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Randomized controlled trial to test additional benefits of blended cognitive behavioral therapy over standard cognitive behavioral therapy for panic disorder and agoraphobia in adults

Submission date
11/06/2024

Recruitment status
Recruiting

Registration date
11/06/2024

Overall study status
Ongoing

Last Edited
30/12/2025

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Over the past decade, there has been a growing interest in internet-delivered cognitive behavioral therapy (iCBT) solutions for the treatment of cognitive and psychological disorders. These programs consist of digital interventions based on cognitive behavioral therapy (CBT) that are usually delivered via the Internet through a smartphone or computer. Internet-delivered CBT programs provide several advantages, for example, they can be readily accessed when needed and they can drastically increase the functional capacity of the healthcare system. The aim of this study, which is to follow up the earlier pilot study ISRCTN16328317 (https://www.isrctn.com/ISRCTN16328317) with a larger study, is to test the additional benefits of a digital health program (elona therapy) for the blended treatment of panic disorder and agoraphobia in adult patients.

Who can participate?
Patients aged 18 to 65 years old with panic disorder and/or agoraphobia receiving cognitive behavioral therapy (CBT) in outpatient clinics

What does the study involve?
Participants in the intervention group will get access to a digital health application (elona therapy) in addition to their outpatient psychotherapy aiming to support and amplify the therapeutic process. This group of patients will be compared to a control group who receive only conventional cognitive behavioral therapy and access to the app after they participate in the study. All patients will fill out online questionnaires at the beginning and the end of the 8 weeks of the study duration. The study will take place in outpatient clinics.

What are the possible benefits and risks of participating?
Participants could benefit from a better and/or faster recovery of their symptoms, while the

potential negative effects of the smartphone program is small due to the constant weekly face-to-face therapy sessions. It is expected that patients receiving both CBT and the support of the digital health application (intervention group) will report fewer symptoms and/or greater improvement in other areas of their personal lives than patients receiving CBT without additional support (control group). As all patients will be receiving CBT, which is a validated and efficient psychotherapeutic approach, the risks of the intervention are low.

Where is the study run from?
Elona Health GmbH (Germany)

When is the study starting and how long is it expected to run for?
May 2024 to March 2027

Who is funding the study?
Elona Health GmbH (Germany)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific

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Type(s)
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Additional identifiers

Protocol serial number
EL-M01ANX

Study information

Scientific Title
Randomized controlled trial to test the superiority of blended cognitive behavioral therapy with elona therapy over standard cognitive behavioral therapy for panic disorder and agoraphobia in adults

Study objectives
Primary hypotheses:
P1: Patients receiving blended cognitive-behavioural therapy (bCBT) with elona therapy experience stronger improvements in self-rated symptoms of panic disorder and agoraphobia (assessed with the Panic and Agoraphobia Scale (PAS)) compared to patients receiving treatment as usual (TAU) after 8 weeks of treatment.

Secondary hypotheses:
S1: Patients receiving bCBT with elona therapy experience stronger improvements in their symptoms of anxiety (assessed with the Beck Anxiety Inventory (BAI)) compared to patients receiving TAU after 8 weeks of treatment.

S2: Patients receiving bCBT with elona therapy experience stronger improvements in their symptoms of depression (assessed with the Beck Depression Inventory-II (BDI-II)) compared to patients receiving TAU after 8 weeks of treatment.

S3: Patients receiving bCBT with elona therapy experience stronger improvements in their quality of life (assessed with the World Health Organization Quality of Life-Brief version (WHOQOL-BREF)) compared to patients receiving TAU after 8 weeks of treatment.

S4: Patients receiving bCBT with elona therapy show higher adherence to treatment (assessed through self and psychotherapist report using a self-validated 4-item instrument) compared to patients receiving TAU after 8 weeks of treatment.

S5: Patients receiving bCBT with elona therapy show stronger improvements in their functional impairment (assessed with Work and Social Adjustment Scale (WSAS)) compared to patients receiving TAU after 8 weeks of treatment.

S6: Patients receiving bCBT with elona therapy show a stronger improvement in their overall symptoms assessed by the clinician (assessed through Clinical Global Impression-Improvement (CGI-I)) compared to patients receiving TAU after 8 weeks of treatment.

S7: Patients receiving bCBT with elona therapy show a stronger improvement in the severity of their symptoms assessed by the clinician (assessed through Clinical Global Impression-Severity (CGI-S)) compared to patients receiving TAU after 8 weeks of treatment.

Mixed linear models with the intention-to-treat (ITT) data set will be used as the primary method of data analysis. For the missing values, multiple imputations will be used. In addition, per-protocol (PP) analyses will be performed as an additional sensitivity analysis. Primary and secondary hypotheses will be tested in a fixed sequence procedure (hierarchical testing), where they will be tested in the predefined order until the first non-significant result.

An interim analysis will be conducted when at least one-third of the planned sample size has completed all study procedures (i.e. completed T1). Only one interim analysis will be carried out.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/05/2024, Ethics Committee of the Georg-Elias-Müller-Institute for Psychology of the Georg-August-University Göttingen (Waldweg 26, Göttingen, 37073, Germany; +49 (0)551 / 39-21110; ethikkommission@psych.uni-goettingen.de), ref: Application no. 349 (Amendment no. 378)

Primary study design
Interventional

Study design
Multi-centre randomized single-blind controlled study

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Panic disorder and/or agoraphobia

Interventions
elona therapy is a digital health application that supports patients in outpatient psychotherapy in the treatment of mental illnesses (depression, anxiety/panic disorders, hypochondriacal disorders) through an intelligent delivery of therapeutic content between regular therapy sessions. With elona therapy, psychotherapists can assign interventions, helpful activities, exercises, and psychoeducational resources that provide patients with information and treatment techniques related to their mental illness. Thus, 400 different types of interventions, techniques, exercises, and psychoeducation based on CBT are available beyond the regular therapy session through the elona therapy smartphone application. The content is based on current and evidence-based therapeutic methods in cognitive behavioral therapy (CBT). By using psychometric questionnaires and exercises, elona therapy individualizes the content to the

needs of the patient. The application is designed to strengthen the active cooperation and participation of patients in outpatient psychotherapy and to integrate therapeutic contents into the daily life of the patient.

To test the additional benefits and safety of bCBT with elona therapy, an RCT for patients with a clinical diagnosis of panic disorder and/or agoraphobia (including ICD-10: F40.0x, F41.0) based on ICD-10 criteria is planned. The RCT comprises two arms. Participants assigned to the intervention group will get access to the elona therapy smartphone application. The control group will get access to elona therapy after 8 weeks. All groups will have full access to TAU (weekly face-to-face psychotherapeutic treatment in CBT) over 8 weeks. For the primary and secondary objectives, a 2x2 intention-to-treat analyses (pre vs mid vs post) design will be used. Participants assigned to the intervention group will work with the elona therapy app as an add-on to TAU.

After agreeing to the informed consent, randomization will take place during enrollment in the electronic data capture system (EDC) via the therapists in an online randomization tool.

Assessments will take place at baseline (T0) and 8 weeks after treatment start (T1) as a self-report. Patients' self-report data are collected, including basic demographic questions via the EDC. The questionnaire includes the German version of the Panic and Agoraphobia Scale (PAS), Beck Anxiety Inventory (BAI), Beck Depression Inventory-II (BDI-II), and the brief version of the quality of life scale by the World Health Organization (WHOQOL- BREF) to assess medical benefits. Additionally, patients will provide data on patient-relevant and structural improvement measures in the Work and Social Adjustment Scale (WSAS), and on their self-reported adherence to therapy.

Psychotherapists will also provide a third-party report on patients' symptom severity at baseline (T0) and posttreatment (T1) through the Clinical Global Impression Scale-Severity (CGI-S) and overall symptom improvement through the Clinical Global Impression Scale-Improvement (CGI-I) only at T1. Moreover, they will report their patients' adherence to the treatment at T1 using a self-validated instrument.

Intervention Type
Behavioural

Primary outcome(s)
Symptoms of panic and agoraphobia measured using the PAS online questionnaire at the beginning of the treatment and 8 weeks

Key secondary outcome(s)
1. Symptoms of anxiety assessed with the Beck Anxiety Inventory (BAI) at the beginning of the treatment and after 8 weeks
2. Symptoms of depression assessed with the Beck Depression Inventory-II (BDI-II) at the beginning of the treatment and after 8 weeks
3. Physical health-related quality of life assessed with the World Health Organization Quality of Life-Brief version (WHOQOL-BREF) at the beginning of the treatment and after 8 weeks
4. Psychological health-related quality of life assessed with the World Health Organization Quality of Life-Brief version (WHOQOL-BREF) at the beginning of the treatment and after 8 weeks
5. Functional impairment of the patient assessed with the Work and Social Adjustment Scale (WSAS) at the beginning of the treatment and after 8 weeks

6. Adherence to treatment assessed through self and psychotherapist report using a self-validated 4-item instrument after 8 weeks

In addition to that, psychotherapists participating in this study will fill out the following questionnaires for their patients:
7. Overall symptoms assessed by the clinician (assessed through Clinical Global Impression - Improvement (CGI-I)) at the beginning of the treatment and after 8 weeks
8. Improvement in the severity of their symptoms assessed by the clinician through Clinical Global Impression-Severity (CGI-S) at the beginning of the treatment and after 8 weeks

Additionally, the study will evaluate whether the proportion of patients experiencing clinically significant improvements (i.e., ≥50% symptom reduction on the PAS) differs significantly between the two study groups after 8 weeks.

Completion date
01/03/2027

Eligibility

Key inclusion criteria
1. All participants without the inclusion ICD-10 diagnosis criteria as well as participants with the following comorbid ICD-10 diagnoses are excluded:
1.1 F0x.x: Organic, including symptomatic, mental disorders
1.2. F1x.x Mental and behavioural disorders due to psychoactive substance use (except F17.x)
1.3. F2x.x: Schizophrenia, schizotypal and delusional disorders
1.4. F31: Bipolar affective disorder
1.5. F32.3: Severe depressive episode with psychotic symptoms
1.6. F33.3: Recurrent depressive disorder, current episode severe with psychotic symptoms
2. Individuals with acute suicidality (operationalized via BDI-II screening question greater than 1 or first checkup) are excluded from this study first checkup)
3. Participants under the age of 18 years
4. Participants without any access to a smartphone (iOS or Android operating system) with internet access
5. Participants without German language proficiency
6. Participants who are currently enrolled in a potentially confounding drug or device trial
7. Participants who plan to change the dose of their current psychiatric medication or start a new one during the study period (a stable dose of psychiatric medication is allowed)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit

65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. All participants without the inclusion ICD-10 diagnosis criteria as well as participants with the following comorbid ICD-10 diagnoses are excluded:
1.1 F0x.x: Organic, including symptomatic, mental disorders
1.2. F1x.x Mental and behavioural disorders due to psychoactive substance use (except F17.x)
1.3. F2x.x: Schizophrenia, schizotypal and delusional disorders
1.4. F31: Bipolar affective disorder
1.5. F32.3: Severe depressive episode with psychotic symptoms
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5. Participants without German language proficiency
6. Participants who are currently enrolled in a potentially confounding drug or device trial
7. Participants who plan to change the dose of their current psychiatric medication or start a new one during the study period (a stable dose of psychiatric medication is allowed)

Date of first enrolment
14/06/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
Germany

Study participating centre
Praxis am Volksgarten Dr. Peter Neudeck
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Study participating centre

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Sponsor information

Organisation
Elona Health GmbH

Funder(s)

Funder type
Industry

Funder Name
Elona Health GmbH

Results and Publications

Individual participant data (IPD) sharing plan
Participant-level data (anonymized data) is available upon request from Ece Atik (atik.ece@uni-goettingen.de), there is participant consent for 10 years for other research institutions, but only including bCBT studies in Germany.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes