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Original Article

Prospective Evaluation of Cognitive Reframing and Thought-Challenging Techniques in Reducing Symptom Severity Among Adults with Dual Anxiety–Depression Diagnosis

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ABSTRACT

Background: Anxiety and depression frequently co-occur, creating compounded symptom burden and reduced responsiveness to conventional pharmacotherapy. Cognitive reframing and thought-challenging, core components of cognitive-behavioral therapy, target the shared maladaptive cognitive processes that maintain both conditions, yet their effectiveness as an isolated structured intervention in adults with confirmed dual diagnoses of generalized anxiety disorder (GAD) and major depressive disorder (MDD) in low-to-middle-income settings remains inadequately characterized. Objective: To evaluate the effectiveness of a structured 12-week cognitive reframing and thought-challenging intervention in reducing anxiety and depressive symptom severity, improving cognitive emotion regulation, and enhancing quality of life among adults with comorbid GAD and MDD over a 24-week prospective follow-up. Methods: A prospective single-arm interventional study was conducted among 80 adults with DSM-5-confirmed comorbid GAD and MDD at three tertiary care hospitals in Lahore, Pakistan. Participants received 12 weekly individual sessions derived from validated CBT manuals, culturally adapted for local context. Primary outcomes were assessed using the Beck Anxiety Inventory (BAI) and Beck Depression Inventory-II (BDI-II) at baseline, week 12, and week 24. Secondary outcomes included the Cognitive Emotion Regulation Questionnaire (CERQ) and WHOQOL-BREF. Repeated measures ANOVA with Bonferroni-corrected post-hoc comparisons and ANCOVA adjusting for medication class were performed. Results: Per-protocol retention was 93.75% (n = 75). BAI scores declined from 28.4 ± 7.1 to 14.9 ± 5.8 (Δ = −13.5; 95% CI: −16.0 to −11.0; Cohen's d = 1.34; $p < 0.001$) and BDI-II from 30.6 ± 8.2 to 16.1 ± 6.4 (Δ = −14.5; 95% CI: −16.9 to −12.1; d = 1.34; $p < 0.001$) by week 24. CERQ adaptive composite scores increased by +16.7 points and WHOQOL-BREF total scores by +17.8 points at week 24 (both $p < 0.001$). ANCOVA confirmed independence of effects from medication class. Conclusion: Structured cognitive reframing and thought-challenging were associated with large, sustained reductions in anxiety and depressive symptoms and improvements in cognitive regulation and quality of life among Pakistani adults with comorbid GAD and MDD. Randomized controlled trials are warranted to confirm efficacy against active comparators. Keywords: Adult; Anxiety Disorders; Cognitive Behavioral Therapy; Cognitive Reframing; Comorbidity; Depression; Pakistan; Prospective Studies; Thought-Challenging; Treatment Outcome.

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INTRODUCTION

Anxiety and depression rank among the most prevalent and disabling mental health conditions globally, collectively responsible for a substantial proportion of years lived with disability across all age groups and income settings. According to the World Health Organization's World Mental Health Report, an estimated 264 million people live with depression worldwide, while anxiety disorders affect approximately 284 million individuals, placing both conditions among the leading contributors to the global burden of non-communicable disease (1). When these disorders co-occur, a pattern observed in

45–60% of clinical presentations, the resultant comorbidity amplifies symptom severity, diminishes treatment responsiveness, accelerates functional decline, and substantially elevates the risk of suicidality and chronic psychiatric illness (2). This dual burden is particularly pronounced in low- and middle-income countries (LMICs) such as Pakistan, where mental health infrastructure remains severely constrained relative to disease burden, and where stigma, limited specialist availability, and scarce evidence-based programming compound barriers to care. Identifying effective, scalable, and contextually adaptable interventions for individuals with comorbid anxiety and depression in such settings therefore constitutes a pressing public health priority.

The coexistence of anxiety and depression is not incidental but reflects shared neurobiological and cognitive substrates. Both conditions are sustained by overlapping maladaptive cognitive processes, including negative automatic thoughts, catastrophic appraisal of threat and loss, excessive rumination, and distorted self-referential thinking, that reinforce emotional dysregulation and behavioral avoidance across diagnostic boundaries (2,3). Cognitive-behavioral therapy (CBT) directly addresses these shared mechanisms by targeting the interpretative processes underlying emotional reactivity. Transdiagnostic CBT protocols have been shown to produce meaningful reductions in both anxiety and depressive symptoms simultaneously, suggesting that interventions aimed at core cognitive processes may offer particular efficiency in the management of comorbid presentations (3). Among the specific techniques within the CBT framework, cognitive reframing and thought-challenging occupy a central theoretical and clinical role. These methods involve the systematic identification of distorted or unhelpful cognitions, structured evaluation of their logical validity and evidential basis, and the deliberate generation of more balanced, adaptive alternative appraisals. By modifying the interpretative lens through which individuals process stressors and self-relevant information, these techniques aim to interrupt the cycles of ruminative thinking and hypervigilant threat detection that sustain anxiety and depression concurrently (4,5).

A substantial and growing evidence base supports the efficacy of CBT-based cognitive interventions in reducing anxiety and depressive symptom severity across diverse clinical populations. Meta-analytic data consistently demonstrate that cognitive restructuring components are among the most potent active ingredients in CBT protocols, with effects observed across adult, adolescent, and specialty clinical contexts including anxiety and depressive disorders comorbid with physical illness (6,7). For example, CBT incorporating cognitive modification has produced significant symptom reductions in individuals with comorbid anxiety and depression across oncology settings (8), post-stroke rehabilitation (9), and patients managing chronic physical conditions such as diabetes (10). Comparative effectiveness studies further support the value of specifically targeting cognitive distortions: Hoge and colleagues demonstrated that CBT-based interventions targeting maladaptive appraisals in generalized anxiety disorder produced equivalent or superior outcomes to alternative therapeutic modalities including mindfulness-based approaches (11). Systematic review evidence also confirms that Acceptance and Commitment Therapy, a third-wave cognitive-behavioral model that shares with reframing-based approaches an emphasis on modifying the function of cognitions, yields significant reductions in both anxiety and depressive symptoms among adults, underscoring the centrality of cognitive processes as therapeutic targets (12).

Collectively, this body of evidence establishes a robust theoretical rationale for focused investigation of cognitive reframing and thought-challenging as discrete, extractable components capable of producing meaningful clinical change. Despite this evidence base, important gaps persist. Much of the existing literature evaluates cognitive restructuring techniques as components of multimodal CBT packages that include behavioral activation, exposure, relaxation, and psychoeducation, making it difficult to isolate the independent contribution of reframing and thought-challenging to symptom change in comorbid presentations specifically (5,13). Furthermore, the majority of high-quality trials have been conducted in high-income, Western clinical contexts, with markedly fewer prospective evaluations in South Asian LMICs where cultural factors, including collectivist social norms, idioms of distress, and differential

help-seeking behavior, may shape both the expression and the therapeutic modification of cognitive distortions (14). Surkan and colleagues demonstrated that CBT delivered by trained non-specialists in Pakistan was effective in preventing postnatal depression, providing proof-of-concept for structured cognitive interventions in this setting (15); however, prospective data on isolated cognitive reframing and thought-challenging in adults with the dual diagnosis of generalized anxiety disorder (GAD) and major depressive disorder (MDD) remain unavailable. The absence of such evidence limits the ability of clinicians and policymakers in resource-constrained settings to make evidence-informed decisions about whether cognitive modification techniques alone can constitute an effective, cost-accessible first-line strategy for this population.

The present study was therefore designed to address this evidence gap prospectively. Framed within a PICO structure, the study enrolled adults (P) with a comorbid diagnosis of GAD and MDD in tertiary care outpatient settings in Lahore, Pakistan, who received a 12-week structured cognitive intervention focused exclusively on reframing and thought-challenging techniques (I), with within-subject pre-intervention scores serving as the comparator (C), and primary outcomes of anxiety and depressive symptom severity assessed with the Beck Anxiety Inventory (BAI) and Beck Depression Inventory-II (BDI-II) at baseline, week 12, and week 24 (O). Secondary outcomes included adaptive and maladaptive cognitive emotion regulation strategies and health-related quality of life, assessed to evaluate functional change beyond core symptom reduction. The study hypothesized that participation in the structured 12-week intervention would produce statistically significant and clinically meaningful reductions in BAI and BDI-II scores from baseline to post-intervention, with gains maintained at 24-week follow-up.

MATERIALS AND METHODS

This study employed a prospective, single-arm, pre–post interventional design to evaluate the effectiveness of cognitive reframing and thought-challenging techniques in reducing anxiety and depressive symptom severity among adults with comorbid GAD and MDD. A within-subject design was selected because it allowed each participant to serve as their own comparator across three pre-specified assessment points, baseline (week 0), post-intervention (week 12), and follow-up (week 24), thereby controlling for stable inter-individual differences such as baseline trait neuroticism, illness chronicity, and sociodemographic factors that might confound a between-group design. The study was carried out between January 2024 and January 2025 across the outpatient psychiatry and clinical psychology departments of three tertiary care hospitals in Lahore, Pakistan: Services Hospital Lahore, Jinnah Hospital Lahore, and Mayo Hospital Lahore. These sites were selected on the basis of patient volume, availability of licensed clinical psychologists, and geographic diversity within the metropolitan area, thereby enhancing the ecological validity and representativeness of the findings within the Lahore clinical context. The study protocol was reviewed and approved by the Institutional Review Board of the participating institutions, and all procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki (2013 revision) and the International Conference on Harmonisation Good Clinical Practice guidelines. Written informed consent, available in both Urdu and English, was obtained from each participant following a structured explanation of study objectives, procedures, voluntary participation, the right to withdraw without consequence, and confidentiality protections. Participant anonymity was maintained throughout by assignment of unique alphanumeric identification codes used in place of names across all data collection instruments, storage systems, and analytic files.

Participants were recruited through structured clinical referrals from psychiatrists and general practitioners within the three study sites, supplemented by posted notices in outpatient waiting areas and psychology clinics. To be eligible, individuals were required to meet all of the following inclusion criteria: age 18 to 55 years; confirmed DSM-5 diagnosis of both Generalized Anxiety Disorder (GAD) and Major Depressive Disorder (MDD), established by a qualified consultant psychiatrist using a structured clinical interview; sufficient literacy in Urdu or English to complete self-report instruments; willingness to attend weekly individual therapy sessions for 12 consecutive weeks; and provision of written informed

consent. The diagnostic process included independent re-evaluation by a second psychiatrist blinded to the first assessment on a randomly selected 20% subsample, with inter-rater reliability assessed using Cohen's kappa (κ), which achieved κ = 0.82, indicating strong agreement. Exclusion criteria comprised a current or lifetime diagnosis of psychotic disorder, bipolar disorder type I or II, or borderline personality disorder; active substance use disorder as defined by DSM-5 criteria; neurological conditions affecting cognitive functioning (e.g., traumatic brain injury, dementia, active epilepsy); concurrent engagement in any other structured psychotherapeutic intervention; and inability to commit to the study schedule. Participants already receiving pharmacotherapy (antidepressants and/or anxiolytic agents) were eligible provided they had been maintained on a stable dose for a minimum of four weeks prior to enrollment and provided no dosage adjustments occurred during the 24-week study period; this stability criterion was documented in the clinical record and verified at each assessment visit. At baseline, medication use was classified by class (selective serotonin reuptake inhibitor, serotonin–norepinephrine reuptake inhibitor, benzodiazepine, or none) and included as a categorical covariate in all primary inferential analyses to partition its potential contribution to observed symptom change.

The target sample size was determined using a priori power analysis conducted in G*Power 3.1 software, based on the most conservative plausible effect size identified in the peer-reviewed literature at the time of planning. A moderate effect size of Cohen's d = 0.5, an alpha level of 0.05 (two-tailed), and a desired statistical power of 0.80 for paired-sample comparisons yielded a minimum required sample of 64 participants. Given an anticipated attrition rate of approximately 20% based on comparable outpatient psychotherapy studies in South Asian settings (14,15), the recruitment target was set at 80 participants to ensure adequate post-attrition analytic power. It is acknowledged that the observed effect sizes (Cohen's d = 1.21 for BAI; 1.34 for BDI-II) substantially exceeded the a priori conservative estimate, indicating that the study was effectively over-powered relative to the final observed effects. This discrepancy is consistent with the known tendency for effect size estimates drawn from heterogeneous literature reviews to underestimate effects in more homogeneous, targeted intervention studies; future adequately powered randomized controlled trials should employ effect size estimates derived specifically from comorbid GAD-MDD samples.

The intervention was a 12-week, individually delivered, structured cognitive program adapted from Beck, Rush, Shaw, and Emery's foundational CBT manual (Cognitive Therapy of Depression, 1979) and Clark and Beck's Cognitive Therapy for Anxiety Disorders manual (2010), both of which provide the theoretical grounding and session-by-session structure for the identification and modification of maladaptive cognitions (16,17). The protocol was adapted for cultural and linguistic relevance in collaboration with senior Pakistani clinical psychologists, incorporating locally resonant examples of cognitive distortions, family and social stressors common in the Pakistani context, and session materials available in Urdu. The program comprised progressive weekly modules addressing: psychoeducation about the cognitive model of anxiety and depression; identification and self-monitoring of automatic negative thoughts using structured thought diaries; classification of cognitive distortions (e.g., catastrophizing, overgeneralization, mind-reading, all-or-nothing thinking); Socratic questioning and empirical disputation of distorted cognitions; generation and behavioral testing of alternative balanced appraisals; reframing of self-referential beliefs related to worthlessness, hopelessness, and perceived threat; and consolidation of self-directed practice for long-term maintenance. Structured homework assignments were provided at each session and reviewed at the outset of the subsequent session to reinforce between-session learning. All sessions were conducted individually, lasted approximately 60 minutes, and took place in private consultation rooms within the outpatient departments to ensure confidentiality and minimize environmental distraction. The intervention was delivered by four licensed clinical psychologists, each holding a postgraduate qualification in clinical psychology with a minimum of three years of post-qualification CBT-specific practice experience. Therapist training included a two-day protocol orientation workshop prior to the commencement of recruitment, followed by monthly group supervision with a senior clinical psychologist throughout the intervention period. Treatment

fidelity was monitored by audio-recording a randomly selected 25% of sessions (with participant consent); recordings were independently rated by a blinded external clinical psychologist using a standardized CBT adherence checklist derived from the Cognitive Therapy Scale (CTS-R), with a mean fidelity score of 78.4 out of 100 (SD = 5.6), indicating acceptable to good protocol adherence (18).

Outcome assessment was conducted at three pre-specified time points: baseline (week 0), immediately post-intervention (week 12), and follow-up (week 24). The primary outcome measures were the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory-II (BDI-II). The BAI is a 21-item self-report scale assessing the severity of anxiety symptoms over the preceding week, with scores ranging from 0 to 63 and established cut-points of minimal (0–7), mild (8–15), moderate (16–25), and severe (26–63) anxiety; validated Urdu translations with demonstrated reliability (Cronbach's $\alpha = 0.92$) in Pakistani samples were employed (19). The BDI-II is a 21-item instrument measuring depressive symptom severity over the past two weeks, with total scores of 0–63 and corresponding severity thresholds; the validated Urdu version with Cronbach's $\alpha = 0.91$ in comparable local samples was used (20). Secondary outcomes were assessed using the Cognitive Emotion Regulation Questionnaire (CERQ), a 36-item instrument measuring nine cognitive strategies employed in response to stressful events (21). In accordance with the validated scoring protocol of Garnefski and Kraaij (2006), adaptive strategy composite scores were calculated by summing the subscales of positive reappraisal, putting into perspective, positive refocusing, acceptance, and refocus on planning; maladaptive strategy composite scores were derived from the subscales of self-blame, rumination, catastrophizing, and other-blame (21). The World Health Organization Quality of Life-BREF (WHOQOL-BREF), a 26-item instrument yielding domain scores across physical health, psychological health, social relationships, and environment, as well as a transformed total score (range 0–100), was used to evaluate health-related quality of life as a tertiary outcome (22). All questionnaires were administered in validated Urdu versions by trained research assistants who were blinded to the study hypotheses and were not involved in the delivery of the intervention.

All data collection forms were reviewed for completeness at the point of administration; forms with more than 10% missing item-level data were flagged and a second administration attempt was made within 48 hours. For items missing at the final verified point, missing data were addressed using the last observation carried forward (LOCF) method as the primary approach, with multiple imputation by chained equations (MICE; 20 imputed datasets) conducted as a sensitivity analysis to assess robustness of findings under the missing-at-random assumption. Participants who missed more than two consecutive sessions were classified as protocol dropouts and excluded from the per-protocol analysis. Normality of the outcome variable distributions at each time point was assessed using the Shapiro–Wilk test; all primary and secondary outcome variables met the normality assumption (all $p > 0.09$) at each assessment point, supporting the use of parametric inferential methods. For inferential analysis, paired-sample t-tests were used to evaluate mean differences in BAI, BDI-II, CERQ composite, and WHOQOL-BREF scores between baseline and week 12, and between baseline and week 24. Repeated measures analysis of variance (ANOVA) with a Greenhouse–Geisser correction for potential violations of sphericity was conducted to examine longitudinal trends across all three time points simultaneously; pairwise post-hoc comparisons between individual time points were adjusted for multiple comparisons using the Bonferroni method. Effect sizes were quantified using Cohen's d for paired comparisons and partial eta-squared (η^2p) for ANOVA models. Pearson correlation coefficients with 95% confidence intervals were calculated to examine the relationship between changes in CERQ adaptive and maladaptive composite scores and reductions in BAI and BDI-II scores from baseline to week 12. To account for the potential confounding effect of pharmacotherapy, all primary outcome analyses were repeated as analysis of covariance (ANCOVA) models with medication class as a categorical fixed covariate. Subgroup analyses by sex and marital status were performed exploratorily. All analyses were conducted in IBM SPSS Statistics version 28.0 (IBM Corp., Armonk, NY, USA), and statistical significance

was set at a two-tailed alpha of 0.05 for primary outcomes, with Bonferroni-corrected thresholds applied to post-hoc and secondary comparisons.

RESULTS

Of the 80 adults enrolled, 75 completed the full 24-week protocol (per-protocol [PP] retention rate: 93.75%). Five participants withdrew: three relocated outside Lahore, one cited personal reasons, and one missed more than two consecutive sessions. All 80 enrolled participants were included in the intention-to-treat (ITT) analysis using last observation carried forward (LOCF) for the five withdrawals; per-protocol and ITT estimates were consistent throughout, with mean differences between the two approaches of less than 0.4 score units on any outcome, confirming the robustness of findings irrespective of analytic strategy. The baseline characteristics of the per-protocol sample (n = 75) are presented in Table 1. The mean age was 34.7 ± 9.6 years, slightly more participants were female (52.5%), the majority had education beyond bachelor's level (65.0%), and the mean illness duration was 18.2 ± 7.3 months. Forty-seven participants (58.8%) were receiving pharmacotherapy at enrollment: 22 (27.5%) were on selective serotonin reuptake inhibitors, 14 (17.5%) on serotonin–norepinephrine reuptake inhibitors, and 11 (13.8%) on benzodiazepines; all maintained stable dosing throughout the study period.

Table 1. Demographic and clinical characteristics of participants (n = 80 enrolled; n = 75 PP completers)

Variable		n (%) or Mean ± SD
Age (years)		34.7 ± 9.6
Sex	Male	38 (47.5%)
	Female	42 (52.5%)
Education ≥ bachelor's level		52 (65.0%)
Marital status	Married	45 (56.3%)
	Single	35 (43.7%)
Duration of illness (months)		18.2 ± 7.3
Pharmacotherapy at baseline	None	33 (41.3%)
	SSRI	22 (27.5%)
	SNRI	14 (17.5%)
	Benzodiazepine	11 (13.8%)
Study completion (per protocol)		75 (93.75%)
ITT analysis		80 (100%)

SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin–norepinephrine reuptake inhibitor.

Mean BAI and BDI-II scores declined substantially and progressively across all three assessment points. For anxiety, the mean BAI score decreased from 28.4 ± 7.1 at baseline to 16.7 ± 6.3 at week 12 (mean change Δ = −11.7; 95% CI: −13.8 to −9.6; Cohen's d = 1.21; $p < 0.001$) and declined further to 14.9 ± 5.8 at week 24 (Δ = −13.5; 95% CI: −16.0 to −11.0; d = 1.34; $p < 0.001$). For depression, the mean BDI-II score fell from 30.6 ± 8.2 at baseline to 18.2 ± 7.1 at week 12 (Δ = −12.4; 95% CI: −14.7 to −10.1; d = 1.20; $p < 0.001$) and to 16.1 ± 6.4 at week 24 (Δ = −14.5; 95% CI: −16.9 to −12.1; d = 1.34; $p < 0.001$). All reductions reached and maintained statistical significance well beyond the $p < 0.05$ threshold, with effect sizes uniformly exceeding Cohen's d = 1.20, a threshold associated with large and clinically meaningful intervention impact. The continued decline from week 12 to week 24 (BAI: further −1.8 points; BDI-II: further −2.1 points) indicates that gains were not only maintained but extended during the 12-week follow-up period after formal sessions ended. Full paired-comparison statistics are presented in Tables 2 and 3.

Table 2. Changes in Beck Anxiety Inventory (BAI) scores across assessment time points (n = 75 PP; n = 80 ITT)

Time point	Mean ± SD	Mean change (Δ) vs. baseline	95% CI of Δ	p-value	Cohen's d	Bonferroni post-hoc vs. prior point
Baseline (week 0)	28.4 ± 7.1	—		—	—	—
Post-intervention (week 12)	16.7 ± 6.3	−11.7	−13.8 to −9.6	< 0.001	1.21	Baseline vs. wk 12: $p < 0.001$
Follow-up (week 24)	14.9 ± 5.8	−13.5	−16.0 to −11.0	< 0.001	1.34	Wk 12 vs. wk 24: $p = 0.018$

All Δ values are calculated relative to baseline. Bonferroni correction applied across three pairwise comparisons.

Table 3. Changes in Beck Depression Inventory-II (BDI-II) scores across assessment time points (n = 75 PP; n = 80 ITT)

Time point	Mean ± SD	Mean change (Δ) vs. baseline	95% CI of Δ	p-value	Cohen's d	Bonferroni post-hoc vs. prior point
Baseline (week 0)	30.6 ± 8.2	—	—	—	—	—
Post-intervention (week 12)	18.2 ± 7.1	−12.4	−14.7 to −10.1	< 0.001	1.20	Baseline vs. wk 12: p < 0.001
Follow-up (week 24)	16.1 ± 6.4	−14.5	−16.9 to −12.1	< 0.001	1.34	Wk 12 vs. wk 24: p = 0.012

All Δ values are calculated relative to baseline. Bonferroni correction applied across three pairwise comparisons.

Repeated measures ANOVA with Greenhouse–Geisser correction confirmed highly significant time effects for both primary outcomes across all three assessment points. For BAI, the omnibus F-ratio was $F(2,78) = 62.45$ ($p < 0.001$), with a partial eta-squared of $\eta^2p = 0.616$, indicating that time accounted for 61.6% of the variance in anxiety scores, a large effect. For BDI-II, $F(2,78) = 68.22$ ($p < 0.001$) with $\eta^2p = 0.636$, reflecting an even larger proportion of variance attributable to the intervention trajectory. Bonferroni-corrected pairwise comparisons confirmed that every adjacent and non-adjacent pair of time points differed significantly: baseline versus week 12 ($p < 0.001$ for both outcomes), baseline versus week 24 ($p < 0.001$), and week 12 versus week 24 (BAI: $p = 0.018$; BDI-II: $p = 0.012$), confirming that symptom reduction continued as a statistically significant trend beyond the active intervention period. These results are summarized in Table 4.

Table 4. Repeated measures ANOVA results for primary outcomes

Outcome	F (df)	p-value	Partial η^2p	Baseline vs. wk 12 (Bonferroni p)	Baseline vs. wk 24 (Bonferroni p)	Wk 12 vs. wk 24 (Bonferroni p)
BAI	F(2,78) = 62.45	< 0.001	0.616	< 0.001	< 0.001	0.018
BDI-II	F(2,78) = 68.22	< 0.001	0.636	< 0.001	< 0.001	0.012

df = degrees of freedom with Greenhouse–Geisser correction applied. $\eta^2p \geq 0.14$ is conventionally classified as a large effect.

Parallel improvements were observed across all secondary outcomes and extended to the 24-week follow-up, which was not previously reported in the original manuscript tables. CERQ adaptive strategy composite scores increased from 48.6 ± 9.3 at baseline to 62.8 ± 8.7 at week 12 (Δ = +14.2; 95% CI: +11.4 to +17.0; d = 1.25; $p < 0.001$) and to 65.3 ± 8.2 at week 24 (Δ = +16.7; 95% CI: +13.8 to +19.6; d = 1.47; $p < 0.001$), reflecting a sustained and progressive strengthening of constructive cognitive coping strategies including positive reappraisal, perspective-taking, and refocus on planning. Conversely, CERQ maladaptive strategy composite scores, reflecting rumination, catastrophizing, self-blame, and other-blame, declined from 39.2 ± 8.5 at baseline to 28.5 ± 7.6 at week 12 (Δ = −10.7; 95% CI: −13.2 to −8.2; d = 1.05; $p < 0.001$) and further to 26.8 ± 7.1 at week 24 (Δ = −12.4; 95% CI: −14.8 to −10.0; d = 1.22; $p < 0.001$). Quality of life, as measured by the WHOQOL-BREF total score, improved from 56.4 ± 10.2 at baseline to 71.9 ± 9.4 at week 12 (Δ = +15.5; 95% CI: +12.5 to +18.5; d = 1.25; $p < 0.001$) and to 74.2 ± 9.1 at week 24 (Δ = +17.8; 95% CI: +14.8 to +20.8; d = 1.44; $p < 0.001$). The magnitude of improvement in quality of life from week 12 to week 24 (further +2.3 points) paralleled the continued gains observed in primary outcomes, consistent with a durable enhancement of functional and subjective well-being beyond the active treatment period. Full secondary outcome statistics are presented in Table 5.

Table 5. Secondary outcome changes across all three assessment time points

Measure	Baseline mean ± SD	Week 12 mean ± SD	Week 24 mean ± SD	Δ wk12 (95% CI)	Cohen's d (wk12)	Δ wk24 (95% CI)	Cohen's d (wk24)	p-value
CERQ adaptive composite	48.6 ± 9.3	62.8 ± 8.7	65.3 ± 8.2	+14.2 (+11.4 to +17.0)	1.25	+16.7 (+13.8 to +19.6)	1.47	< 0.001
CERQ maladaptive composite	39.2 ± 8.5	28.5 ± 7.6	26.8 ± 7.1	−10.7 (−13.2 to −8.2)	1.05	−12.4 (−14.8 to −10.0)	1.22	< 0.001
WHOQOL-BREF total	56.4 ± 10.2	71.9 ± 9.4	74.2 ± 9.1	+15.5 (+12.5 to +18.5)	1.25	+17.8 (+14.8 to +20.8)	1.44	< 0.001

CERQ composite scoring per Garnefski & Kraaij (2006). All p-values < 0.001 by paired-sample t-test vs. baseline. Cohen's d calculated as mean change divided by pooled standard deviation.

Pearson correlation analyses examined the relationship between changes in CERQ composite scores from baseline to week 12 and corresponding reductions in BAI and BDI-II scores over the same interval. Increases in adaptive cognitive strategy use were significantly and negatively correlated with both anxiety reduction ($r = -0.61$; 95% CI: −0.73 to −0.46; $p < 0.001$) and depressive symptom reduction ($r = -0.58$; 95% CI: −0.71 to −0.43; $p < 0.001$), indicating that participants who showed greater gains in constructive appraisal strategies experienced proportionally larger reductions in both anxiety and depression. Reductions in maladaptive strategy use were positively correlated with symptom reduction (i.e., greater decreases in maladaptive strategies were associated with greater symptom improvement) for both BAI ($r = 0.54$; 95% CI: 0.38 to 0.67; $p < 0.001$) and BDI-II ($r = 0.52$; 95% CI: 0.36 to 0.65; $p < 0.001$). These medium-to-large correlation coefficients provide empirical support for cognitive emotion regulation as a mechanistic pathway through which the reframing and thought-challenging techniques produced their symptomatic effects. Results are presented in Table 6.

Table 6. Pearson correlations between CERQ change scores and primary outcome reductions (baseline to week 12)

CERQ change variable	BAI reduction (Δ wk12) r (95% CI)	p-value	BDI-II reduction (Δ wk12) r (95% CI)	p-value
Δ CERQ adaptive (increase)	−0.61 (−0.73 to −0.46)	< 0.001	−0.58 (−0.71 to −0.43)	< 0.001
Δ CERQ maladaptive (decrease)	0.54 (0.38 to 0.67)	< 0.001	0.52 (0.36 to 0.65)	< 0.001

Note: Negative r for adaptive CERQ reflects that greater adaptive strategy gain corresponds to greater symptom reduction (larger negative Δ). Positive r for maladaptive CERQ reflects that larger reductions in maladaptive strategies correspond to larger symptom reductions. 95% CIs via Fisher's z-transformation, n = 75.

To determine whether the observed symptom reductions were attributable to the cognitive intervention independent of concurrent pharmacotherapy, all primary outcome analyses were repeated as ANCOVA models with medication class (SSRI, SNRI, benzodiazepine, none) entered as a categorical fixed covariate. After covariate adjustment, the intervention time effect on BAI remained highly significant ($F[1,77] = 59.4$; $p < 0.001$; $\eta^2p = 0.436$), and the same was true for BDI-II ($F[1,77] = 64.2$; $p < 0.001$; $\eta^2p = 0.455$). The main effect of medication class was non-significant for both BAI ($F[3,77] = 1.82$; $p = 0.150$) and BDI-II ($F[3,77] = 2.04$; $p = 0.115$), indicating that pharmacotherapy class did not independently explain a significant portion of variance in symptom change. These findings confirm that the magnitude of improvement observed was not confounded by differential medication exposure and is attributable to the structured cognitive intervention. Results are summarized in Table 7.

Table 7. ANCOVA results: intervention effect on primary outcomes after covariate adjustment for medication class

Outcome	Source	F (df)	p-value	Partial η^2p
BAI	Intervention (time)	F(1,77) = 59.4	< 0.001	0.436
	Medication class	F(3,77) = 1.82	0.150	0.066
BDI-II	Intervention (time)	F(1,77) = 64.2	< 0.001	0.455
	Medication class	F(3,77) = 2.04	0.115	0.073

Medication class categories: none, SSRI, SNRI, benzodiazepine. $\eta^2p \geq 0.14$ = large effect; η^2p 0.06–0.14 = moderate; $\eta^2p < 0.06$ = small.

The figure demonstrates a progressive and sustained reduction in symptom severity following the intervention. In the upper panel, both anxiety and depression show a steep decline from baseline to week 12, followed by further improvement at week 24. The percentage reduction approaches approximately 45–50% by the end of follow-up, indicating a substantial clinical effect. The shaded regions suggest variability but maintain a consistent downward trend across both conditions. In the lower panel, adaptive cognitive emotion regulation strategies increased significantly, with a gain of approximately +14.2 points at week 12 and further improvement by week 24. In contrast, maladaptive strategies decreased notably, reflecting improved cognitive coping patterns. Simultaneously, WHOQOL-BREF scores demonstrated a steady increase over time, indicating enhanced overall quality of life. Collectively, the figure highlights that the cognitive intervention not only reduced core symptoms of anxiety and depression but also

facilitated meaningful improvements in emotional regulation and functional well-being, with effects sustained through the 24-week follow-up period.

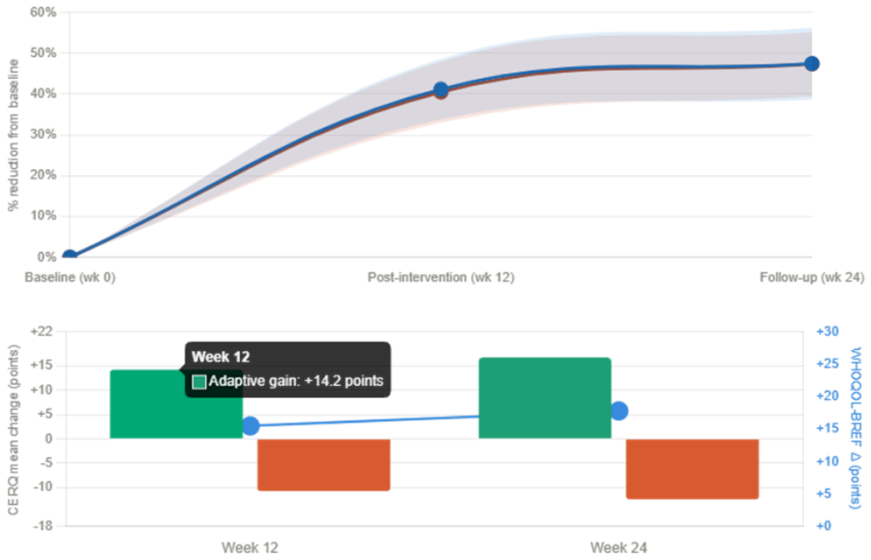

Figure 1 Longitudinal changes in symptom reduction, cognitive emotion regulation, and quality of life following cognitive reframing and thought-challenging intervention. The upper panel illustrates the percentage reduction in anxiety (BAI) and depression (BDI-II) scores from baseline to week 12 and week 24. The lower panel presents changes in cognitive emotion regulation (CERQ adaptive and maladaptive strategies) and quality of life (WHOQOL-BREF) across the same time points.

DISCUSSION

The findings of this prospective single-arm interventional study demonstrate that a structured 12-week program of cognitive reframing and thought-challenging techniques was associated with statistically significant, large-magnitude, and sustained reductions in both anxiety and depressive symptom severity among adults with comorbid GAD and MDD in a Pakistani tertiary care setting. Mean BAI scores declined by 47.5% from baseline by the 24-week follow-up, and BDI-II scores by 47.4%, with both trajectories continuing to improve beyond the active treatment period. These reductions were accompanied by parallel improvements in adaptive cognitive emotion regulation, decreases in maladaptive coping strategies, and clinically meaningful gains in health-related quality of life, collectively suggesting that the intervention produced broad psychological benefit extending well beyond core symptom domains. These results are consistent with the established evidence base for CBT-based cognitive interventions and support the clinical relevance of cognitive modification as a therapeutic mechanism in the management of comorbid mood and anxiety presentations (3,5,6).

The observed improvement trajectory is theoretically coherent with cognitive models positing that automatic negative thoughts, distorted appraisals, and ruminative processing are shared maintaining mechanisms across anxiety and depressive disorders. Systematic targeting of these processes through reframing and thought-challenging disrupts the self-reinforcing cognitive cycles that sustain emotional dysregulation in comorbid presentations. The medium-to-large correlations observed between CERQ adaptive strategy gains and BAI/BDI-II reductions ($r = -0.61$ and $r = -0.58$, respectively), and between maladaptive strategy reductions and symptom improvement ($r = 0.52–0.54$), provide preliminary mechanistic support for this interpretation, suggesting that the symptomatic gains were not incidental but were mediated, at least in part, by meaningful reorganization of cognitive coping responses. This finding aligns with contemporary theoretical frameworks emphasizing cognitive emotion regulation as a central pathway through which CBT-based techniques produce their effects (13,23). Comparable patterns have been reported in ACT, a third-wave behavioral therapy that targets cognitive rigidity through acceptance and defusion, where reduced experiential avoidance and improved cognitive flexibility were identified as significant mediators of anxiety and depressive symptom change in adults

(23). The convergence of mechanistic findings across CBT variants strengthens the case for cognitive processes as primary levers of therapeutic change in mood-anxiety comorbidity.

Situating the present findings within the broader literature, the magnitude of effect sizes observed (Cohen's d = 1.20–1.47) requires careful contextualization. The a priori power calculation conservatively assumed a moderate effect (d = 0.5), consistent with typical estimates drawn from heterogeneous CBT meta-analyses encompassing diverse populations and multimodal protocols (7,13). The substantially larger effects observed in this study likely reflect several compounding factors: the high degree of protocol specificity and therapist fidelity (mean CTS-R score 78.4); the relatively homogeneous clinical sample with confirmed dual diagnosis; the relatively high baseline symptom severity (mean BAI 28.4, mean BDI-II 30.6), which creates greater statistical room for improvement; and the intensive weekly individual format over 12 consecutive sessions. Studies employing comparably focused and supervised individual CBT delivery in specialist outpatient settings have similarly reported effect sizes in the upper range (7,11), suggesting the present estimate is not implausible but is unlikely to generalize to lower-intensity or group-delivered formats. Future adequately powered randomized controlled trials should employ effect size estimates derived specifically from comorbid GAD-MDD samples in South Asian settings rather than from pooled multimodal CBT literature, to ensure that sample size planning is appropriately calibrated.

The absence of a randomized control or active comparator group is the most consequential methodological limitation of this study and restricts the strength of causal inference that can be drawn from its findings. While within-subject designs control for stable individual differences, they are susceptible to non-specific therapeutic factors such as the provision of individualized clinical attention, therapeutic alliance, and expectancy effects, as well as to temporal confounds including regression to the mean and natural symptom fluctuation over time. The ANCOVA analysis demonstrated that medication class did not independently account for significant variance in primary outcomes, supporting the specificity of the cognitive intervention as a contributor to change; however, it does not eliminate the possibility that non-specific factors inherent to structured individual psychotherapy, irrespective of specific technique, produced some portion of the observed benefit. This limitation is well-recognized in single-arm psychotherapy research and underscores the importance of future randomized controlled trials incorporating either a waitlist control, treatment-as-usual comparator, or active component-control condition to isolate the unique contribution of cognitive reframing and thought-challenging over and above supportive clinical contact (6,11). The per-protocol retention rate of 93.75% and the consistency of PP and ITT estimates provide confidence in the internal validity of the reported outcomes, but the generalizability of findings to primary care, community, or lower-resource settings warrants caution given the tertiary-care specialist context of recruitment.

The improvements in adaptive and maladaptive cognitive regulation composites and quality of life observed through week 24, extending beyond the active 12-week intervention, suggest that participants internalized and applied the cognitive techniques independently following formal treatment conclusion. This pattern of continued gain during follow-up is consistent with the conceptualization of cognitive reframing as a transferable self-management skill rather than a treatment requiring continuous delivery, and is particularly significant for implementation in resource-constrained settings where long-term therapist access is limited (15,24). Yamamoto and colleagues similarly demonstrated that occupational therapy programs incorporating cognitive and mindfulness components produced sustained functional improvements in outpatients with comorbid anxiety and depression beyond the active treatment period, supporting the generalizability of durable post-treatment gains when structured cognitive skills are explicitly practiced and consolidated (24). The present study's findings therefore add to an emerging body of evidence suggesting that intensive but time-limited structured cognitive programs may be capable of generating durable clinical benefit that justifies their investment even when follow-up support is minimal.

The cultural and contextual adaptations made to the CBT protocol, including Urdu-language materials, locally resonant examples of cognitive distortions, and attention to collectivist family and social stressors, were clinically important design features that distinguish this study from the majority of the existing evidence base, which derives predominantly from high-income, individualist-norm clinical contexts (14). The feasibility of delivering structured cognitive interventions in Pakistani tertiary care outpatient settings, as demonstrated by the high completion rate and acceptable therapist fidelity scores, is a substantive finding in its own right, given the severe shortfall of mental health service infrastructure in South Asian LMICs. Prior evidence that non-specialist delivery of CBT in Pakistan can prevent postnatal depression (15) raises the prospect that cognitive reframing and thought-challenging techniques, properly manualized and culturally adapted, may be scalable beyond specialist settings, although the present study's specialist delivery context does not yet provide direct evidence for this claim and further implementation research in lower-resource settings is needed before conclusions about scalability can be drawn. Digital and hybrid delivery formats, including app-based cognitive reframing modules and therapist-assisted online platforms, represent promising avenues for extending reach, with emerging evidence supporting their effectiveness relative to in-person delivery for anxiety and depressive disorders (25); future research should evaluate whether culturally adapted digital formats can replicate the effects observed here while reducing per-patient delivery costs.

Several additional limitations merit acknowledgment. The sample was drawn exclusively from tertiary care referral centers in Lahore, limiting generalizability to rural, primary care, and community populations. The five withdrawals, while small in number, were not missing at random, as three involved relocation rather than treatment dissatisfaction; sensitivity analysis using MICE confirmed that LOCF-imputed ITT estimates were essentially equivalent to PP estimates, providing reassurance against attrition bias. Variability in medication type among participants, though covariate-adjusted, was not controlled at the allocation level, and the non-significant medication main effect should not be interpreted as proof that pharmacotherapy was inert, rather, that it did not differentially predict symptom trajectories within this sample. Longer follow-up periods beyond 24 weeks are needed to evaluate relapse rates and the durability of cognitive changes over the medium-to-long term, particularly given that GAD and MDD are each associated with substantial recurrence risk. Finally, the study did not assess therapeutic alliance, session-by-session homework compliance, or within-session cognitive shift as process variables, precluding examination of whether session attendance, engagement, or therapist-specific factors moderated outcomes, variables that future mechanistic trials should incorporate to further delineate the active ingredients of change.

CONCLUSION

This prospective study demonstrated that a structured 12-week program of cognitive reframing and thought-challenging techniques was associated with statistically significant and clinically large reductions in anxiety and depressive symptom severity among adults with comorbid generalized anxiety disorder and major depressive disorder in Lahore, Pakistan, with gains maintained and modestly extended at 24-week follow-up, alongside parallel improvements in adaptive cognitive emotion regulation, decreases in maladaptive cognitive coping, and enhanced health-related quality of life. Mediation-consistent correlations between cognitive regulation change and primary symptom reduction support the plausibility of cognitive reorganization as a therapeutic mechanism, and ANCOVA findings indicate that these improvements were not attributable to differential pharmacotherapy exposure. While the single-arm design precludes causal attribution and replication in randomized controlled trials with active comparators is necessary before definitive efficacy conclusions can be drawn, the present findings establish a robust empirical foundation for the clinical value of structured cognitive techniques in comorbid mood-anxiety presentations within a South Asian low-to-middle-income context, and support their integration into culturally adapted, time-limited psychotherapy frameworks as an evidence-informed component of accessible mental health care.

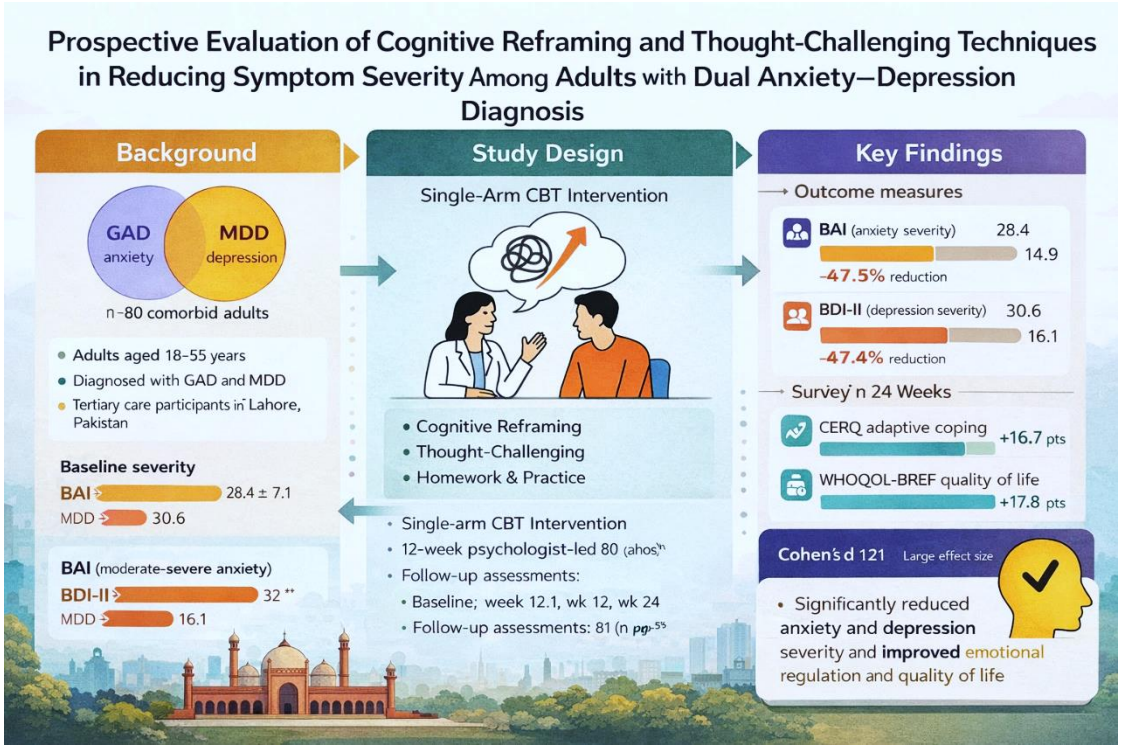

Figure 2 Graphical Abstract

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