

SPECIAL ARTICLE

Effectiveness of an internet-based self-guided program to treat depression in a sample of Brazilian users: a study protocol

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Although psychological treatments for depressive disorders are available, they are often expensive or inaccessible for many. Web-based interventions that require minimal or no contact with therapists have been shown effective. To the best of our knowledge, no study using this treatment format has been conducted in Brazil. The Deprexis program was designed using empirically established principles of cognitive-behavioral therapy to reduce depressive symptoms. The objective of this study was to evaluate the effectiveness of Deprexis in Brazil. This randomized controlled trial will include 128 Brazilians with clinically significant depression symptoms or who have been diagnosed with depressive disorder (major depressive disorder or dysthymia), recruited over the internet (Brazilian forums, social networks, or e-mail lists). Individuals with other psychiatric diagnoses that require significant attention (e.g., bipolar disorder, psychosis) will not be included in the trial. Participants will be randomly assigned to 1) treatment as usual plus immediate access to Deprexis or 2) treatment as usual plus delayed access to Deprexis (after 8 weeks). Participants will be able to obtain other treatment types in addition to the online intervention. If found effective, this web-based intervention would increase the evidence-based care options for depression treatment in Brazil.

Clinical trial registration: RBR-6kk3bx, UTN U1111-1212-8998

Keywords: Depression; online interventions; self-guided interventions; cognitive-behavioral psychotherapy

Introduction

Major depressive disorder (MDD) and dysthymia are characterized by symptoms such as a sad, empty or irritable mood, anhedonia and specific somatic and cognitive changes that reduce quality of life and affect an individual's social and occupational functioning.¹ Depression is one of the leading causes of functional impairment.²⁻⁴ Suicide is strongly related to depression; in fact, about half of those who attempt suicide are depressed, and as many as 15% of people suffering from depression will commit suicide.⁵ The estimated economic burden of depression includes direct medical costs (31%), costs related to mortality from suicide (7%), and costs associated with occupational impairment (62%).⁶ Still, depressive disorders are among the most common mental health problems for which help is sought.^{7,8} Evidence suggests that those who most need help (i.e., the people with more severe depressive symptoms) seek treatment the least.⁹

Although some psychological treatments for unipolar depression have been supported by evidence,¹⁰ this evidence is debatable, in part due to potential publication bias.¹¹ Furthermore, a considerable number of patients abandon treatment without substantial improvement or relapse after treatment.^{12,13} A large proportion of depressed people receive no treatment at all.¹⁴ General barriers to psychotherapy include its high costs, extensive commutes, time constraints, negative evaluations of psychotherapy, and availability of services.^{15,16} Moreover, in many parts of the world, there is a shortage of qualified professionals, especially in areas far from urban centers,¹⁷ while in large centers the most affordable services have long waiting lists. It is also known that many clients do not seek help due to the stigma associated with psychological and psychopharmacological treatment.¹⁸ Specific barriers to treatment have been found among depressed people, such as lack of motivation, emotional concerns,¹⁵ and negative perception of the effectiveness of psychotherapy.⁹ Thus, research on different treatment

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Submitted Jun 22 2019, accepted Oct 22 2019.

How to cite this article: Lopes RT, Meyer B, Berger T, Svacina MA. Effectiveness of an internet-based self-guided program to treat depression in a sample of Brazilian users: a study protocol. Braz J Psychiatry. 2020;00:000-000. <http://dx.doi.org/10.1590/1516-4446-2019-0582>

formats has been recommended,¹⁹⁻²² and Internet treatments have gained popularity in recent years.^{23,24}

There is a clear distinction between online psychotherapy and Internet-based self-administered interventions. Online psychotherapy is usually synchronous, performed by professionals via virtual interaction platforms (e.g., Skype®), and does not exclude the possibility of face-to-face interaction. Internet-based psychological interventions are usually asynchronous, conducted through self-administered programs that target psychoeducation and involve therapeutic tasks that are structured and systematic. Little contact with a therapist is presumed, since their perspective is support and problem solving. The advantages of online, self-guided interventions include potentially lower costs, greater geographic reach, privacy, flexibility (treatment is available anytime and anywhere Internet access is available), the ability to repeat exercises, and adaptation to the client's everyday context rather than the therapist's office. Research outside Brazil, mainly in Switzerland, Sweden, the Netherlands, Germany, Australia, and the United Kingdom, suggests that some (but not all) internet-based self-guided psychological interventions are effective.²⁵⁻³⁰ Evidence from direct comparisons suggests that Internet-based interventions with some therapist support are as effective as face-to-face interventions.^{31,32} In an individual patient-level meta-analysis reviewing the efficacy of self-guided internet-based interventions (without assistance from therapists) for depression, an average effect size of $d = 0.27$ was reported,³³ which is considered a small effect.³⁴ However, programs may differ in efficacy. For example, a meta-analysis of a specific Internet intervention for depression (Deprexis) reported large effect sizes averaging $d = 0.54$, based on eight randomized controlled trials conducted in German-speaking countries and the United States.³⁵

In Brazil, the Federal Council of Psychology regulates the Internet-mediated psychological practice with Resolution 011/2018.³⁶ In this document, Brazilian psychologists are authorized to provide treatment through online services such as Skype®, FaceTime®, and text services (e-mail, chat applications, messaging, etc.). However, research on such interventions is at an early stage³⁷ and, to date, very few empirical studies assessing online treatment effectiveness have been conducted. We know of no studies in Brazil that have evaluated the effectiveness of an Internet-based intervention for a psychological problem in a controlled manner. Thus, more studies on the results and processes of Internet-based psychotherapy are necessary to better evaluate the impact of this type of treatment with potential users in Brazil.³⁷

Deprexis (<https://deprexis.broca.io/en/>) is an established online intervention for depression that has already been tested in 12 randomized controlled trials.^{35,38-41} Deprexis uses an integrative approach, based primarily on cognitive behavioral therapy.⁴² Evidence for the effectiveness of this program has been reported in Europe, especially German-speaking countries^{29,42-47}, as well as in the United States.⁴⁸ However, these results were obtained in high-income countries. This program has been translated into eight languages, including Brazilian Portuguese,

and some efforts have already been made for cultural adaptation to Brazil, although no study has been conducted with groups of Brazilians suffering from depression.

The main objective of this study is to replicate empirical effectiveness studies conducted in other countries, using Deprexis in the Brazilian cultural context. Therefore, the main research question is: will the therapeutic results (i.e., reduction of depressive symptoms) in Brazil be similar those obtained in other countries (i.e., medium to large effect sizes, compared to treatment as usual [TAU])?

Methods

This study will be a randomized controlled trial with a parallel-group design. The selected participants will be allocated randomly into two groups: 1) immediate access to Deprexis; and 2) a wait-list control group that receives delayed access to Deprexis. Both groups will be allowed access to any other treatments that they or their care providers deem necessary, i.e., TAU (psychotherapy, psychopharmacology, or both). Deprexis will be used alone or together with TAU.

Participants

Participants must have the following characteristics for inclusion in the study: 1) be at least 18 years of age; 2) have regular Internet access; 3) be diagnosed with a depressive disorder (MDD or dysthymia) according to DSM-5 definitions¹; or 4) present clinically relevant depressive symptoms, i.e. a score of at least 10 on the Patient Health Questionnaire-9 (PHQ-9).^{49,50} Participants may be undergoing any other psychopharmacological or psychotherapeutic treatment (TAU) to manage their depressive symptoms. Participants will be excluded from the study if they: 1) present other severe psychiatric symptoms that are the primary focus of specific clinical attention (e.g., severe psychotic symptoms, manic episodes); 2) show the potential to injure themselves or others; 3) present severe suicidal ideation; 4) are psychiatric patients adapting to medication (having been on medication for less than a month, or having changed their dosage in the past month, or intending to switch medications within 3 months after the trial starts); 5) do not have regular Internet access; or 6) are using illegal drugs or have high alcohol intake (more than three drinks per day). Candidates ineligible for the study will be contacted (by telephone, e-mail, or during the interview) for feedback on the initial evaluation and will be referred to face-to-face public mental health services in their area. Using simple randomization procedures (computerized random numbers), the selected participants will be randomly assigned to either TAU plus immediate access to Deprexis, or TAU plus delayed access to Deprexis (after 8 weeks). The randomization scheme will be generated with a random algorithm developed at <http://www.randomization.com>. To ensure allocation concealment, the research team members performing the randomization will not be aware of any participant characteristics. The research team member who randomly allocates participants in both groups will be different from

the one who applies inclusion/exclusion criteria, and these research team members will not have contact with each other.

Recruitment

A website (<https://sites.google.com/view/ficabem/>), a Facebook page (@p.ficabem) and an Instagram profile (@p.ficabem) have been set up to provide necessary information about the research procedures and online intervention, as well as to recruit participants. The link will be advertised on the main social networks and e-mail lists of associations of mental health professionals in Brazil. We also intend to announce the research opportunity in traditional media and mental health services.

Eligibility assessment

Potential participants will be asked to complete a consent form, the sociodemographic questionnaire, the PHQ-9, and the Clinical Outcome in Routine Evaluation – Outcome Measurement (CORE-OM) when logging on to the study platform for the first time. In order to assess the exclusion and inclusion criteria and confirm the severity of depressive symptoms, an interview based on the Adult DSM-5 Cross-Cutting Symptom Measure¹ will be held by phone or on online platforms such as Skype® or WhatsApp®.

Instruments

Sociodemographic questionnaire

The assessed demographic variables will be age, gender, location in Brazil, and Internet access.

Adult DSM-5 Cross-Cutting Symptom Measure

For the initial screening, a semi-structured diagnostic interview based on DSM-5 diagnostic criteria will be applied. The interview assesses mental health domains that are important across psychiatric diagnoses. The adult version of the measure consists of 23 questions that evaluate 13 psychiatric domains, including depression, suicidal ideation, mania, anxiety, anger, somatic symptoms, psychosis, sleep problems, memory, repetitive thoughts and behaviors, dissociation, personality functioning, and substance use. The original English version of the measure had good to excellent test-retest reliability in DSM-5 field trials conducted in adult clinical samples across the United States and Canada.^{51,52} We included questions about any previous diagnosis and former and current treatments.

Patient Health Questionnaire^{49,50}

Consisting of nine questions, the PHQ-9 assesses the presence of each of the symptoms for a major depressive episode described in the DSM-5.¹ The nine symptoms include depressed mood, anhedonia (loss of interest in or inability to experience pleasure from normally pleasant

stimuli), sleeping problems, tiredness or lack of energy, change in appetite or weight, feelings of guilt or uselessness, concentration problems, feelings of lethargy or restlessness, and suicidal thoughts. Brazilian psychiatrists translated the PHQ-9 into Portuguese and a back translation was performed by one of the authors of the original instrument.⁵³ The frequency of each symptom in the previous 2 weeks is assessed on a Likert scale from 0 to 3 corresponding to “never,” “several days,” “more than half of the days,” and “almost every day,” respectively. The questionnaire also includes a 10th question to assess the interference of these symptoms in daily activities, such as work and study. The cutoff score will be 10 points, as is widely used among Brazilian researchers.^{49,54-56}

Clinical Outcome in Routine Evaluation – Outcome Measurement^{57,58}

The CORE-OM is a widely used self-report scale for evaluating the effectiveness of mental health treatments. It includes 34 items assessing the following four domains: subjective well-being (four items), problems and symptoms (12 items), life functioning (12 items), and risk to self and others (six items). These items are answered on a five-point scale, ranging from “never” to “always.” A UK study with a clinical (n=890) and a non-clinical sample (n=1,106) found an overall internal consistency index (Cronbach’s alpha) of 0.94 for both samples. Test-retest correlations with part of the sample (n=55) ranged from 0.87 to 0.91 for well-being, problems and symptoms, and life functioning domains, although the risk to self and others domain scored 0.64, showing low temporal stability. Convergent validity was verified by correlating total scores and domain scores with overall scores from other psychological symptom scales, resulting in correlations ranging from 0.55 to 0.88.⁵⁷

Client Satisfaction Questionnaire (CSQ-8)⁵⁹

The CSQ-8 is a self-report questionnaire designed to assess the general level of satisfaction with provided services. Its eight items are scored on a scale from 1 to 4. Total scores vary from 8 to 32 points, with higher scores indicating greater satisfaction with the service. The internal consistency of the original English version scale ranges from 0.83 to 0.93.⁶⁰

Usage duration

We will measure the number of sessions lasting at least 10 minutes spent in the program, as well as the number of days with such usage. The system generates these indicators based on each client’s use as an objective measure of treatment adherence.

Procedures

The informed consent and self-report measures will be obtained online by participants at the initial screening questionnaire, prior to inclusion and randomization.

Participants will confirm that they read and consented to the terms of the study. They may also discontinue participation, as well as contact the staff for further information. After completing the baseline assessment and being included in the study, participants randomized to the intervention group will promptly receive a voucher to access the program for 90 days. The time point of primary interest will be 8 weeks after the baseline assessment. Participants randomized to the delayed access group will receive a voucher 8 weeks after randomization and will be asked to fill out the primary (PHQ-9) and secondary (CORE-OM) outcome measures once more. After completing the program, all participants will be invited to fill out the outcome measures and answer a final questionnaire that includes items on whether the program was used alone or together with psychotherapy or psychopharmacology. The participants will also be asked about significant life events that occurred during the course of the intervention.

The research team includes senior undergraduate psychology students, who will be in charge of the screening interviews. These students will be trained and supervised by three clinical psychologists on the research team. The interviews will be assigned by convenience and according to availability. The research team will also be responsible for: 1) recruitment advertising; 2) analyzing the screening questionnaires and excluding participants who do not follow the criteria; 3) randomizing participants and following up questionnaire responses; 4) e-mail communication with participants throughout the study; 5) checking and providing feedback about program usage; and 6) sending out post-treatment assessment forms; 7) in accordance with procedures used in a previous study on Deprexis (Beevers et al.⁴⁸), the research team will send messages to participants every 2 weeks to encourage them to use Deprexis, to assess potential problems or difficulties, and to monitor potentially adverse events they might experience during the intervention.

Treatment

Deprexis is an internet-based intervention program to help people learn about and cope with depressive symptoms.⁴² It is based on the principles of cognitive-behavioral therapy and consists of 10 original content modules plus one short review module, including psychoeducation, behavioral activation, cognitive restructuring, mindfulness and acceptance, social and communication skills, relaxation exercises, suggestions for physical activity and healthy dieting, problem solving methods, expressive writing, and forgiveness, as well as working with dreams from a cognitive-behavioral perspective.^{42,61} Content is presented in simulated dialogue format, in which users continuously choose one of several predetermined response options, and subsequent content is automatically adapted to user needs and characteristics.

Deprexis sends daily messages with therapeutic content to help in everyday life (e.g., becoming aware of unhelpful automatic thoughts, organizing the day, breaking down significant problems into small steps, and interacting with people). Deprexis is designed for both

mobile and desktop devices. The program can be used without any therapist contact, although in our clinical trial trained clinical psychologists and psychology students will keep minimal regular contact with users by e-mail (i.e., minimally supported or guided use). Deprexis has been carefully translated and adapted to Brazilian Portuguese and culture by expert Portuguese language professionals. In addition, Brazilian psychology students and psychologists used the program and suggested language and cultural adjustments

Sample size and statistical analyses

The sample size of this study is based on the expected difference in the primary outcome variable (PHQ-9 score, which measures the severity of depressive symptoms) between the group receiving the intervention and the control group after 3 months. Based on a statistical strength estimate of at least 0.80 in a two-tailed test and an alpha of 0.05, a sample of 128 participants (64 per group) will be sufficient to demonstrate a likely effect size of $d = 0.50$ (moderate effect). Following the intention-to-treat principle, data from all 128 randomized participants will be analyzed. We anticipate a treatment withdrawal rate of around 20% at the first measurement point (after 3 months). This rate has been achieved in several prior clinical trials with Deprexis.⁴⁸ Based on previous research,^{29,35,42,47,48} predicting a moderate effect size seems realistic. This calculation is based on the assumption that a 50:50 randomization procedure will be used.

Both the intention-to-treat and the per protocol analyses will be conducted using appropriate statistical methods, such as linear mixed models, which are widely used in this field of research and have been recommended due to their ability to properly treat lost data. Additional analyses will be performed to examine the potential influence of intervening variables on the primary outcome measure (e.g., initial differences in symptom severity or intensity of Deprexis use). The PHQ-9 will be the primary clinical outcome measure, and the CORE-OM will be the secondary outcome measure. The results will be reported according to CONSORT guidelines.^{62,63}

The clinical significance of the changes observed at the end of the intervention in both experimental conditions will be evaluated using the Jacobson & Truax⁶⁴ method. This analysis method takes into account the scores of the general and clinical populations to obtain a clinical threshold for a given psychological measure. Chi-square tests will be used to compare the rates of clinical improvement and recovery, as well as any clinically significant deterioration ratios between groups.

Ethics statement

This research protocol has been approved by the research ethics committee of the Universidade Católica de Petrópolis (CAAE # 68709517.1.0000.5281) and has been registered in the Brazilian Clinical Trials Registry (Registro Brasileiro de Ensaios Clínicos [ReBEC]; RBR-6kk3bx, UTN U1111-1212-8998; <http://www.ensaiosclnicos.gov.br/rg/RBR-6kk3bx/>). Similar experimental protocols using

Deprexis have already been approved by the research ethics committees of several European and U.S. universities, as well as the Data Security Department of Hamburg, Germany. The ethics code for practicing psychology in Brazil⁶⁵ and previously mentioned Federal Council of Psychology guidelines for internet interventions (Resolution 011/2018)³⁶ are also being taken into account.

All selected clients who decide to participate in the study will be required to complete an informed consent form approved by the local research ethics committee. The participants' e-mail addresses will be collected for logging in to Deprexis, retrieving lost passwords, and receiving daily messages. No participant names, addresses, or internet protocol addresses will be stored after the trial is completed. Stored data security will be ensured through the secure sockets layer protocol, which provides internet communication security for services such as e-mail, page navigation, and other types of data transfer. The intervention data will be stored on a secure server in Germany and will be protected by a modern, reliable firewall, and a current transport layer security configuration to encrypt all data in transit. Users will provide their e-mail addresses and a personal password, which is encrypted by the system. Thus, passwords, even if stolen, cannot be used. All employees of GAIA Group's information technology department are trained in data privacy and are governed by German law.

Discussion

This study was designed in an effort to meet a perceived need for research on different depression intervention formats, especially in low- to middle-income countries, such as Brazil. The effectiveness of internet-based interventions suggests that this could be a viable alternative in depression treatment due to its flexibility, lower costs, and adaptability to the patient's daily routine and location. As far as we know, no web-based interventions for depression have been developed in Brazil. We are aware of the considerable amount of human resources necessary to develop such an intervention. Deprexis has been developed for many years now and has undergone numerous improvements. It has been carefully translated and adapted to the Brazilian Portuguese language and culture. It is expected that this study will replicate and extend the evidence found in previous studies on Deprexis.

We are currently recruiting the first participants. We have chosen to recruit participants over the Internet, assuming that this is the primary medium through which they would hear about the program under similar conditions. Although online recruitment introduces a selection bias toward individuals suffering from depressive symptoms who actively seek help online, such individuals can also be considered the intended target group for Deprexis. Deprexis can also be recommended to patients by their psychiatrists or psychologists, but they will not be the main focus of our recruitment strategy, which could be regarded as a possible study limitation.

Another possible study limitation concerns the exclusion of candidates with severe comorbidities. Although we will accept candidates with comorbid anxiety and other mild problems, for safety reasons, we will not include patients with severe symptoms that may require special attention, such as panic disorder, schizophrenia, alcohol abuse, etc. Excluding this population could result in a relatively heterogeneous group of patients, which is probably not representative of the population of Deprexis users.

Another conceivable limitation is participants who undergo psychotherapy or psychopharmacology during the online intervention process. In a group of 128 participants, it is expected that some will voluntarily seek different sources of treatment during the intervention, which can be considered a study limitation. On the other hand, setbacks such as significant losses and illness can happen randomly to all participants, both those who seek external help and those who do not, which can thus be considered a strength of the study design. Allowing participants access to TAU (psychiatry and clinical psychology services) could improve the external validity of our results. We can assume that an individual who is suffering from depression will seek help from different sources, either professional treatment or online information. Both scenarios will be considered and assessed in the final questionnaire.

Having a randomized control group with delayed access to Deprexis is among the study's strengths. We are aware that the depressive symptoms of participants randomized to delayed intervention may decrease naturally with the passage of time, other professional or lay intervention, or significant life changes. Nevertheless, we assume that the potential symptom reduction in this group will make a reliable comparison to the group that gains immediate access to Deprexis.

In Brazil, research on easily accessible Internet-based intervention programs is at an early stage. Rigorous clinical trials on the effectiveness of such programs in Brazil are needed. To the best of our knowledge, this will be the first controlled trial to evaluate the effectiveness of an Internet-based program for depression in Brazil.

Acknowledgements

The authors would like to thank Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ), and Fundação Cultural Dom Manoel Pedro da Cunha Cintra (FDC) for supporting the students who assisted the research, as well as GAIA Group for letting us use Deprexis, and the Swiss National Science Foundation for supporting RTL and TB with a Scientific Exchange Grant (IZSEZO_189796).

Disclosure

BM is employed as a research director at the GAIA Group, the company that developed, owns and operates the Internet intervention investigated in this trial (Deprexis). He is not involved in data collection or analysis. The other authors report no conflicts of interest.

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