

Improving the effectiveness of cognitive based therapy for depression with digital interventions: findings from a randomized control trial

Submission date 07/02/2023	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 08/02/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 17/08/2023	Condition category Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

elona therapy is the first digital health application (DiGA) for therapy support in the treatment of depression and is reimbursed by all statutory health insurers in Germany. Psychotherapists can individualize the available content based on the progress of the therapy. This study follows a pilot study (<https://www.isrctn.com/ISRCTN16328317>) and aims to evaluate the efficacy and safety of the digital health application elona therapy (Depression module) for blended cognitive behavioral therapy (bCBT) compared to standard cognitive behavioral therapy (CBT) for depression.

Who can participate?

Patients aged 18 - 65 years with a unipolar depressive disorder

What does the study involve?

Participants will either receive bCBT with elona therapy or standard CBT over 12 weeks. All patients will fill out online questionnaires at the beginning (week 0) and at the end (week 12) of the study period.

What are the possible benefits and risks of participating?

During the use of the application, all participants will receive the usual behavioral therapy (TAU). All participants will benefit from cognitive-based therapy. One group will also additionally benefit from the prior pilot-study tested mental health application. The participants could face a worsening of their general depression symptoms in this setting. In addition, similar to other forms of psychotherapy, the increase in these symptoms could trigger other symptoms of other mental illnesses. In general, because all participants will receive the usual cognitive-based therapy, risks are very low.

Where is the study run from?

Heinrich-Heine-Universität Düsseldorf Clinical Psychology (Germany)

When is the study starting and how long is it expected to run for?
September 2022 to January 2025

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

Who is the main contact?
Jan Kalde of the University of Duesseldorf, jan.kalde@hhu.de

Contact information

Type(s)
Principal Investigator

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Mr Jan Kalde

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Dep_RCT_1

Study information

Scientific Title
Enhancing the efficacy of CBT for patients with unipolar depression by integrating digital interventions into treatment: Results from a randomized controlled trial

Study objectives

Current study hypothesis as of 10/08/2023:

Primary hypothesis (confirmatory)

P1: Patients receiving bCBT with elona therapy experience stronger improvements in depression symptoms (assessed with the PHQ-9) compared to patients receiving TAU over 12 weeks of treatment.

Primary safety hypotheses

PS: Patients receiving bCBT with elona therapy do not experience more adverse events or serious adverse events (assessed through therapist report via eCRF, see 5.4) over the course of 12 weeks of treatment.

Secondary hypotheses (exploratory)

S1: Patients receiving bCBT with elona therapy experience stronger improvements in generalized anxiety symptoms (assessed with the GAD-7) compared to patients receiving TAU over 12 weeks of treatment.

S2: Patients receiving bCBT with elona therapy experience stronger improvements in their psychological health-related quality of life (assessed with the psychological health subscale of the WHOQOL- BREF) compared to patients receiving TAU over 12 weeks of treatment.

S3: Patients receiving bCBT with elona therapy experience stronger improvements in their depression literacy (assessed with the D-Lit) compared to patients receiving TAU over 12 weeks of treatment.

S4: Patients receiving bCBT with elona therapy show higher adherence (assessed through self and psychotherapist report using a self-validated 4-item instrument) compared to patients receiving TAU over 12 weeks of treatment.

S5: The proportion of patients showing clinically significant improvement (i.e., $\geq 50\%$ symptom reduction on the PHQ-9; Israel, 2006; Keller, 2003; McMillan et al., 2010) is larger for patients receiving bCBT with elona therapy compared to patients receiving TAU over 12 weeks of treatment.

S6: Patients receiving bCBT with elona therapy experience stronger improvements in their therapist-rated CGI-S scores compared to patients receiving TAU over 12 weeks of treatment.

S7: Patients receiving bCBT with elona therapy experience stronger improvements in their overall symptoms compared to patients receiving TAU over 12 weeks of treatment (indicated by higher therapist-reported CGI-I scores at T1).

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Ethics approval required

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Ethics approval(s)

Approved 05/08/2023, Ethics Committee HHU Duesseldorf (Moorenstrasse 5, Building 14.82, Dusseldorf, 40225, Germany; +49 211 81-19591; Ethikkommission@med.uni-duesseldorf.de), ref: 2022-2183-andere Forschung erstvotierend

Study design

Interventional randomized controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Other therapist office

Study type(s)

Treatment

Participant information sheet

See additional files (in German)

Health condition(s) or problem(s) studied

Outpatient psychotherapeutic treatment of unipolar depression

Interventions

Current interventions as of 10/08/2023:

elona therapy (Depression module) is a digital health application that supports patients in outpatient psychotherapy for unipolar depression through the 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. Overall, over 400 different types of interventions, techniques, exercises, and psychoeducation 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 CBT. elona therapy allows individualizing 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 content in the daily life of the patient.

To test the efficacy and safety of elona therapy (Depression module), a randomized controlled trial (RCT) with patients with a clinical diagnosis of depression (including ICD-10: F32.x, F33.x, F34.1) based on ICD-10 criteria, is planned. Randomization is achieved 1:1 and stratified according to the subgroups of depression (mild/moderate/severe/dysthymia). This study follows a pilot study (<https://www.isrctn.com/ISRCTN16328317>).

The RCT comprises two arms: Participants assigned to the treatment group will receive access to the elona therapy (Depression module) application in addition to face-to-face cognitive behavioral therapy (CBT) for 12 weeks (blended CBT; bCBT). The other group (active control group) will receive face-to-face CBT for 12 weeks (treatment as usual; TAU). The active control group will receive access to elona therapy after the study period. For evaluating the primary and secondary objectives of this study (see below) a 2 (group: bCBT, TAU) x 2 (time: pre, post) design will be used.

Previous interventions:

elona therapy (Depression module) is a digital health application that supports patients in outpatient psychotherapy for unipolar depression through the 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. Overall, over 400 different types of interventions, techniques, exercises, and psychoeducation 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 CBT. elona therapy allows individualizing 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 in the daily life of the patient.

To test the efficacy and safety of elona therapy (Depression module), a randomized controlled trial (RCT) with patients with a clinical diagnosis of depression (including ICD-10: F32.x, F33.x, F34.1) based on ICD-10 criteria is planned. Randomization via online tool ('Climedo')

The RCT comprises two arms: Participants assigned to the treatment group will receive access to the elona therapy (Depression module) application in addition to face-to-face cognitive behavioral therapy (CBT) for 12 weeks (blended CBT; bCBT). The other group (active control group) will receive face-to-face CBT for 12 weeks (treatment as usual; TAU). The active control group will receive access to elona therapy after the study period. For evaluating the primary and secondary objectives of this study (see below) a 2 (group: bCBT, TAU) x 2 (time: pre, post) design will be used.

Intervention Type

Behavioural

Primary outcome measure

Current primary outcome measure as of 17/08/2023:

Assessments will take place at baseline (T0) and 12 weeks after treatment start (T1):

Primary efficacy objective

Depressive symptoms (PHQ-9)

Primary safety objective

Number or seriousness of adverse events measured using patient records

Previous primary outcome measure as of 10/08/2023 to 17/08/2023:

Assessments will take place at baseline (T0), 6 weeks after treatment start (T1) and 10 weeks after treatment start (T2):

Primary efficacy objective

Depressive symptoms (PHQ-9)

Primary safety objective

Number or seriousness of adverse events measured using patient records

Previous primary outcome measure:

Assessments will take place at baseline (T0) and 12-week after treatment start (T1):

Primary efficacy objective

Depressive symptoms (PHQ-9)

Primary safety objective

Number or seriousness of adverse events measured using patient records

Secondary outcome measures

Assessments will take place at baseline (T0) and 12-week after treatment start (T1):

1. Generalized anxiety symptoms (measured with the GAD-7)
2. Psychological health (measured with the psychological health subscale of the WHOQOL-BREF)
3. Depression literacy (measured with the D-Lit)
4. Self efficacy (GSE)
5. Overall therapist-rated symptoms (measured with the Clinical Global Impression (CGI) Scale Item 1, CGI-S (Severity), and Item 2, CGI-I (Improvement)).
6. Adherence (assessed with a 4-item scale from the patient and therapist perspective)
7. Proportion of patients experiencing clinically significant improvements (i.e., $\geq 50\%$ symptom reduction on the PHQ-9; Israel, 2006; Keller, 2003; McMillan et al., 2010)

Overall study start date

01/09/2022

Completion date

31/01/2025

Eligibility

Key inclusion criteria

1. All participants must have been diagnosed with one of the following ICD-10 diagnoses:
F32: Depressive episode

F32.0: Mild depressive episode
F32.1: Moderate depressive episode
F32.2: Severe depressive episode without psychotic symptoms
F33: Recurrent depressive disorder
F33.0: Recurrent depressive disorder, current episode mild
F33.1: Recurrent depressive disorder, current episode moderate
F33.2: Recurrent depressive disorder, current episode severe without psychotic symptoms
F34.1: Dysthymia
2. Between the age of 18 and 65 years
3. Sufficient German language skills (in writing and reading)
4. Possess a smartphone (iOS or Android operating system) with internet access
5. Provide signed and dated informed consent, and be willing to comply with the protocol

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

324 participants (162 in each group).

Key exclusion criteria

1. All individuals without the included ICD-10 diagnoses as well as individuals with the following comorbid ICD-10 diagnoses are excluded:
F00-F09: Organic, including symptomatic, mental disorders
F10-F19 Mental and behavioural disorders due to psychoactive substance use (except F17.1, F17.2, F17.3)
F20-F29: Schizophrenia, schizotypal and delusional disorders
F30: Manic episode
F31.0, F31.1, F31.2, F31.5, F31.6, F31.8, F31.9: Bipolar disorder current hypomanic or manic episode
F32.3: Severe depressive episode with psychotic symptoms
F33.3: Recurrent depressive disorder, current episode severe with psychotic symptoms
2. Individuals with acute suicidality (assessed via clinical assessment by the responsible therapist),
3. Individuals without any access to a smartphone (iOS or Android operating system) with internet access, and
4. Individuals with insufficient German language proficiency are excluded from this study
5. If an individual is currently enrolled or is planning to participate in a potentially confounding drug or device trial during the study, enrollment into this study is not possible
6. Participants will also be excluded for the respective measurement point if they fail to complete the study questionnaires within 14 days after having received them

Date of first enrolment

17/08/2023

Date of final enrolment

31/05/2024

Locations

Countries of recruitment

Germany

Study participating centre

Psychotherapeutische Institutsambulanz der Heinrich-Heine-Universität

Graf-Adolf-Straße 63

40210 Düsseldorf, Germany

Düsseldorf

Germany

40210

Study participating centre

AVT GmbH Akademie für Verhaltenstherapie

Venloer Str 47-53

50672 Köln, Germany

Köln

Germany

50672

Study participating centre

Hochschulambulanz für Psychotherapie am Institut für Psychologie der Universität Würzburg

Marcusstraße 9-11

97070 Würzburg, Germany

Würzburg

Germany

97070

Study participating centre

Zentrum für Psychotherapie – Hochschulambulanz der Arbeitseinheit Klinische Psychologie und Psychotherapie der Ruhr-Universität Bochum

Massenbergstraße 9 - 13

44787 Bochum, Germany

Bochum

Germany

44787

Study participating centre

Institutsambulanz und Tagesklinik für Psychotherapie IAP-AVM-Dresden GmbH

Königstraße 7

01097 Dresden, Germany

Dresden

Germany

01097

Study participating centre

Psychotherapeutische Hochschul-Ambulanz - Technische Universität Chemnitz GmbH

Zwickauer Str. 58

09112 Chemnitz, Germany

Chemnitz

Germany

09112

Study participating centre

Praxis am Volksgarten Dr. Peter Neudeck

Volksgartenstraße 36

50677 Köln, Germany

Köln

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50677

Study participating centre

Psychotherapie an der Königsallee Dr. Peter Neudeck

Grünstraße 23

40212 Düsseldorf, Germany

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Sponsor information

Organisation

Heinrich-Heine-Universität Düsseldorf

Sponsor details

Heinrich-Heine-Universität Düsseldorf Clinical Psychology

Clinical Psychology

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Sponsor type

University/education

Website

<https://hhu.de>

Funder(s)

Funder type

Industry

Funder Name

Elona Health GmbH

Results and Publications

Publication and dissemination plan

The results are planned to be published in a peer-review academic journal after the end of the trial.

Intention to publish date

31/12/2024

Individual participant data (IPD) sharing plan

Participant level data (anonymised data) is available upon request from Jan Kalde (jan.kalde@hhu.de).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	in German		08/02/2023	No	Yes