challenges faced by individuals in this region. By recognizing areas for improvement in the mental health infrastructure of Pakistan, this study offers a vital pathway towards more accessible and efficient mental health interventions for the mental well-being of individuals affected by MDD in Pakistan.

Acknowledgments

The authors extend their appreciation to the King Salman center for Disability Research for funding the publication related expenses of this work through Research Group no KSRG-2023-263.

Authors' Contributions

AK is a postgraduate scholar in the field of Counseling Sciences at UNIMAS. He is the main conceiver of this idea and is working under the research supervision of AM. Both authors are responsible for designing, conceptualizing, and executing the study. MH is responsible for promoting the study, recruiting participants, conducting informed consent procedures, and collecting data from clinics. SUD and SH drafted the manuscript, reviewed it, and refined it. They have also funded this study. All authors share responsibility for submitting this manuscript for publication.

Conflicts of Interest

There are no conflicts of interest declared by the authors of this study.

Reference

1. Dickinson S. Post-traumatic growth in the twenty-first century: how current trends may threaten our ability to grow after trauma. *J Posit Psychol*. 2021;16(4):503-511.
2. Global Burden of Disease. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Psychiatry*. 2022;9(2):137-150.
3. Santomauro D, Herrera M, Shadid J, et al. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet*. 2022;398(10312):1700-1712.
4. Mya Care. Depression as a disease of modern-day living. https://myacare.com/blog/depression-as-a-disease-of-modernday-living. Published 2023.
5. Priya A, Garg S, Tigga NP. Predicting Anxiety, Depression and Stress in Modern Life using Machine Learning Algorithms. *Procedia Comput Sci*. 2021;167:1258-1267.
6. Nawaz D, Khan SA, Batool S, Rasool A. Governance Issues and Deep-Rooted Corruption in Pakistan. *Int J Mod Agric*. 2021;10(2):2699-2706.
7. WHO. WHO Pakistan celebrates World Mental Health Day. https://www.emro.who.int/pak/pakistan-news/who-pakistan-celebrates-world-mental-health-day.html#:~:text=In Pakistan%2C mental disorders account,in need of psychiatric assistance. Published 2024.
8. Ullah I, Ali S, Ashraf F, et al. Prevalence of depression and anxiety among general population in Pakistan during COVID-19 lockdown: An online-survey. *Curr Psychol*. 2022. doi:10.1007/s12144-022-02815-7
9. Shahid H, Hasan MA, Ejaz O, et al. The Severity of Depression, Anxiety, and Stress: Recommendations From Joint Work of Research Center and Psychology Clinics in COVID-19 Pandemic. *Front psychiatry*. 2022;13.
10. Noor ZU, Zahid S, Jamil M. Stress, anxiety, and depression among patients admitted to orthopedic wards in two public hospitals of Peshawar. *J Rehman Med Inst*. 2022;8(3):17-19.
11. Khattak HG, Arshad H, Anwar K, et al. Frequency of Depression, Anxiety and Stress among Medical Students of Rawalpindi and Islamabad. *Pakistan J Med Heal Sci*. 2022;16(10):61.
12. Kamenov K, Twomey C, Cabello M, Prina AM, Ayuso-Mateos JL. The efficacy of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in depression: a meta-analysis. *Psychol Med*. 2018;47(3):414-425.
13. Leichsenring F, Steinert C, Rabung S, Ioannidis JPA. The efficacy of psychotherapies and pharmacotherapies for mental disorders in adults: an umbrella review and meta-analytic evaluation of recent meta-analyses. *World Psychiatry*. 2022;21(1):133-145.

14. Ramic E, Prasko S, Gavran L, Spahic E. Assessment of the Antidepressant Side Effects Occurrence in Patients Treated in Primary Care. *Mater Sociomed*. 2020;32(2):131.
15. Sethi R, Ravishankar DA, Nagireddy R. Phenibut Dependence and Withdrawal. *Prim Care Companion CNS Disord*. 2021;23(1):26029.
16. Prescott D, White ND. When Is Pharmacotherapy Initiation Beneficial in Patients With Depressive Disorders? *Am J Lifestyle Med*. 2017;11(3):220-222.
17. Malhi GS, Bell E, Singh AB, et al. The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders: major depression summary. *Bipolar Disord*. 2020;22(8):788-804.
18. Shapiro F. *Eye Movement Desensitization and Reprocessing (EMDR) Therapy, Third Edition: Basic Principles, Protocols, and Procedures*. Guilford Publications; 2017. https://books.google.com.pk/books?id=pYG6DgAAQBAJ.
19. Beck JS. *Cognitive Behavior Therapy, Third Edition: Basics and Beyond*. Guilford Publications; 2020. https://books.google.com.pk/books?id=yb_nDwAAQBAJ.
20. Sherazee M. Beyond drugs: New options for the mentally ill in Pakistan.July 2014.
21. Farrell D. Developing EMDR Therapy in Pakistan as Part of a Humanitarian Endeavor. *J EMDR Pr Res*. 2014;8(4):233-2014. doi:10.1891/1933-3196.8.4.233
22. Gandhi M. *The Story of My Experiments with Truth: An Autobiography*. Courier Corporation; 1983.
23. Shapiro F. The role of eye movement desensitization and reprocessing (EMDR) therapy in medicine: addressing the psychological and physical symptoms stemming from adverse life experiences. *Perm J*. 2014;18(1):71.
24. Proudlock S, Peris J. Using EMDR therapy with patients in an acute mental health crisis. *BMC Psychiatry*. 2020;20(1):1-9.
25. Winkler O, Dhaliwal R. Web-Based Eye Movement Desensitization and Reprocessing for Adults With Suicidal Ideation: Protocol for a Randomized Controlled Trial. *JMIR Res Protoc*. 2021;10(11):e30711.
26. Every-Palmer, Flewett T, Dean S, Hansby O. Eye movement desensitization and reprocessing (EMDR) therapy for posttraumatic stress disorder in adults with serious mental illness within forensic and rehabilitation services: a study protocol for a randomized controlled trial. *Trials*. 2019;20(1):1-14.
27. Mazzoni GP, Miglietta E, Ciull T, et al. Group Eye Movement Desensitization Reprocessing (EMDR) Psychotherapy and recurrent interpersonal traumatic episodes: a pilot follow-up study. *Clin Neuropsychiatry*. 2022;19(6):379.
28. Schäfer I, Chuey-Ferrer L, Hofmann A, Lieberman P, Mainusch G, Lotzin A. Effectiveness of EMDR in patients with substance use disorder and comorbid PTSD: study protocol for a randomized controlled trial. *BMC Psychiatry*. 2018;17(1):1-7.
29. Bayhan BB, Tarquinio C, Rydberg J, Korkmazlar Ü. The study of the group intervention containing EMDR therapy for children and mothers in the field of trauma after a mine explosion in Turkey. *Eur J Trauma Dissociation*. 2022;6(1):100248.
30. Wakusawa K, Sugiyama T, Hotta H, et al. Triadic Therapy Based on Somatic Eye Movement Desensitization and Reprocessing for Posttraumatic Stress Disorder: A Pilot Randomized Controlled Study. *J EMDR Pract Res*. 2023.
31. Zhao J, Chen D-Y, Li X-B, et al. EMDR versus waiting list in individuals at clinical high risk for psychosis with post-traumatic stress symptoms: A randomized controlled trial. *Schizophr Res*. 2023;256:1-7.
32. Qayyum R, Malik MM, Siddique S. EMDR: An Effective Therapeutic Technique For Psychiatric Disorders. *Pakistan Armed Forces Med J*. 2012;(2):138.
33. Muhammad Sami B, Mowadat Hussain R, Safi Ullah K, Rashid Q. Efficacy of eye movement desensitization and reprocessing beyond complex post traumatic stress disorder: a case study

of EMDR in Pakistan. 2016.
34. Khan A, Khan S, Shah ST. Efficacy of eye movement desensitization & reprocessing versus cognitive behavioral therapy in Post-Traumatic Stress and Depressive Symptoms: Study protocol for a Randomized Controlled Trial. *Contemp Clin trials Commun*. 2019;16:100439.
35. Shah, Sun T, Xu W, Jiang W, Yuan Y. The mental health of China and Pakistan, mental health laws and COVID-19 mental health policies: a comparative review. *Gen Psychiatry*. 2022;35(5):e100885.
36. Ali, Rana. Eye Movement Desensitization and Reprocessing (EMDR) in Post Traumatic Stress Disorder (PTSD) patients of 2005 earthquake in Pakistan. In: *First International Conference on Psycho-Trauma, Islamabad, Pakistan*. ; 2008:30-31.
37. Bilal, Rana. The use of Eye Movement Desensitization and Reprocessing (EMDR) in battle hardy soldiers with post traumatic stress. In: *First International Conference on Psycho-Trauma, Islamabad, Pakistan, 30–31 August*. ; 2008:1-13.
38. Bilal, Hussain, Khan, Qayyum. Efficacy of eye movement desensitization and reprocessing beyond complex post traumatic stress disorder: a case study of EMDR in Pakistan. *Prof Med Journal-Quarterly*. 2015;22(4):514-521.
39. Farrell D, Keenan P, Knibbs L, Hicks C. A Q-methodology evaluation of an EMDR Europe HAP facilitators training in Pakistan. *J EMDR Pract Res*. 2013;7(4):174-185.
40. Seponski DM. Exploring eye movement desensitization and reprocessing (EMDR) as a culturally responsive Cambodian model of therapy. 2015.
41. Rasolkhani-Kalhorn T. Translation and adaptation of the EMDR protocol to the Iranian culture. 2009.
42. Acarturk C, Konuk E, Cetinkaya M, et al. The efficacy of eye movement desensitization and reprocessing for post-traumatic stress disorder and depression among Syrian refugees: Results of a randomized controlled trial. *Psychol Med*. 2016;46(12):2583-2593.
43. Lehnung M, Shapiro E, Schreiber M, Hofmann A. Evaluating the EMDR Group traumatic episode protocol with refugees: A field study. *J EMDR Pract Res*. 2017;11(3):129-138.
44. Mbazzi FB, Dewailly A, Admasu K, et al. Cultural Adaptations of the Standard EMDR Protocol in Five African Countries. *J EMDR Pract Res*. 2021;15(1):29-43.
45. Laliotis D, Luber M, Oren U, et al. What Is EMDR Therapy? Past, Present, and Future Directions. *J EMDR Pract Res*. 2022;15(4).
46. Cope SR, Smith JG, El-Leithy S, et al. MODIFI: protocol for randomised feasibility study of eye-movement desensitisation and reprocessing therapy (EMDR) for functional neurological disorder (FND). *BMJ Open*. 2023;13(6):e073727.
47. Strelchuk D, Turner K, Smith S, Bisson J, Wiles N, Zammit S. Provision of online eye movement and desensitisation therapy (EMDR) for people with post-traumatic stress disorder (PTSD): a multi-method service evaluation. *Eur J Psychotraumatol*. 2023;14(2):2281182.
48. Marich J, Dekker D, Riley M, O'Brien A. Qualitative research in EMDR therapy: Exploring the individual experience of the how and why. *J EMDR Pract Res*. 2020.
49. Tripp T. Art Therapy and EMDR: Integrating Cognitive, Somatic, and Emotional Processing for Treating Trauma. In: Davis E, Fitzgerald J, Jacobs S, Marchand J, eds. *EMDR and Creative Arts Therapies*. Routledge Abingdon and New York; 2023:176-207.
50. Whalley M, Lee D. Integrating Compassion into EMDR for PTSD. *OBM Integr Complement Med*. 2023;8(4):1-18.
51. Lohrasbe RS. EMDR Therapy and Somatic Psychology: Interventions to Enhance Embodiment in Trauma Treatment, by Arielle Schwartz and Barb Maiberger. 2020.
52. Yurtsever A, Bakalim O, Karaman Ş, Konuk E. The effect of the online eye movement desensitization and reprocessing early intervention protocol (EMDR R-TEP) for the risk groups with post-traumatic stress symptoms during the COVID-19 pandemic. *Front Psychol*. 2022;13:935782.

53. Smith K. BilateralBase. https://www.bilateralbase.com. Published 2023.
54. Yaşar AB, Kavakçı Ö, Çiftçi ZZ, et al. The Effectiveness of Online EMDR 2.0 Group Protocol on Posttraumatic Stress Disorder Symptoms, Depression, Anxiety, and Stress in Individuals Who Have Experienced a Traffic Accident: A Preliminary Study. *J EMDR Pract Res*. 2023;1(2).
55. Farrell D, Fadeeva A, Zat Z, et al. A Stage 1 Pilot Cohort Exploring the Use of EMDR Therapy as a Videoconference Psychotherapy During COVID-19 With Frontline Mental Health Workers: A Proof of Concept Study Utilising a Virtual Blind 2 Therapist Protocol. *Front Psychol*. 2022:2383.
56. SPIRIT. SPIRIT-Standard Protocol Items: Recommendations for Interventional Trials. https://www.spirit-statement.org/spirit-statement/. Published 2023.
57. Matthijssen SJMA, Lee CW, de Roos C, et al. The current status of EMDR therapy, specific target areas, and goals for the future. *J EMDR Pract Res*. 2020;14(4):241-284.
58. Leeds A. The Adaptive Information Processing Model: The Theoretical Framework for EMDR Therapy. In: Farrell D, Schubert SJ, Kiernan MD, eds. *The Oxford Handbook of EMDR*. Oxford Academic; 2023.
59. Santarnecchi E, Bossini L, Vatti G, et al. Psychological and brain connectivity changes following trauma-focused CBT and EMDR treatment in single-episode PTSD patients. *Front Psychol*. 2020;10:129.
60. Rydberg JA, Machado J. Integrative psychotherapy and psychotherapy integration: The case of EMDR. *Eur J Trauma Dissociation*. 2021;4(3):100165.
61. Grissmer DW, Subotnik RF, Orland M. *A Guide to Incorporating Multiple Methods in Randomized Controlled Trials to Assess Intervention Effects*.; 2017. http://www.apa.org/ed/schools/cpse/activities/mixed-methods.asp.
62. CONSORT. Consolidated Standards of Reporting Trials. http://www.consort-statement.org. Published 2023.
63. Chowdhary N, Jotheeswaran AT, Nadkarni A, et al. The methods and outcomes of cultural adaptations of psychological treatments for depressive disorders: a systematic review. *Psychol Med*. 2014;44(6):1131-1146.
64. Wiltsey Stirman S, Gamarra JM, Bartlett BA. Empirical examinations of modifications and adaptations to evidence-based psychotherapies: Methodologies, impact, and future directions. *Clin Psychol Sci Pract*. 2017;24(4):396.
65. Naeem F, Phiri P, Rathod S, Ayub M. Cultural adaptation of cognitive behavioural therapy. *BJPsych Adv*. 2019;25(6):387-395.
66. Husain MO, Chaudhry IB, Mehmood N, et al. Pilot randomised controlled trial of culturally adapted cognitive behavior therapy for psychosis (CaCBTp) in Pakistan. *BMC Health Serv Res*. 2017;17:1-8.
67. Ishtiaq M, Afridi MI, Khan SA. Depression: prevalence & risk factors of depression among adult population of district peshawar. *Prof Med J*. 2018;25(08):1229-1234.
68. Umar Z, Tahir Z, Nizami A. Impact of severe mental illnesses on health-related quality of life among patients attending the Institute of Psychiatry, Rawalpindi from 2019 to 2021: A cross-sectional study. *PLoS One*. 2023;18(8):e0289080.
69. Kumar R. *Nursing Research & Statistics*. Jaypee Brothers Medical Publishers Pvt. Limited; 2019.
70. Khan A. Structured Diagnostic Interview for Screening DSM-5 (TR) Disorders. In: *Clinical Protocols and Diagnostic Tools for Psychiatrists and Psychologists*. Unpublished Forth Comming Book; 2023.
71. Walters SJ, Jacques RM, dos Anjos Henriques-Cadby IB, Candlish J, Totton N, Xian MTS. Sample size estimation for randomised controlled trials with repeated assessment of patient-reported outcomes: what correlation between baseline and follow-up outcomes should we

assume? *Trials*. 2020;20(1):566. doi:10.1186/s13063-019-3671-2
72. Schuster R, Kaiser T, Terhorst Y, Messner EM, Strohmeier L-M, Laireiter A-R. Sample size, sample size planning, and the impact of study context: systematic review and recommendations by the example of psychological depression treatment. *Psychol Med*. 2021;51(6):902-908.
73. Ma W, Qin Y, Li Y, Hu F. Statistical Inference for Covariate-Adaptive Randomization Procedures. *J Am Stat Assoc*. 2020;115(531):1488-1497. doi:10.1080/01621459.2019.1635483
74. Lin Y, Zhu M, Su Z. The pursuit of balance: an overview of covariate-adaptive randomization techniques in clinical trials. *Contemp Clin Trials*. 2016;45(8):21-25.
75. Hofmann A, Hase M, Liebermann P, et al. DeprEnd-EMDR Therapy Protocol for the Treatment of Depressive Disorders. In: Luber M, ed. *Eye Movement Desensitization and Reprocessing (EMDR) Therapy Scripted Protocols and Summary Sheets: Treating Anxiety, Obsessive-Compulsive, and Mood-Related Conditions.* Springer Publishing Company, LLC; 2016:289-313.
76. FUCI. Find and Update Company Information Service United Kingdom. https://find-and-update.company-information.service.gov.uk/company/11481195/officers. Published 2023.
77. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23(1):56.
78. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385-401.
79. Newman MG, Zuellig AR, Kachin KE, et al. Preliminary reliability and validity of the Generalized Anxiety Disorder Questionnaire-IV: A revised self-report diagnostic measure of generalized anxiety disorder. *Behav Ther*. 2002;33(2):215-233.
80. Wolpe J. Subjective units of distress scale. *J EMDR Pract Res*. 1969.
81. Matthijssen S, Brouwers T, Roozendaal V. The effect of EMDR versus EMDR 2.0 on emotionality and vividness of aversive memories in a non-clinical sample. *Eur J Psychotraumatol*. 2021;12(1):1956793.
82. Smyk A. The System Usability Scale & How It's Used in UX. https://xd.adobe.com/ideas/process/user-testing/sus-system-usability-scale-ux/. Published 2020.
83. Békés V, Aafjes-van Doorn K, McCollum J, Prout TR, Hoffman L. The development of a self-report scale to assess therapists' acceptance of telepsychotherapy. *J Clin Psychol*. 2022;78(6):1240-1260.
84. CPSHIT. Opportunities to Build a Safer System for Health IT. In: *Health IT and Patient Safety: Building Safer Systems for Better Care*. Committee on Patient Safety and Health Information Technology, Institute of Medicine, Washington, USA; 2012.
85. Dorsey S, Sedlar G, Jungbluth N. *Everyday Competence and Fidelity for EBP Organizations: Practical Guide*.; 2013.
86. Korn DL, Maxfield L, Stickgold R, Smyth NJ. EMDR Fidelity Rating Scale.
87. Kohrt BA, Jordans MJD, Rai S, et al. Therapist competence in global mental health: development of the ENhancing Assessment of Common Therapeutic factors (ENACT) rating scale. *Behav Res Ther*. 2015;69:11-21.
88. Bursnall M, Thomas BD, Berntsson H, Strong E, Brayne M, Hind D. Clinician and Patient Experience of Internet-Mediated Eye Movement Desensitisation and Reprocessing Therapy. *J Psychosoc Rehabil Ment Heal*. 2023;9(3):251-262.
89. Oei TPS, Green AL. The Satisfaction With Therapy and Therapist Scale--Revised (STTS-R) for group psychotherapy: Psychometric properties and confirmatory factor analysis. *Prof Psychol Res Pract*. 2009;39(4):435.
90. George D, Mallery P. *IBM SPSS Statistics 26 Step by Step: A Simple Guide and Reference*. Routledge; 2020.

91. Lee S, Lee DK. What is the proper way to apply the multiple comparison test? *Korean J Anesthesiol*. 2018;71(5):353-360.
92. David Garson G. Introductory Guide to HLM with SPSS Software. In: *Hierarchical Linear Modeling: Guide and Applications*. SAGE Publications Inc; 2014:121-146.
93. Hair J, Fávero LP. Multilevel modeling for longitudinal data: concepts and applications. *RAUSP Manag J*. 2019;54:459-489.
94. IBM. Likelihood Ratio Tests. https://www.ibm.com/docs/en/spss-statistics/27.0.0?topic=model-likelihood-ratio-tests. Published 2023.
95. Heck R, Thomas S, Tabata L. *Multilevel Modeling of Categorical Outcomes Using IBM SPSS*. Taylor & Francis; 2017. https://books.google.com.pk/books?id=PJsTMAuPv6kC.
96. Kalin NH. The critical relationship between anxiety and depression. *Am J Psychiatry*. 2020;177(5):365-367.
97. Zhang, Zyphur M, Preacher K. Testing multilevel mediation using hierarchical linear models: Problems and solutions. *Organ Res Methods*. 2010;12(4):695-719.
98. Baron RM, Kenny DA. The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*. 1986;51(6):1173.
99. Kenny DA, Korchmaros JD, Bolger N. Lower level mediation in multilevel models. *Psychol Methods*. 2003;8(2):115.