Comparing Blended and Standard Cognitive Behavioral Therapy for Patients with Unipolar Depression, Panic Disorder, and Agoraphobia

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Zusammenfassung

Diese Arbeit umfasst Untersuchungen zur Wirksamkeit der „Blended Cognitive Behavioral Therapy“ (bCBT) unter Zuhilfenahme der digitalen Gesundheitsanwendung „*elona therapy“* im Vergleich zur kognitiven Verhaltenstherapie (CBT) bei unipolarer Depression und Angststörungen in der ambulanten psychotherapeutischen Versorgung.In Kombination von bCBT und face-to-face Therapie werden gezielt digitale therapeutische Elemente als Unterstützung über Smartphone oder Webanwendungen mit Hilfe strukturierter Interventionen eingebracht, die in den Alltag der Patient:innen integriert werden.

Drei multizentrische, randomisierte, zweiarmige kontrollierte Studien durchgeführt in ambulanten Psychotherapeutischen Praxen und Ambulanzen in Deutschland bilden die Grundlage der vorliegenden Untersuchungen: zwei Pilotstudien zu unipolarer Depression und Angststörungen sowie eine Folgestudie mit Fokus auf unipolare Depression. Die Teilnehmenden wurden jeweils randomisiert entweder der bCBT-Gruppe (face-to-face Standardtherapie plus digitale Anwendung) oder der CBT-Gruppe (nur face-to-face) zugewiesen. Erhoben wurden Depressions- und Angstsymptome sowie weitere testdiagnostische Ergebnisse zu Beginn und nach der Intervention (Woche 12). In den Pilotstudien wurde zusätzlich eine Zwischenmessung in Woche 6 durchgeführt.

Während die Ergebnisse der Pilotstudien uneinheitlich ausfielen, zeigte die Folgestudie signifikante Verbesserungen in der bCBT-Gruppe hinsichtlich depressiver und ängstlicher Symptomatik, Lebensqualität, Selbstwirksamkeit, Psychoedukatives Wissen und des allgemeinen Krankheitsverlaufs im Vergleich zur Kontrollgruppe.

Zusammenfassend liefern die Pilotstudien Hinweise auf die Machbarkeit und Anwendung von blended Therapien. Die größere Folgestudie belegt das Potenzial von bCBT insbesondere bei

unipolarer Depression. Die uneinheitlichen Ergebnisse bei Angststörungen verdeutlichen jedoch den weiteren Forschungsbedarf in diesem Bereich.

Summary

This thesis evaluates the effectiveness of blended cognitive behavioral therapy (bCBT) using the digital health application *elona therapy*, compared to standard CBT for unipolar depression and anxiety disorders in outpatient care. bCBT combines digital therapeutic components with traditional face-to-face CBT, extending therapeutic support into patients' daily lives via structured interventions delivered through smartphone- or web-based applications.

The work comprises three multicenter, randomized, two-arm controlled trials conducted in Germany: two pilot studies targeting unipolar depression and anxiety disorders, and a follow-up trial focused on unipolar depression. Participants were randomized to receive either standard face-to-face CBT combined with the digital application (bCBT group) or standard face-to-face CBT alone. Symptoms of depression and anxiety, along with patient-related variables, were assessed at baseline and post-intervention (week 12). In the pilot studies, an additional mid-intervention assessment was conducted at week 6.

While the pilot studies yielded mixed results, the follow-up trial showed that patients in the bCBT group experienced significantly larger improvements in depressive symptoms, anxiety, quality of life, self-efficacy, depression literacy, and overall disease severity compared to those in the CBT group.

Taken together, the pilot studies provided insights into the feasibility and application of blended treatments. The larger third trial confirmed the potential benefits of bCBT for a broader population with unipolar depression. However, the mixed results for anxiety disorders suggest that further research is needed in this area.

General Introduction

Depression and anxiety disorders, including panic disorder and agoraphobia, are among the most prevalent mental health conditions worldwide. They significantly impair emotional well-being, social functioning, and quality of life, with contribute substantially to global disability and economic costs (GBD 2019 Diseases and Injuries Collaborators, 2020; Gillham et al., 2000). Cognitive behavioral therapy (CBT) has consistently demonstrated effectiveness in treating these disorders, supported by extensive empirical research (APA, 2019; Hofmann et al., 2012; NICE, 2009). However, the implementation of CBT in outpatient clinics faces several limitations, such as restricted accessibility, limited session duration, and inconsistent patient engagement with therapeutic materials outside of sessions, potentially compromising its effectiveness (Helbig & Fehm, 2004; Shafran et al., 2009).

In response to these challenges, recent advances in digital health interventions have led to the development of blended cognitive behavioral therapy (bCBT). This approach integrates digital therapeutic elements with conventional face-to-face CBT, extending therapeutic support into patients' daily lives through structured digital interventions with smartphone or web applications (Andersson & Titov, 2014; Erbe et al., 2017). bCBT typically involves therapists assigning specific digital exercises, psychoeducational content, and self-monitoring tasks aligned with session themes to patients, which they complete independently between face-to-face therapy sessions. Methods commonly used in bCBT include interactive exercises (e.g. relaxation, psychoeducational content), session reflections, symptom-tracking diaries, guided self-help activities, personalized reminders, and automated feedback systems (Atik et al., 2023).

Initial empirical studies suggest that digital integration in CBT can enhance patient adherence, improve symptom reduction, and potentially amplify overall therapeutic outcomes

(Berger et al., 2018; Schuster et al., 2020; Thase et al., 2018). Nevertheless, the current literature on bCBT yields mixed findings, with some studies highlighting its superiority over traditional CBT, while others report no significant differences between the two approaches (Ly et al., 2015; Pérez et al., 2021).

The ongoing evolution of bCBT is part of a broader trend toward digital health solutions aimed at enhancing the accessibility and personalization of psychological treatments to strengthen (digital) therapy congruence. This refers to the alignment between digital interventions and the therapeutic content of face-to-face sessions. Patients are more likely to find digital components meaningful and engaging—particularly when combined with high levels of autonomy and tailored support (Tang & Kreindler, 2017; Urech et al., 2019).

Despite promising initial results, further research is needed to address methodological inconsistencies and enhance the reliability of digital interventions across diverse clinical contexts (Kazantzis et al., 2010; Klein et al., 2016). This dissertation contributes to this evolving field by systematically exploring the potential of digitally blended CBT approaches in improving clinical outcomes across anxiety and depressive disorders.

bCBT application

The bCBT application (*elona therapy*) was used in all three trials in addition to standard face-to-face CBT.

The application comprises two integrated interfaces: A smartphone application for patients and a web-based platform for therapists. The therapist interface allows for the creation of individualized treatment plans by assigning digital content tailored to each patient. This content includes psychoeducational materials, therapeutic techniques, and interactive exercises selected from a structured library of over 400 evidence-based CBT resources. Therapists were encouraged

to exercise their clinical judgment when choosing content aligned with each patient's symptoms, therapeutic goals, and current treatment focus. Patients had continuous access to their assigned digital content via their smartphones throughout the treatment period. In addition to therapist-assigned content, patients had access to core modules covering emotional awareness, goal setting, depression education, and CBT principles. The system also offers automated content suggestions to complement therapist input.

The bCBT application includes additional features such as daily mood tracking, session reflections, a digital therapy schedule, and customizable reminders and notifications. Integration between the therapist and patient platforms enables real-time monitoring, allowing therapists to respond promptly in the event of symptom worsening or non-engagement.

Overview of the studies

This dissertation comprises three publications of studies investigating the effectiveness of blended cognitive behavioral therapy (bCBT) using the *elona health* application, compared to standard face-to-face CBT. In all three studies, adult patients were randomly assigned to receive either standard CBT or bCBT, which combined standard CBT with the digital application over 12 weeks of weekly therapy sessions.

Studies 1 and 2 were designed as pilot trials: Study 1 focused on patients with unipolar depression, and Study 2 on patients with anxiety disorders. The pilot design was chosen to test the usability of an early-access version of the bCBT program. The pilot design also allowed for smaller sample sizes and the inclusion of a broader set of outcome measures. These diverse outcome measures were intended to explore which variables are most sensitive and relevant to detecting intervention effects. Earlier studies of other bCBT applications (e.g., Berger et al., 2018; Schuster et al., 2020; Thase et al., 2018) focused on inconsistent outcomes, for example the BDI-II or PHQ-9 for depression. Following the 12-week intervention period, participants could report adverse events or technical difficulties, facilitating a preliminary evaluation of the bCBT application's usability and safety.

Study 3 was a larger-scale trial focusing on patients with unipolar depression. It aimed to replicate the findings of Study 1 while addressing key methodological limitations of the earlier studies.

Full details are provided in the original research articles (Studies 1 and 2) and the manuscript for Study 3 (submitted for publication), all included in the Appendix.

Study 1: Pilot Study: Unipolar Depression

Enhancing the effectiveness of CBT for patients with unipolar depression by integrating digital interventions into treatment: A pilot randomized controlled trial

Kalde, J., Atik, E., Stricker, J., Schückes, M., Neudeck, P., Pittig, A., & Pietrowsky, R. (2023). Enhancing the effectiveness of CBT for patients with unipolar depression by integrating digital interventions into treatment: A pilot randomized controlled trial. *Psychotherapy Research*, *34*(8), 1131–1146. https://doi.org/10.1080/10503307.2023.2277866

Study Registration, Ethical Approval

The pilot trials 1 and 2 were registered and approved by the ethical committee as one study, but with two separate samples (depression and anxiety patients). The two samples were randomized and treated separately, resulting in two different research articles.

The study was preregistered with the ISRCTN registry (ISRCTN-ID: 16328317). Ethical approval for the study protocol was obtained from the ethics committee at Heinrich Heine University Düsseldorf, Germany (Reference: 2021-1470_1). All participants provided written informed consent after receiving detailed study information. The trial was conducted in accordance with the Declaration of Helsinki and adhered to Good Clinical Practice guidelines for clinical investigations involving medical devices with human subjects (ISO 14155).

Methods

Study Aim and Hypotheses

The first pilot trial aimed to investigate the efficacy and safety of a digital application integrated into blended cognitive behavioral therapy (bCBT), in comparison to standard CBT for adults with unipolar depression over a 12-week treatment period. A broad range of outcome

variables was examined, and hypotheses were formulated based on existing evidence on bCBT interventions.

The primary hypothesis posited that participants in the bCBT group—who received weekly 50-minute face-to-face CBT sessions combined with access to the *elona therapy* application—would show greater reductions in depressive symptoms, as measured by the Beck Depression Inventory-II (BDI-II; Beck et al., 1996; Kühner et al., 2007), compared to participants receiving standard CBT alone, at both the 6- and 12-week assessments. To complement the primary outcome, the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001; Löwe et al., 2002) was included as a secondary depression measure.

Secondary hypotheses anticipated that the bCBT group would exhibit greater improvements than the CBT-only group in the following areas:

– Anxiety symptoms, assessed using the Generalized Anxiety Disorder Scale-7 (GAD-7; Mundt et al., 2002; Hinz et al., 2017) and the Beck Anxiety Inventory (BAI; Beck & Steer, 1988; Margraf & Ehlers, 2007)

– Worry, assessed with the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990; Stöber, 1998)

– Functional impairment, assessed using the Work and Social Adjustment Scale (WSAS; Meyer et al., 2009; Heissel et al., 2021)

– Self-efficacy, measured with the General Self-Efficacy Scale (GSE; Schwarzer & Jerusalem, 1995; Schwarzer et al., 1999)

– Mental health literacy, assessed with a short version of the Mental Health Literacy Scale (MHLS; O'Connor & Casey, 2015; Lalk, 2021)

– Overall quality of life, measured using the WHO Quality of Life—BREF (WHOQOL-BREF; WHOQOL Group, 1998; Skevington et al., 2004)

Additionally, it was hypothesized that participants in the bCBT group would report stronger therapeutic alliance (Working Alliance Inventory – Short Revised; WAI-SR; Hatcher & Gillaspy, 2006; Flückiger et al., 2018), fewer adverse therapy-related experiences (Negative Effects Questionnaire; NEQ; Rozental et al., 2016), and greater adherence to the treatment protocol than those in the standard CBT group.

Adherence was measured using four patient-rated and four therapist-rated items assessing engagement in therapy-related activities between sessions. These items were developed through a consensus process involving five experienced clinical psychologists and therapists. Additional information is provided in Table S1 of the first publication.

Recruitment

Participants were recruited between January 31 and May 30, 2022, from five outpatient psychotherapy clinics located in North Rhine-Westphalia, Germany. All participants provided informed consent. Therapists received a compensation of up to €150 for each enrolled participant (regardless of group allocation) who completed all study assessments. Participants did not receive financial compensation.

Randomization

After enrollment, participants were individually randomized (1:1) using the electronic data capture system's integrated randomization tool. No restrictions were placed on concurrent mental healthcare, including medication use. Recruitment occurred during standard intake sessions prior to therapy onset, which focused on assessment rather than treatment.

To maintain blinding, participants were informed they were part of a study examining optimal timing for integrating a bCBT application, with group allocation determining access time

(between weeks 0–12). Following study completion, all participants were debriefed and could request access to the app or deletion of their data.

All patients received 12 weeks of standard, individualized face-to-face CBT without a treatment manual, reflecting typical clinical care. Therapy was provided by licensed CBT therapists (n = 6) or advanced CBT trainees (n = 14), all qualified to deliver outpatient treatment under supervision in Germany. Therapists received a briefing on the structure and content of the bCBT application.

Following informed consent and randomization, participants received email invitations to complete baseline assessments (T0) via the electronic data capture system. At T0, demographic data—including age, gender, prior psychotherapy experience, and employment status—were also collected. Follow-up assessments were conducted online at six weeks (T1) and twelve weeks (T2). Most outcome measures were assessed at all three time points, except those assessing working alliance (WAI-SR), negative effects (NEQ), and treatment adherence, which were only evaluated at T1 and T2.

Outcome Measures

Online study questionnaires, including standardized outcome measures, were distributed to participants via email through the electronic data capture (EDC) system. The baseline assessment (T0) was completed after participants provided informed consent and were randomly assigned to one of the two study groups. At T0, demographic information -such as participants' occupation, age, gender, and prior experience with psychotherapy- was also collected.

Follow-up assessments were conducted at six weeks (T1) and twelve weeks (T2), during which participants received additional questionnaires. All primary and secondary outcome measures were administered at T0, T1, and T2, except for those related to working alliance

(patient- and therapist-rated), adverse therapeutic effects (therapist-rated), and patient adherence (patient- and therapist-rated). These specific measures were administered only at T1 and T2.

Intervention

Patients in the intervention group received access to the digital health application *elona therapy* depression module in addition to standard face-to-face CBT for a period of 12 weeks. The primary difference between the intervention and control groups was the use of the *bCBT* application during the treatment period.

Sample Characteristics and Diagnostic Procedures

Of the 82 participants initially randomized, 77 provided data at one or more time points and were thus included in the intention-to-treat (ITT) analysis. There were no significant demographic differences between the treatment groups. The number of therapy sessions attended did not significantly differ between groups (CBT: $M = 10.16$, $SD = 2.31$; bCBT: $M = 10.15$, $SD = 2.59$), $t(62) = 0.02$, $p = .987$, $d < .01$.

Diagnostic procedures were conducted as part of routine clinical practice. In 52 cases, diagnoses were made based on symptom comparison with ICD-10 criteria. For 22 participants, structured diagnostic interviews (e.g., Mini-DIPS or SCID) were used in combination with ICD-10-based symptom evaluation. Four participants were diagnosed using structured interviews alone. Three were assessed through ICD-10 comparisons and another diagnostic tool (e.g., supervision or standardized measures such as the SCL-90-R). One diagnosis was made using a structured interview and a prior diagnosis from earlier treatment.

Results

Most outcome measures demonstrated acceptable internal consistency (Cronbach's α = .71–.94), except for the WHOQOL-BREF subscales for quality of life and general health, physical health, social relationships, and the patient-reported adherence scale.

In total, seven participants from the bCBT group and nine from the CBT group dropped out over the course of the study. The proportion of participants who discontinued between baseline (T0) and the first follow-up (T1) did not differ significantly between the intervention groups, $\chi^2(1, N = 82) = 0.24$, $p = .626$, nor did dropout rates differ from T0 to the final measurement (T2), $\chi^2(1, N = 82) = 0.01$, $p = .913$. Similarly, no statistically significant baseline differences were observed between the two treatment groups across any outcome measure (all $ps \geq .111$).

No adverse events, serious incidents, or device-related complications were reported in either group throughout the study.

Primary Hypothesis

Between-group analyses showed that symptom reduction, as measured by the BDI-II, was descriptively larger in the bCBT group compared to the CBT group at 12 weeks ($d = –0.21$). However, the interaction effect between time and treatment condition did not reach statistical significance (B = 0.62, p = .190).

Secondary Hypotheses

For generalized anxiety symptoms (GAD-7), the interaction between time and condition was statistically significant ($B = 0.50$, $p = .022$), with the T2 contrast indicating greater improvement in the bCBT group compared to CBT ($B = –1.60$, $p = .007$). A similar pattern was

observed for psychological health (subscale of the WHOQOL-BREF), where the time × condition interaction was also significant (B = –0.49, p = .008), and the T2 contrast favored the bCBT group (B = 1.60, p = .003).

For all other outcomes, no significant time × condition interactions (ps = .215 to .896) or group contrasts at T1 (ps = .304 to .992) and T2 (ps = .160 to .869) were observed. However, descriptive comparisons suggested greater improvements in the bCBT group for PHQ-9 (d = –0.20), PSWQ (d = –0.22), WHOQOL-BREF physical health (d = 0.24), and general self-efficacy (GSE; d = 0.20).

At T1, bCBT participants reported significantly higher adherence compared to CBT, $t(66)$ = –2.14, p = .036, d = –0.52. Other comparisons related to adherence, working alliance (WAI-SR), and negative effects were not statistically significant at either time point (ps ≥ .096). Nonetheless, effect sizes ($|d| \geq .20$) favored bCBT for patient-rated working alliance (T1: d = –0.38; T2: d = –0.42), fewer negative effects (d = 0.28), and higher adherence (self-rated: d = –0.34; therapist-rated: d= –0.26) at T2.

Participants in the bCBT group showed significant improvements in all secondary outcomes from T0 to T2 (ps < .001 to .003), except for the mental health literacy scale (MHLS: p = .828). A similar pattern was found in the CBT group, with significant improvements across all outcomes (ps < .001 to .046) except MHLS (p = .519).

Conclusion

Although the primary hypothesis was not supported, with no statistically significant difference on the BDI-II, the bCBT group showed descriptively greater symptom reductions.

Notably, bCBT led to significantly greater reductions in generalized anxiety symptoms and improved psychological health compared to CBT. The GAD-7, which captures cognitive

aspects of anxiety such as worry, tension, and restlessness, appears better suited than the BAI for detecting anxiety changes in depressed populations (e.g., Toussaint et al., 2020). This may explain why significant effects were found for the GAD-7 but not the BAI.

Improvements in psychological well-being further support the intervention's impact, as this domain reflects an important therapeutic goal (Katschnig, 2006; Webb et al., 2011). Descriptive between-group differences also suggested potential benefits of bCBT in additional areas, including worry, physical health, self-efficacy, therapeutic alliance, perceived side effects, and treatment adherence.

Study 2: Pilot Study: Anxiety Disorders

Advancing CBT for panic disorder and agoraphobia by integrating a digital intervention into treatment: a pilot randomized controlled trial

Atik, E., Kalde, J., Stricker, J., Schückes, M., Neudeck, P., Pietrowsky, R., & Pittig, A. (2025). Advancing CBT for panic disorder and agoraphobia by integrating a digital intervention into treatment: a pilot randomized controlled trial. *Cognitive Behaviour Therapy*, 1–21. https://doi.org/10.1080/16506073.2025.2503834

The second pilot study followed the same procedures, ethical approval, exclusion criteria, outcome measurements, general design, statistical analyses, etc. as the first.
Participants in the bCBT group of the anxiety pilot study received the anxiety module of the bCBT application instead of the depression module.

Inclusion criteria were: (i) meeting ICD-10 diagnostic criteria for panic disorder and/or agoraphobia (with or without panic disorder), while ii-viii matching the criteria from the first pilot study.

Methods

Study Aim and Hypotheses

The primary hypothesis was that bCBT would lead to greater reductions in anxiety symptoms (BAI) than standard CBT after 12 weeks. Secondary hypotheses anticipated superior outcomes in depression, quality of life, work and social adjustment, self-efficacy, and mental health literacy in the bCBT group. Also, a stronger working alliance, fewer adverse effects, and better adherence compared to standard CBT was expected.

Sample Characteristics and Diagnostic Procedures

A total of 56 individuals with panic disorder and/or agoraphobia were randomized to either the CBT or bCBT group. Of these, 50 completed at least one assessment and were included in the ITT analysis.

Neither demographic variables (all ps ≥ .137; see Table 2) nor baseline values of outcome measures (ps ≥ .364) differed significantly between the two study groups. There was no significant difference in the number of therapy sessions received during the study period between the CBT group (M = 11.12, SD = 1.32 sessions) and the bCBT group (M = 10.56, SD = 1.83 sessions), $t(40) = 1.08$, $p = .287$.

A total of 23 psychotherapists participated in the study. For most participants (n = 46), diagnoses were established by matching the presenting symptoms with ICD-10 criteria. For 22 of these participants, the diagnosis was additionally supported by standardized diagnostic instruments. Two participants were diagnosed exclusively via a structured clinical interview, while two others were diagnosed using alternative methods deemed appropriate by the respective therapist.

Results

Most outcome measures showed acceptable reliability (α = .70–.93). Lower internal consistency (α < .70) was observed at some time points for select WHOQOL-BREF subscales and the adherence ratings from patients and therapists. Dropout rates did not differ significantly between groups from T0 to T1 ($\chi^2(1, N = 50) = 0.77$, $p = .381$) or T0 to T2 ($\chi^2(1, N = 50) = 0.25$, $p = .617$).

No significant baseline differences were found across outcome variables (all ps ≥ .364). No adverse events, serious incidents, or technical issues occurred in either group.

Primary and Secondary Outcomes

No significant between-group differences were found in the primary hypothesis of the reduction of anxiety symptoms (BAI). Regarding between-group differences, the time x condition interaction ($B = 0.60$, $p = .158$) did not reach statistical significance, despite an observable descriptive difference.

A significant between-group effect was found for depressive symptoms assessed by the BDI-II at T2 ($B = –2.57$, $p = .028$), though the overall time × condition interaction was not significant ($B = 0.60$ $p = .158$).

All other contrasts and interactions were non-significant (ps = .082–.997). Descriptively, bCBT showed small-to-moderate advantages for depression ($d = –0.46$), general health ($d = 0.20$), and physical health ($d = 0.22$). No significant group differences were found in patient-rated (T1: $d = –0.11$; T2: $d = –0.25$) or therapist-rated (T1: $d = –0.23$; T2: $d = 0.05$) working alliance. Self-reported adherence was descriptively higher in the bCBT group at T1 ($d = –0.45$) and T2 ($d = –0.44$), but not statistically significant. The same trend held for therapist-rated adherence (T1: $d = –0.26$; T2: $d = –0.23$). No significant differences were observed between groups in

frequency or severity of negative effects, as measured by the NEQ, at either T1 (frequency: d = 0.07; severity: d = 0.08) or T2 (frequency: d = 0.21; severity: d = 0.15).

Conclusion

The results suggest that anxiety symptoms improved more in the bCBT group than in the CBT group by week 6 (T1); however, this difference diminished by week 12 (T2) and did not reach statistical significance at either time point. However, bCBT demonstrated significantly greater efficacy than standard CBT on a secondary outcome measure of depression after 12 weeks. For quality of life, improvements were descriptively greater in the bCBT group as well, though these differences were not statistically significant.

Given the pilot nature of the trial and the relatively small sample size, the study was likely underpowered to detect subtle between-group differences, particularly for secondary outcomes.

Study 3: Larger Scale Study unipolar depression

Blended Cognitive Behavioral Therapy Versus Standard CBT for Unipolar Depression: A Multicenter Randomized Controlled Trial

Kalde, J., Atik, E., Stricker, J., Schückes, M., Neudeck, P., Abel, P., Hollank, J., Pittig, A., & Pietrowsky, R. (2025). *Blended cognitive behavioral therapy with a digital app vs. standard CBT for unipolar depression: A multicenter randomized controlled trial* [Manuscript submitted for publication to *Psychotherapy and Psychosomatics*].

Like Studies 1 and 2, Study 3 was also a two-arm, multicenter, pragmatic randomized controlled trial (RCT) designed to investigate the additional benefits of a bCBT treatment program. This larger-scale trial aimed to confirm and extend the previous findings in patients

with unipolar depression, as compared to the standard CBT treatment evaluated in Study 1, while addressing some of the limitations. It was also conducted in outpatient clinics and clinics affiliated with training institutes for CBT therapists in several large cities in Germany as part of routine care over a 12-week period.

Methods

Study design and hypotheses

The main differences between Study 1 and Study 3 concerned the outcome measures and study design. The BDI-II, BAI, WSAS, PSWQ, and all WHOQOL-BREF subscales except the Psychological Health subscale were excluded. Overall disorder severity and improvement were measured using the Clinical Global Impression-Severity (CGI-S; Guy, 1976; CIPS, 1996) and the Clinical Global Impression-Improvement (CGI-I; Guy, 1976; CIPS, 1996), with higher scores indicating greater severity (CGI-S) or less improvement (CGI-I).

In addition, a larger number of patients and therapists participated, and the number of assessment time points was reduced to two (baseline and 12 weeks, instead of baseline, 6 weeks, and 12 weeks). Furthermore, the bCBT application was further developed by adding therapeutic features, redesigning the user interface, and improving overall usability for both patients and therapists. Therapists were either licensed professionals or trainees under clinical supervision (1:4 ratio) at affiliated clinics.

The study received ethical clearance from the Ethics Committee of the Medical Faculty at Heinrich Heine University Düsseldorf (Reference No.: 2022-2183). It was prospectively registered in the ISRCTN registry (ISRCTN ID: 11129335). All participants were informed about the study through written documentation and verbal explanation and subsequently gave their informed consent.

As in Study 1, participants were required to meet the diagnostic criteria for a depressive episode (F32.0, F32.1, F32.2), recurrent depressive disorder (F33.0, F33.1, F33.2), or dysthymia (F34.1) according to the ICD-10. The inclusion and exclusion criteria remained the same, except that participants planning to change the dose of their current psychiatric medication or initiate a new one during the study period (a stable medication dose was permitted), were excluded to address a limitation of Study 1.

Participants

A total of 283 patients were recruited between August 2023 and May 2024. Of these, 144 were randomized to the bCBT group and 139 to the CBT group. Randomization followed a 1:1 allocation ratio and was stratified by depressive symptom severity (mild, moderate, severe depression, or dysthymia) into four groups: Group 1 (F32.0, F33.0), Group 2 (F32.1, F33.1), Group 3 (F32.2, F33.2), and Group 4 (F34.1). In contrast to Study 1, which employed simple randomization without stratification, this approach aimed to ensure balanced allocation across varying levels of symptom severity.

Statistical analyses

The primary hypothesis proposed that bCBT would result in greater reductions in depressive symptoms compared to standard CBT. Secondary hypotheses included stronger improvements in anxiety symptoms, psychological quality of life, self-efficacy, depression literacy, and therapist-rated symptom severity in the bCBT group. Higher treatment adherence, greater therapist-rated improvement, and a larger proportion of patients achieving clinically significant symptom reduction (≥50% on the PHQ-9; Israel, 2006; Keller, 2003; McMillan et al.,

2010) were also expected for bCBT. The safety hypothesis assumed no increase in adverse or serious adverse events in the bCBT group relative to standard CBT.

The study analyses were based on the ITT sample including all randomized participants before baseline testing (T0). In Study 1, randomization occurred prior to the baseline assessment; however, some patients were randomized without subsequently completing the baseline questionnaires. Consequently, these individuals could not be included in the ITT analyses, representing a methodological limitation of the previous studies. In contrast, the present study ensured the inclusion of all randomized participants.

Results

Significant baseline differences were observed between the two study groups for PHQ-9 ($p = .010$) and GAD-7 scores ($p = .041$). No significant baseline differences emerged for the remaining outcome measures (WHOQOL-Psychological Health, GSE, D-Lit, CGI-S, CGI-I). The bCBT group attended more sessions ($M = 10.95$, $SD = 1.38$) than the CBT group ($M = 10.10$, $SD = 2.19$), $t(262) = 3.79$, $p < .001$, $d = .47$.

There were no group differences in the baseline demographic characteristics, except for the employment status ($p = .023$; all other ps $> .05$). The rate of patients who dropped out in the CBT group (11.51%) was significantly higher than the rate of patients who dropped out in the bCBT group (4.17%), χ^2 (1, $N = 283$) = 5.32, $p = .021$.

Primary and Secondary Outcomes

Patients in the bCBT group demonstrated significantly larger improvements across a range of clinical and psychological outcomes compared to those receiving standard CBT.

Regarding the primary outcome**,** depressive symptoms, as measured by the PHQ-9, improved significantly more in the bCBT group ($d = 0.62$, $p < .001$), with a between-group difference of 95% CI [1.19, 3.29].

For secondary outcomes**,** participants receiving bCBT showed significantly larger improvements in generalized anxiety symptoms (GAD-7, $d = 0.61$, $p < .001$), psychological quality of life (WHOQOL-Psychological Health, $d = 0.42$, $p < .001$), self-efficacy (GSE, $d = 0.41$, $p = .003$), and mental health literacy (D-Lit, $d = 0.66$, $p < .001$).

Treatment adherence was higher among bCBT participants, as indicated by both self-reports ($d = .27$, $p = .034$) and therapist evaluations ($d = .41$, $p = .002$). Clinician-rated outcomes also favored bCBT, with significantly larger improvements on the CGI-S ($d = .45$, $p = .004$) and CGI-I ($d = .60$, $p < .001$).

The proportion of adverse events reported in the bCBT group (2 of 144) and the CBT group (1 of 139) did not differ significantly, χ^2 (1, $N = 283$) = 0.30, $p = .583$ (safety outcome).

Conclusion

The third trial found that blended CBT (bCBT) lead to greater improvements than standard CBT across multiple domains, including depressive and anxiety symptoms, quality of life, self-efficacy, and treatment adherence over a 12-week period. These results point to a therapeutic advantage of the evaluated bCBT program. Participants in the bCBT group also attended more therapy sessions on average, which could align with higher treatment engagement. The consistent improvements across several outcome measures suggest that bCBT may offer broader and more robust benefits than previously documented. Moreover, this large-scale trial addressed several methodological shortcomings identified in earlier and the pilot studies, such as limited sample sizes and inconsistent control conditions.

General Discussion

This dissertation contributes to the evolving literature on blended cognitive behavioral therapy by systematically examining its effectiveness and potential advantages over traditional CBT approaches in treating depression and anxiety disorders. The studies highlight the advantages of integrating digital therapeutic components with traditional CBT face-to-face therapy.

Findings across these studies underscore the importance of individualized and congruent digital interventions. The successful integration of digital tools such as interactive exercises, self-monitoring diaries, and automated reminders demonstrates how digital platforms can effectively augment traditional psychotherapy. Such digital interventions provide continuous therapeutic support, thereby reinforcing learned strategies and skills beyond therapy sessions and improving clinical outcomes.

Comparable randomized controlled trials examining bCBT and standard CBT with matched face-to-face contact are limited. Among the available studies, only one reported significantly greater reductions in depressive symptoms for bCBT (Berger et al., 2018). In contrast, the present findings revealed a larger between-group effect size for the primary depression outcome, indicating a stronger treatment effect. Results regarding anxiety and quality of life have been mixed, with some studies showing benefits for bCBT (e.g., Berger et al., 2018; Kalde et al., 2023) and others reporting no significant differences between conditions (Romijn et al., 2021; Pérez et al., 2021).

The practical implications of these findings, such as the higher adherence to treatment and higher session attendance suggest, that bCBT may represent a valuable approach to overcoming traditional barriers in psychotherapy, including limited session time, accessibility constraints, and

suboptimal adherence. This finding is in line with prior research suggesting that digital tools can enhance adherence to standard treatments, mainly demonstrated in earlier studies addressing physical health appointments or medication adherence (Topp et al., 2023; Wiecek et al., 2020). These findings of the dissertation extend the evidence to the domain of psychotherapy, indicating that similar adherence-enhancing mechanisms may be operative. Future research should aim to isolate the most effective digital elements (e.g., session reminders, post-session journaling) and assess their specific contributions to treatment engagement and outcomes.

Limitations

Several methodological limitations identified in Studies 1 and 2 were addressed in the design of Study 3. In parallel, feedback from those two studies also prompted further development and expansion of the digital application, enhancing its usability and functionality for both patients and therapists.

In Study 1 and 2, the use of psychopharmacological medication during the treatment period was not systematically assessed. As a result, changes in medication use may have confounded the outcomes. This limitation was addressed in Study 3 by explicitly monitoring and restricting changes in psychiatric medication: participants were only eligible if they maintained a stable dose throughout the study.

Another methodological issue in Studies 1 and 2 was that randomization occurred prior to baseline assessment. Consequently, some participants were randomized but did not complete the baseline questionnaires and were therefore excluded from the ITT analyses. In Study 3, this was resolved through minor changes in the EDC system, ensuring that only participants who completed the baseline assessment were randomized and included in the ITT sample.

Besides the limitations which were addressed in study 3, there were several limitations which couldn't be solved:

The study designs did not allow for a detailed examination of underlying mechanisms. To address this gap, future research could employ qualitative methodologies to explore how patients and therapists perceive and engage with various elements of the bCBT intervention. Moreover, as the study focused on a single digital platform, the generalizability of the results to other bCBT applications is limited. Comparative studies assessing different digital tools within blended care frameworks are necessary to identify which features contribute most to therapeutic efficacy and to inform future app development tailored to the needs of depressed patients.

The face-to-face therapy component of this study was delivered without a standardized manual. This reflects routine clinical conditions and underscores the ecological validity of the intervention but also introduces variability that complicates comparisons between the bCBT and standard CBT groups, thereby limiting the replicability of findings.

Similarly, therapists employed diverse diagnostic strategies—including both structured interviews and clinical judgment—reflecting everyday clinical practice. Although this approach aligns with routine clinical practice (e.g., Mueller & Segal, 2015), it also introduces a limitation, as variations in diagnostic procedures across participants may reduce consistency and comparability.

The findings of all three studies are based solely on quantitative questionnaire data. Conducting qualitative interviews with bCBT users—both patients and therapists—could enrich these findings by offering deeper insights into their experiences, perceived benefits of the digital application, and specific needs.

Furthermore, a limitation of all trials was the lack of data on reasons for non-inclusion among screened individuals who were ultimately not enrolled. This was largely due to practical

limitations and data protection regulations. Screening occurred within the context of routine care at the participating sites, with therapists informing eligible patients about the study. As screenings were not conducted specifically for research purposes, collecting information on exclusions without prior informed consent was deemed ethically inappropriate.

Finally, all conclusions of the studies are limited by the absence of long-term follow-up. The sustainability of treatment gains and potential effects on relapse or continued engagement with therapeutic content remain unknown. Future research should incorporate follow-up assessments at extended intervals, such as three- or six-months post-treatment, to evaluate the persistence and long-term utility of bCBT interventions.

Future Directions

Overall, this dissertation underscores the significant potential of digitally integrated therapeutic models to enhance both the delivery and efficacy of psychological interventions. Future research should aim to identify the specific components of digital interventions that most effectively contribute to therapeutic outcomes. Additionally, the long-term effectiveness and scalability of bCBT should be investigated across diverse clinical populations, with particular attention to varying digital formats and implementation contexts within bCBT frameworks. There is also a need for large-scale trials focused specifically on patients with anxiety disorders to expand the preliminary findings reported here.

While the current studies employed a blended model in which therapists selected individualized tasks and worksheets for patients via a mobile app, emerging technologies - particularly the integration of large language models (LLMs), such as OpenAI's ChatGPT or Google Gemini- represent a potentially transformative development in digital mental health care. These models allow for a more dynamic and interactive experience by changing the interface

from static content delivery to conversational engagement, enabling patients to interact with therapeutic material through natural-language dialogue. However, they also raise concerns regarding misinterpretation, privacy, and ethical oversight (Obradovich et al., 2024; Stade et al., 2024).

General Conclusion

This dissertation, comprising three randomized controlled trials, provides evidence that blended cognitive behavioral therapy (bCBT) leads to greater improvements than standard CBT across multiple outcomes over a 12-week period. While the two pilot studies offered initial insights into the application of blended treatments, the larger third trial expanded these findings across a broader population of patients with unipolar depression. However, results for patients with anxiety disorders remain mixed and warrant further investigation in future research.

Declaration of interest

All three studies received financial support from Elona Health, the developer of *elona therapy*, the digital intervention evaluated in the trials. This support included funding for therapist compensation in all studies and, in Study 3, for patient compensation as well.

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Appendix A - Affidavit

Eidesstattliche Erklärung gemäß § 5 der Promotionsordnung vom 15.06.2018 der Mathematisch-Naturwissenschaftlichen Fakultät der Heinrich-Heine-Universität Düsseldorf:

Ich versichere an Eides Statt, dass die Dissertation von mir selbständig und ohne unzulässige fremde Hilfe unter Beachtung der „Grundsätze zur Sicherung guter wissenschaftlicher Praxis an der Heinrich-Heine-Universität Düsseldorf“ erstellt worden ist.

Die Dissertation wurde in der vorliegenden oder ähnlichen Form noch bei keiner anderen Institution eingereicht. Ich habe bisher keine erfolglosen Promotionsversuche unternommen.

Köln, den 5.2.26 

Jan Kalde

Appendix B: Original Research articles and manuscript

Original article of Study 1:

Kalde, J., Atik, E., Stricker, J., Schückes, M., Neudeck, P., Pittig, A., & Pietrowsky, R. (2023). Enhancing the effectiveness of CBT for patients with unipolar depression by integrating digital interventions into treatment: A pilot randomized controlled trial. *Psychotherapy Research*, *34*(8), 1131–1146. https://doi.org/10.1080/10503307.2023.2277866

I was the corresponding and first author of this article. I contributed to the Conceptualization, Data curation, Resources, Investigation, Methodology, Project administration and execution, Ethics approval, Writing and Validation

Original article of Study 2:

Atik, E., Kalde, J., Stricker, J., Schückes, M., Neudeck, P., Pietrowsky, R., & Pittig, A. (2025). Advancing CBT for panic disorder and agoraphobia by integrating a digital intervention into treatment: a pilot randomized controlled trial. *Cognitive Behaviour Therapy*, 1–21. https://doi.org/10.1080/16506073.2025.2503834

I was the corresponding and second author of this article. I contributed to the Conceptualization, Data curation, Resources, Investigation, Methodology, Project administration and execution, Ethics approval, Writing and Validation

Original manuscript of Study 3:

Kalde, J., Atik, E., Stricker, J., Schückes, M., Neudeck, P., Abel, P., Hollank, J., Pittig, A., & Pietrowsky, R. (2025). *Blended cognitive behavioral therapy with a digital app vs. standard CBT for unipolar depression: A multicenter randomized controlled trial* [Manuscript submitted for publication to *Psychotherapy and Psychosomatics*].

I was the corresponding and first author of this manuscript. I contributed to the Conceptualization, Data curation, Investigation, Methodology, Project administration and execution, Ethics approval, Writing and Validation