

Refining Outcomes in Bipolar Disorder: A Longitudinal Morbidity Analysis of the BipoLife Psychotherapy Trial

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Abstract

Background: Bipolar disorder (BD) is characterized by a fluctuating and partially subthreshold course of affective morbidity that is insufficiently captured by categorical endpoints or cross-sectional symptom measures. Combining the assessment of a pre-treatment phase with a dimensional approach that integrates symptom severity and duration may provide a more sensitive framework for evaluating illness trajectories and treatment effects. The primary analysis of the BipoLife Psychotherapy Trial used time to relapse to compare two adjunctive group psychotherapies and found no meaningful differences between treatments. In a secondary analysis, we apply such a framework to complement these findings.

Methods: The BipoLife Psychotherapy Trial was a randomized, observer-blind study comparing a skill-oriented, material-based cognitive behavioral therapy with a supportive, patient-centered, emotion-focused therapy in euthymic BD (N = 305) over 18 months. In this secondary analysis, longitudinal affective morbidity was assessed in 297 patients with evaluable data, using weekly psychiatric status ratings from the Longitudinal Interval Follow-Up Evaluation across a 6-month pre-treatment phase, treatment, and follow-up. A dimensional morbidity index was derived to quantify depressive, manic, and overall affective morbidity. Changes over time and between treatments were analyzed using mixed-effects models, and the prognostic value of pre-treatment morbidity was examined.

Results: Despite euthymia for at least 4 weeks at study entry, 44.9% of weeks across the full 6-month pre-treatment phase were characterized by affective morbidity. Consistent with prior evidence, symptomatology was predominantly depressive, with more than half occurring at subthreshold levels. Following treatment initiation, time spent in euthymia increased from 55.1% to 74.0%, with depressive morbidity showing the greatest reduction. Overall morbidity decreased significantly and remained lower during follow-up ($p < .001$), with no differences between treatment groups. Higher pre-treatment morbidity predicted greater subsequent morbidity across treatment and follow-up ($p = .011$).

Conclusions: Integrating pre-treatment morbidity with continuous measures of symptom severity may improve the sensitivity of clinical trials to capture illness trajectories and treatment effects in BD.

Background

Bipolar disorder (BD) is characterized by a chronic, fluctuating course of affect that extends well beyond discrete episodes. However, conventional outcome measures fail to capture the heterogeneous illness trajectories and treatment responses characteristic of BD^{1,2}, limiting the ability to meaningfully evaluate psychotherapeutic interventions.

Over two decades ago, two long-term naturalistic weekly mood rating studies by Judd et al. demonstrated patients with BD to be euthymic only about half of the time, with depression dominating the symptomatic course and subsyndromal or minor symptoms occurring roughly three times as often as full syndromal episodes^{3,4}. These findings are particularly salient because even subthreshold symptoms are associated with greater disability across domains of daily functioning, lower mental

health-related quality of life⁵ and impaired cognition⁶. Together, these observations highlight the need to assess a broader range of symptom severity over time, an approach that remains underrepresented in studies evaluating the effectiveness of interventions of all modalities. This limitation reflects a broader issue in BD research, where outcomes are commonly defined using categorical constructs such as response, remission, or recurrence rather than continuous measures of illness burden⁷. Consequently, the largest review of randomized controlled trials of manualized psychotherapies in BD to date converged on episode recurrence as the primary outcome, with affective symptom levels assessed cross-sectionally⁸.

Previous studies have examined aspects of the longitudinal course of BD within clinical trials. Analyses of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) cohort, for example, have characterized symptom trajectories using mood rating scales assessed at 3- to 6-month intervals, identifying distinct patterns of depressive and manic symptoms¹. In addition, a randomized psychotherapy trial of interpersonal and social rhythm therapy used weekly ratings from the Longitudinal Interval Follow-Up Evaluation (LIFE)⁹ to quantify cumulative depressive symptom burden¹⁰. However, systematic analyses of longitudinal affective morbidity based on frequent mood ratings remain scarce.

The Morbidity Index (MI) provides a dimensional measure of illness burden by integrating both the duration and severity of affective symptoms. Originally introduced by Coppen and Abou-Saleh¹¹, the MI is derived from repeated longitudinal assessments and reflects average symptom severity over time, capturing the fluctuating and cumulative course of affective morbidity. Compared with traditional outcomes such as episode counts or time to relapse, it therefore provides a more comprehensive and precise measure of illness burden^{12,13}. Subsequent adaptations have extended the MI framework to include subthreshold symptoms, acknowledging their high prevalence and clinical relevance in BD^{13,14,15}.

In this secondary analysis, we applied this framework to the BipoLife Psychotherapy Trial^{16,17}, which used time to relapse as the primary outcome to compare two adjunctive group psychotherapies. By design, the comparative analysis did not address how affective morbidity changed over the course of treatment and follow-up. Leveraging the trial's large sample and detailed longitudinal ratings on the LIFE, we characterized affective morbidity trajectories over a 2-year period.

Methods

Study design and analytic sample

The present analyses are based on data from the BipoLife Psychotherapy Trial, a randomized controlled study comparing two group psychotherapies for relapse prevention in BD: skill-oriented, material-based cognitive behavioral therapy (*Spezifische, Emotional-Kognitive Psychotherapie*; SEKT) and supportive, patient-centered, emotion-focused therapy (*Emotionsfördernde, Supportive, Psychoedukative Psychotherapie*; FEST). Both interventions were delivered in an open group format of four full-day

workshops held roughly monthly over five months. SEKT was a structured, manual-based programme covering psychoeducation, early warning signs and stress management, and skills in metacognition, emotion regulation, interpersonal functioning, and problem-solving, all supported by worksheets, exercises, and homework. FEST, by contrast, was a supportive group therapy in which participants shared personal experiences, expressed emotions, and offered mutual support, while the therapist facilitated a group-chosen topic and reinforced common therapeutic factors and personal resources rather than prescribing exercises or homework.

Adults with bipolar I or II disorder in a euthymic state were randomized to one of the two interventions and followed longitudinally with repeated clinical assessments. The analytic sample comprised 305 participants (median age 34 years [IQR 18–50]; 53% male), of whom 207 (68%) had bipolar I disorder and 98 (32%) bipolar II disorder. The design, recruitment procedures, and full baseline characteristics have been described in detail elsewhere^{16,17}.

Longitudinal morbidity data and study phases

Longitudinal morbidity data were derived from weekly psychiatric status ratings (PSR) obtained using the LIFE, a well-established instrument for reconstructing the longitudinal course of psychiatric disorders over extended intervals⁹. At the baseline assessment, the LIFE was used to rate weekly psychiatric status for the 24 weeks preceding treatment initiation, allowing morbidity to be characterized across the pre-treatment period rather than relying on a more cross-sectional mood rating at baseline. Trial eligibility required euthymia for the 4 weeks immediately preceding enrollment, based on standardized symptom measures^{16,17}, which did not constrain morbidity earlier in the 24-week pre-treatment phase. The LIFE was repeated at post-treatment and at 12-month and 18-month follow-up, providing comparable retrospective weekly ratings for the intervening periods.

For analytic purposes, the study timeline was divided into four predefined phases: pre-treatment (weeks – 24 to 0), treatment (weeks 0–28), 12-month follow-up (weeks 28–54), and 18-month follow-up (weeks 54–90). Weekly psychiatric status ratings were available for both depressive and manic symptomatology and formed the basis for the MIs described below.

Construction of the Morbidity Index

Weekly PSR obtained from the LIFE were used to derive polarity-specific MIs for depressive (DMI) and manic (MMI) symptomatology. The mapping of LIFE PSR to MI levels is summarized in Table 1. Directly aggregating PSR values across weeks would allow weeks with no or only residual symptoms to contribute to morbidity estimates similarly to weeks with clinically relevant syndromal states. This averaging approach implicitly treats the ordinal PSR scale as interval-level. The MI approach instead provides a clinically informed re-weighting of PSR. Based on established PSR categories, weekly DMI and MMI were operationalized as ordinal severity levels reflecting increasing symptom burden and

clinical significance. The intermediate DMI level 2 is intended to capture clinically relevant situations in which syndromal depression persists despite intensification of pharmacotherapy, reflecting both insufficient treatment response and increased treatment burden.

Because each PSR rating reflects the (manic or depressive) morbidity for the entire week as one value, the MI per phase is equivalent to the area under the morbidity–time curve – a step-function integral – divided by the number of observed weeks, summarizing both the severity and duration of affective morbidity in a single, clinically interpretable value.

To capture overall affective morbidity independent of polarity, a total MI (TMI) was defined as the weekly maximum of depressive and manic morbidity values. This maximum-rule approach yields a single longitudinal measure of overall illness burden while avoiding double-counting during weeks with concurrent depressive and manic morbidity. For polarity-specific classifications, concurrent weeks were assigned to the pole with the higher symptom rating. In the rare event of identical depressive and manic symptom ratings (0.7% of observed weeks), assignments were distributed evenly between depressive and manic categories to avoid systematic overrepresentation of either pole.

Table 1
Definition of morbidity index levels derived from LIFE PSR

Polarity	MI level	LIFE PSR equivalent	Interpretation
DMI	0	PSR 1–2	Euthymic or residual symptoms
	0.5	PSR 3–4	Subthreshold depressive symptoms
	1	PSR 5	Full criteria depression
	2	PSR 5 + TE	Full criteria depression with treatment escalation (TE)
	3	PSR 6	Severe depression / hospitalization
MMI	0	PSR 1–2	Euthymic or residual symptoms
	0.5	PSR 3	Subthreshold manic symptoms
	1	PSR 4	Full criteria hypomania
	2	PSR 5	Full criteria mania
	3	PSR 6	Severe mania / hospitalization
Notes. DMI = Depressive Morbidity Index; MMI = Manic Morbidity Index; LIFE PSR = Psychiatric Status Ratings from the Longitudinal Interval Follow-Up Evaluation; TE = Treatment Escalation.			

Outcome derivation

Weekly morbidity was operationalized using the DMI, MMI, and the combined TMI, with TMI serving as the primary outcome and the polarity-specific indices used for descriptive and secondary analyses.

In the mixed-effects repeated measures models, the pre-treatment phase served as the reference level, allowing changes in morbidity during treatment and follow-up to be interpreted relative to pre-treatment illness burden. For moderation analyses, mean pre-treatment morbidity was used as the predictor of cumulative morbidity across the treatment and follow-up phases.

Statistical analysis

Statistical analyses were performed using JMP 19.0.4 (SAS Institute), with figures generated in Python 3.13. Longitudinal changes in morbidity across study phases were analyzed using mixed-effects models. Phase-level morbidity was modeled with study phase, treatment group, and their interaction as fixed effects, with participant specified as the repeated subject factor and an unstructured covariance matrix to account for within-subject correlations. Models were estimated using likelihood-based methods, allowing all available observations to contribute under a missing-at-random assumption.

Changes relative to the pre-treatment phase were quantified using least-squares mean contrasts comparing each post-treatment phase with the pre-treatment phase. Differences between treatment groups were assessed overall and within study phases.

To examine whether pre-treatment morbidity predicted later illness burden, an analysis of covariance (ANCOVA) was conducted with cumulative morbidity across the treatment and follow-up phases as the outcome and pre-treatment morbidity, treatment group, and their interaction as predictors.

Results

The analytic sample comprised 305 randomized participants, whose baseline characteristics have been described in detail elsewhere^{16,17}. LIFE-based weekly morbidity data were available for 297 participants, who were included in the present analyses (pre-treatment, $n = 297$; treatment, $n = 285$; 12-month follow-up, $n = 232$; 18-month follow-up, $n = 215$; all four phases, $n = 213$). Higher pre-treatment morbidity was associated with a lower likelihood of complete phase coverage ($\beta = -0.99$, $p = .004$), though the explained variance was small ($R^2 \approx .03$) and the association did not differ by therapy ($p = .88$).

Distribution of affective morbidity across study phases

The phase-specific distribution of weekly affective morbidity states is shown in Fig. 1, with the underlying MI level distribution summarized in Table 2. During the pre-treatment period, most weeks were spent in euthymia, whereas non-euthymic weeks were predominantly characterized by depressive morbidity and comparatively fewer (hypo)manic states. Trial inclusion required participants to be euthymic for at least 4 weeks prior to treatment initiation, which likely contributed to the proportion of

euthymic weeks observed before treatment. Across treatment and follow-up, euthymia became more prevalent while depressive morbidity decreased.

Figure 1 legend

Weekly morbidity states were classified according to the MI derived from LIFE PSR. Stacked bars show the proportion of weeks spent in each affective morbidity state during the pre-treatment, treatment, 12-month follow-up, and 18-month follow-up phases. Bar widths are proportional to phase duration. Proportions are pooled across treatment groups. (49/300)

Table 2
Distribution of weekly morbidity index levels across study phases

Morbidity state	MI Level	Pre-treatment	Post-Treatment	12-month follow-up	18-month follow-up
Euthymia	MI 0	55.1%	74.0%	71.3%	70.9%
Depression					
Subthreshold	MI 0.5	20.7%	17.1%	14.5%	17.7%
Clinical	MI 1	10.5%	2.9%	6.3%	5.6%
	MI 2	1.0%	0.1%	0.1%	0.0%
	MI 3	1.7%	0.0%	0.8%	0.4%
(Hypo)mania					
Subthreshold	MI 0.5	5.2%	3.4%	3.9%	3.8%
Clinical	MI 1	2.6%	1.7%	2.1%	0.8%
	MI 2	2.7%	0.5%	0.7%	0.8%
	MI 3	0.5%	0.3%	0.3%	0.1%

Changes in Morbidity across study phases

Adjusted mean TMI for all participants is shown in Fig. 2. Values differed significantly across study phases ($F(3,241) = 32.89, p < .001$), with TMI decreasing by approximately 0.23 units from pre-treatment to the treatment phase and remaining similarly reduced at both follow-up assessments, indicating a lasting reduction following treatment initiation. These changes were primarily driven by reductions in DMI (treatment phase vs pre-treatment: $\beta = -0.163, p < .001$), while MMI also decreased but to a lesser extent ($\beta = -0.073, p = .002$). These reductions were sustained during follow-up, with slight attenuation at 12 months and stable effects at 18 months, mirroring the pattern observed for TMI. Consistent with the findings for the primary trial outcome (time to relapse), there was no significant difference in TMI between the SEKT and FEST groups ($F(1, 278) = 0.55, p = .459$). Likewise, the change in TMI across study

phases did not differ between treatments (study phase $\times$ therapy interaction: $F(3, 241) = 0.46, p = .71$). Phase-specific SEKT–FEST contrasts are shown in Table 3.

Figure 2 legend

Adjusted total morbidity index (TMI) across study phases by treatment group. Points represent model-estimated marginal means from the mixed-effects model, with vertical bars indicating 95% confidence intervals. Estimates are shown for the pre-treatment period, treatment phase, and the 12- and 18-month follow-up phases. Lower values indicate lower overall affective morbidity. FEST = Supportive, Patient-Centered, Emotion-Focused Therapy; SEKT = Skill-Oriented Cognitive Behavioral Therapy. **(60/300)**

Table 3
Mixed-effects model estimates of total morbidity across study phases and treatment

Predictor	Estimate (β)	SE	<i>t</i>	<i>p</i>
Study phase (vs pre-treatment)				
Treatment phase	−0.230	0.033	−6.93	< .001
12-month follow-up	−0.203	0.040	−5.13	< .001
18-month follow-up	−0.218	0.039	−5.59	< .001
SEKT vs FEST comparisons	Difference	95% CI		<i>p</i>
Pre-treatment	0.000	−0.084 to 0.085		.991
Treatment	0.002	−0.047 to 0.050		.948
12-month follow-up	0.046	−0.036 to 0.128		.272
18-month follow-up	0.026	−0.050 to 0.102		.501
<i>Note. Estimates are from the mixed-effects model with pre-treatment as the reference phase. The pre-treatment reference mean total morbidity index (TMI) was 0.399; the between-participant standard deviation of mean pre-treatment TMI was 0.369 (n = 297).</i>				

Influence of pre-treatment morbidity on cumulative morbidity

To examine whether pre-treatment TMI predicted subsequent morbidity burden, an ANCOVA model was estimated with cumulative TMI across the treatment and follow-up phases as the outcome and pre-treatment TMI, treatment group, and their interaction as predictors. Higher pre-treatment TMI was significantly associated with higher cumulative TMI during the treatment and follow-up period ($\beta = 0.092, SE = 0.036, p = .011$). This association did not differ between SEKT and FEST (interaction: $\beta = 0.024, SE = 0.036, p = .492$), indicating that pre-treatment morbidity predicted later morbidity similarly in both

treatment groups. The overall model explained a small proportion of variance in cumulative TMI ($R^2 = .03$, $F(3, 279) = 2.64$).

Discussion

In this secondary analysis of the BipoLife Psychotherapy Trial comparing two adjunctive group psychotherapies in euthymic BD (SEKT vs FEST)^{16,17}, we observed a significant and sustained reduction in overall morbidity following treatment initiation, driven primarily by decreases in depressive morbidity, with no between-group differences. Higher pre-treatment morbidity predicted greater subsequent morbidity independently of treatment allocation.

A central implication of the present findings concerns the conceptualization of “baseline euthymia” in BD. Although trial inclusion required at least 4 weeks of euthymia, the detailed longitudinal ratings on the LIFE revealed substantial affective morbidity across the 6-month pre-treatment phase. This pattern closely parallels the seminal LIFE-based studies by Judd et al., who reported that patients with bipolar I disorder were symptomatic during 47.3% of follow-up weeks, with depressive symptoms (31.9%) predominating over manic/hypomanic symptoms (9.3%), and subsyndromal states occurring approximately three times as often as syndromal episodes³. Similar results were observed in bipolar II disorder, with 53.9% of weeks symptomatic and a marked predominance of depressive and subthreshold symptoms⁴. In the present sample, despite the euthymia criterion at study entry, 44.9% of weeks across this 6-month phase were characterized by affective morbidity, predominantly depressive (33.9%) and less frequently (hypo)manic (11.0%). Thus, pre-treatment morbidity closely resembled the naturalistic course of BD, and its predictive value for subsequent illness burden underscores the clinical importance of characterizing the pre-treatment period beyond a single baseline assessment.

Most randomized controlled trials in BD evaluate outcomes using either episode recurrence or threshold-based changes on symptom rating scales, thereby compressing inherently continuous illness trajectories into categorical states such as response, remission, or relapse^{7,8}. While such outcomes are clinically intuitive, they fail to capture both the fluctuating and cumulative affective burden patients experience over time and the clinical relevance of subthreshold symptoms. This matters given evidence that clinically meaningful impairment occurs along a continuum of affective symptom severity, including at subthreshold levels, with depressive symptoms representing the principal driver^{18,19}.

In the present analysis, improvements were not uniform across morbidity states: Weeks with clinical depressive symptoms showed a pronounced reduction, whereas subthreshold depressive symptoms proved markedly more persistent, with only partial and unstable improvement across follow-up. In contrast, subthreshold and clinical (hypo)manic symptoms exhibited a more parallel pattern of reduction relative to one another.

This differential pattern suggests that a substantial component of illness burden may reside in a more persistent subthreshold depressive “background”, which may reflect either incomplete remission in

transit toward euthymia — with the subthreshold fraction partly replenished through formerly syndromal episodes — or a more enduring, treatment-resistant residual state. Both accounts are consistent with evidence that such symptoms are highly prevalent, often persist between episodes, and contribute importantly to the longitudinal burden of BD^{20,21}. Alternatively, this pattern may reflect sample heterogeneity, with a subgroup of patients characterized by predominantly depressive trajectories that are less amenable to change within the observed time frame. Such patterns would remain largely obscured when using traditional relapse-based endpoints, which primarily capture transitions into and out of fully syndromal states but not the persistence of subthreshold morbidity.

Prior applications of the MI have relied on a variety of mood rating instruments, typically across observation windows of several weeks^{11,13,14,15}. While high-frequency prospective monitoring approaches such as daily mood ratings or ecological momentary assessment may approximate a methodological gold standard for capturing mood symptoms in real time and in naturalistic settings^{22,23,24}, they are often associated with substantial patient burden and limited feasibility in large-scale or long-term studies²⁵. The integration of the MI with the 6-monthly retrospective LIFE, in contrast, allows for an efficient assessment of extended observation periods using a unified framework. This includes pre-treatment phases otherwise difficult to capture in trial settings. It thus offers a pragmatic and scalable approach to capturing longitudinal symptom burden across trial phases.

Similar time-integrated approaches have been adopted in other chronic, fluctuating diseases: In systemic lupus erythematosus and rheumatoid arthritis, cumulative disease activity over time predicts both mortality and structural joint damage^{26,27}. These examples illustrate that, in disorders characterized by fluctuating activity, cumulative dimensional burden may provide information not captured by cross-sectional or categorical disease states.

The 6-month retrospective structure of the LIFE, while enabling feasible long-term longitudinal measurement, is inherently vulnerable to recall bias²⁸, particularly for the precise temporal distribution of symptoms and for less salient (hypo)manic states. Shorter intervals of approximately 3 months may improve recall accuracy and offer a better compromise between feasibility and temporal precision^{25,29,30}.

More broadly, the absence of an untreated control group precludes disentangling the sustained reduction in morbidity following treatment initiation from confounding factors such as regression to the mean, recall bias, and the 4-week euthymia inclusion criterion — the last of which may extend into the early treatment phase as a symptom-free interval that would likely have occurred regardless of treatment. These confounders most plausibly account for part of the reduction observed during the treatment phase itself (for instance, recall bias may favor periods of therapeutic support) but are less able to explain the sustained reduction through the 12- and 18-month follow-ups.

A further consideration concerns the handling of mixed states, which are operationalized differently across diagnostic systems³¹ and are not directly assessed by the LIFE. We assigned weeks with concurrent depressive and manic symptoms to the more severe pole, distributing the rare weeks with

identical symptom ratings evenly between depressive and manic categories. While this approach captures the burden of concurrent symptoms without double-counting, it does not characterize mixed states as a distinct construct. Future studies should prospectively assess the MI using direct clinician ratings and consider shorter LIFE assessment intervals to reduce recall bias.

Conclusions

Including the pre-treatment phase as a longitudinal reference revealed substantial affective morbidity in patients meeting standard criteria for euthymia at entry, and allowed change in morbidity to be evaluated across treatment and follow-up. In contrast to conventional categorical outcomes, the dimensional, longitudinal MI captured the fluctuating and often subsyndromal course of bipolar disorder. Integrating pre-treatment morbidity with continuous, fine-grained measures of symptom severity may therefore improve the sensitivity of clinical trials to capture illness trajectories and treatment effects in bipolar disorder.

Abbreviations

ANCOVA

Analysis of Covariance

BD

Bipolar Disorder

DMI

Depressive Morbidity Index

FEST

Emotionsfördernde, Supportive, Psychoedukative Psychotherapie (Supportive, Patient-Centered, Emotion-Focused Therapy)

LIFE

Longitudinal Interval Follow-Up Evaluation

MI

Morbidity Index

MMI

Manic Morbidity Index

PSR

Psychiatric Status Rating

SEKT

Spezifische, Emotional-Kognitive Psychotherapie (Skill-Oriented Material-Based Cognitive Behavioral Therapy)

TE

Treatment Escalation

TMI

Total Morbidity Index

Declarations

Ethics approval and consent to participate

All investigations in humans or on human tissue described here were conducted with the approval of the responsible ethics committees, in accordance with national law, and in accordance with the Declaration of Helsinki of 1975 (current revised version). Trial registration: German Clinical Trials Register (DRKS): DRKS00006013 (registered 21 May 2015). Written informed consent was obtained from all participating patients after they had been fully informed about the study and the use of the collected data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to ongoing analyses but are available from the corresponding author on reasonable request, subject to appropriate data protection and use agreements.

Competing interests

Martin Lambert received consultant or speaker fees from AstraZeneca, Bristol-Myers Squibb, Lilly Deutschland GmbH, Janssen Cilag GmbH, Lundbeck GmbH, Otsuka Pharma GmbH, Roche Deutschland Holding GmbH, Sanofi Aventis, Trommsdorff GmbH & Co KG, Laboratorios Farmacéuticos Rovi, and Takeda GmbH. ML also holds shares of MiNDNET e-Health AG and MiNDNET e-Health-Solutions GmbH.

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Authors' Contributions

JB and **TJS** conceptualized the study. **JB** conducted the data analyses, including primary and sensitivity analyses, and performed data visualization. **JB** drafted the original manuscript. **GOM** administrated and delivered the intervention, and edited the manuscript. **TJS** served as a Co-Primary Investigator on the intervention study, co-supervised the intervention, and edited the final manuscript. **JF, LMS, PT, FB, EF, CHA, EQ, SS, AW, AR¹, TE, AF, IL, MH², VK, ML, ACZ, FR, MB, JC, LJ, DR, PR, MS, SB, KP, SKS, SM³, VO, AR⁴, IF, TK, IK, SM⁵, EP, KA, MH⁶, TGS, FS, AH, TV, LH, ST, CW, SW** made substantial contributions to the acquisition of data, including conducting the interventions and clinical assessments. All authors critically revised the manuscript and approved the final version for publication.

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Declaration of AI-assisted technologies in the manuscript preparation process

During manuscript preparation, the authors used ChatGPT 5.2 (OpenAI) and Claude Sonnet 4.6 (Anthropic) to support language refinement, stylistic editing, and structural clarity of the text. These tools were used to improve readability and presentation of author-generated content. They were not used for data analysis, statistical procedures, or independent scientific interpretation. All conceptualization, methodological decisions, and substantive content originate from the authors, who assume full responsibility for the accuracy and integrity of the manuscript. The final manuscript was manually reviewed and approved by a native English speaker.

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Figures

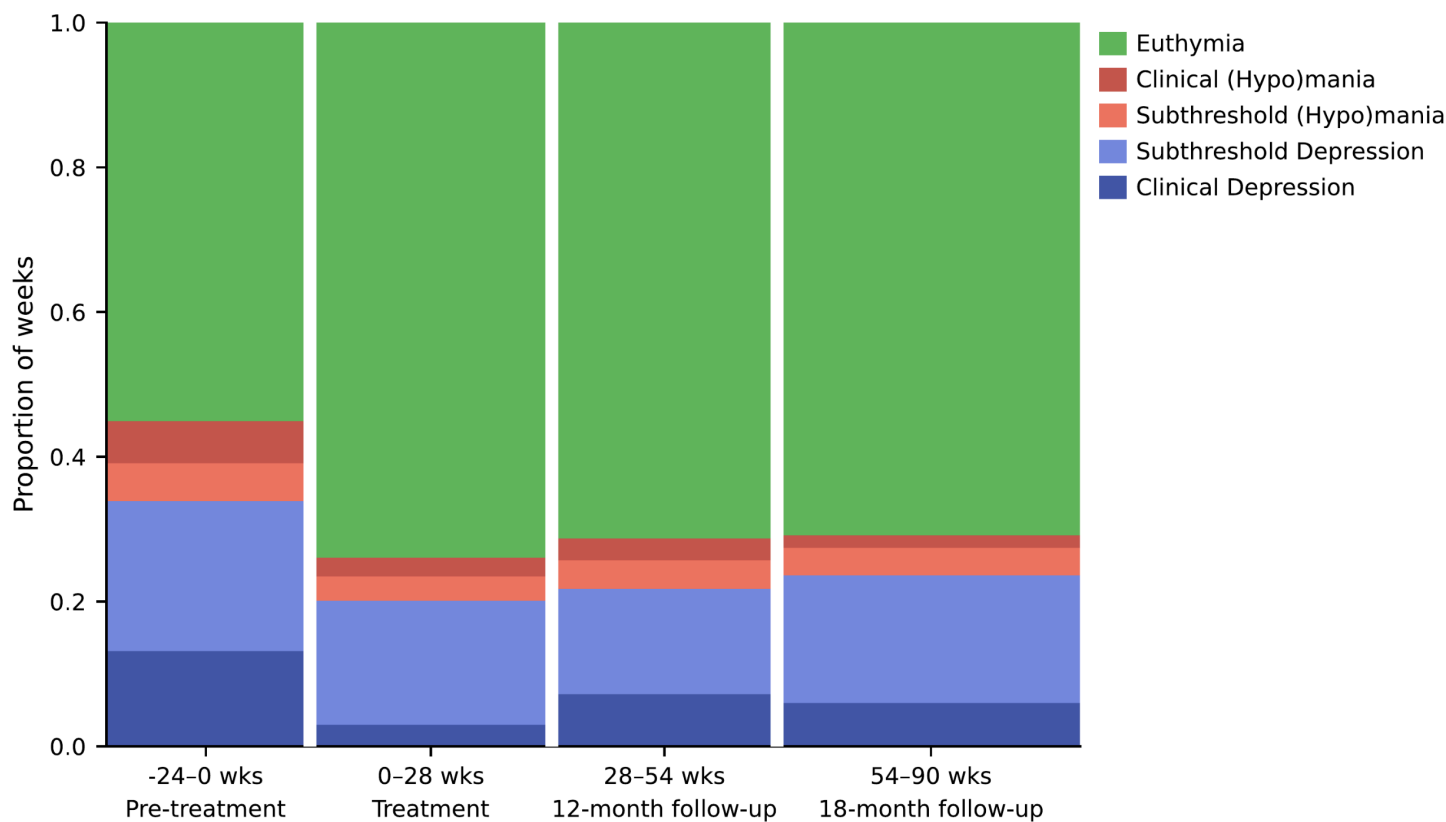


Figure 1

Distribution of Weekly Affective Morbidity Across Study Phases **(8/15)**

Weekly morbidity states were classified according to the MI derived from LIFE PSR. Stacked bars show the proportion of weeks spent in each affective morbidity state during the pre-treatment, treatment, 12-month follow-up, and 18-month follow-up phases. Bar widths are proportional to phase duration. Proportions are pooled across treatment groups. **(49/300)**

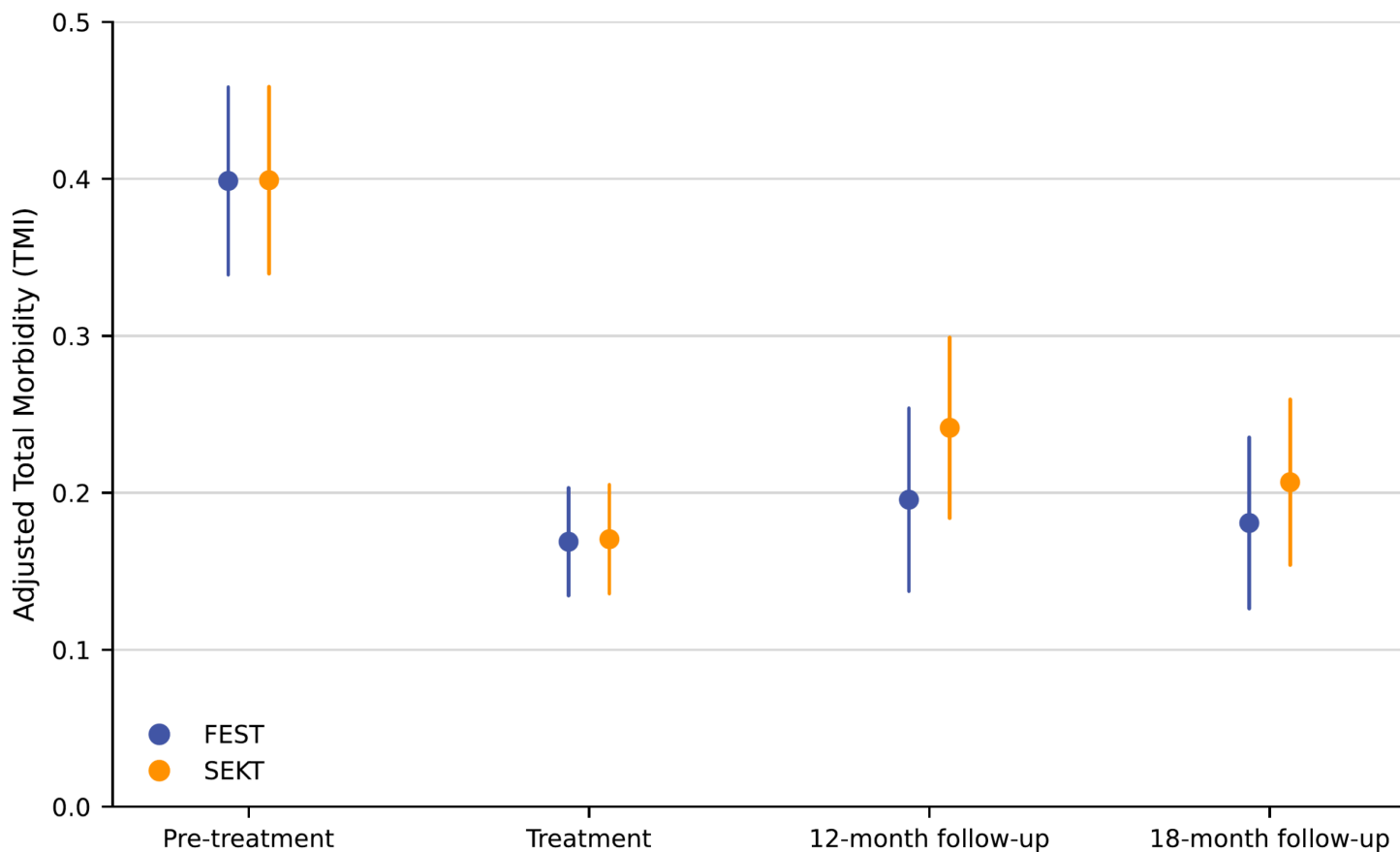


Figure 2

Total Morbidity Across Study Phases by Treatment Group (8/15)

Adjusted total morbidity index (TMI) across study phases by treatment group. Points represent model-estimated marginal means from the mixed-effects model, with vertical bars indicating 95% confidence intervals. Estimates are shown for the pre-treatment period, treatment phase, and the 12- and 18-month follow-up phases. Lower values indicate lower overall affective morbidity. FEST = Supportive, Patient-Centered, Emotion-Focused Therapy; SEKT = Skill-Oriented Cognitive Behavioral Therapy. **(60/300)**