Can adolescents with depression be effectively treated with guided and unguided Cognitive Behavior Therapy on the Internet?

Background

The World Health Organization identifies depression as a leading cause of disability worldwide and a global health priority (1). A risk period for developing depression is adolescence, when there is a sharp increase in prevalence, especially for girls (2). By the end of adolescence, around 20 % have experienced an episode of depression (3). Fortunately, early detection and treatment markedly decreases the likelihood of future depressive symptoms (4).

Depression in adolescents can be effectively treated with Cognitive Behaviour Therapy (CBT) and is recommended as first choice in national treatment guidelines (5). However, a majority of adolescents do not have access to CBT. Internet-delivered CBT (ICBT), an interactive online treatment that mirrors the content, components and strategies from standard face-to-face CBT, has been suggested as a way to increase availability to effective psychological treatments. ICBT has been found to be effective and probably cost-effective for several adult psychiatric disorders, including depression (6). Yet, studies on ICBT for adolescents with depression are scarce, both qualitative and quantitative ones (7).

The limited research available leaves many questions unanswered. First, there is a need for well-designed, methodologically sound and properly powered trials in the field. Second, to what extent therapist support is important in ICBT trials of adolescent depression is a critical question. If ICBT could be entirely self-guided, e.g. without therapist-support, without sacrificing efficacy and safety, it would be much easier to disseminate. Third, the cost-effectiveness of ICBT for adolescent depression has not been evaluated.

Study goals and objectives

The overall goal of our research project is to increase the availability to evidence-based psychological treatments of adolescent depression.

Objectives: 1) To develop two ICBT interventions, guided and unguided, for adolescents with mild to moderate MDD and their primary caregivers. 2) To conduct a randomized feasibility pilot study, comparing guided ICBT, unguided ICBT and treatment as usual (TAU), to test whether the interventions are feasible and acceptable to the adolescents and their caregivers, and provide preliminary efficacy data. 3) To conduct a full-scale RCT of guided ICBT vs unguided ICBT vs TAU to

establish the efficacy and cost-effectiveness of ICBT in mild to moderate MDD. 4) To describe the long-term effects of the interventions.

Primary hypothesis is that guided ICBT will be superior to unguided ICBT and TAU regarding symptom reduction. Research questions: Is guided ICBT for adolescents with mild to moderate depression more efficacious than unguided ICBT and TAU regarding symptom reduction? Are the therapeutic gains of guided ICBT maintained long term (1 year after the intervention)? Is guided ICBT more cost-effective compared to unguided ICBT and TAU?

Research plan

1. Development of ICBT interventions. This project is a continuation of our previous work to develop and test a range of ICBT-programs for pediatric anxiety disorders (e.g. (8) and OCD , (9) presentation of the ICBT platform: https://goo.gl/qnVJAt). The MDD treatment protocol, "BIP Depression", will be designed in line with current expert guidelines by psychologists with thorough clinical expertise in CBT and MDD. Adolescents, parents and experienced clinicians will be involved in the iterative development of the treatment program through the use of focus groups.

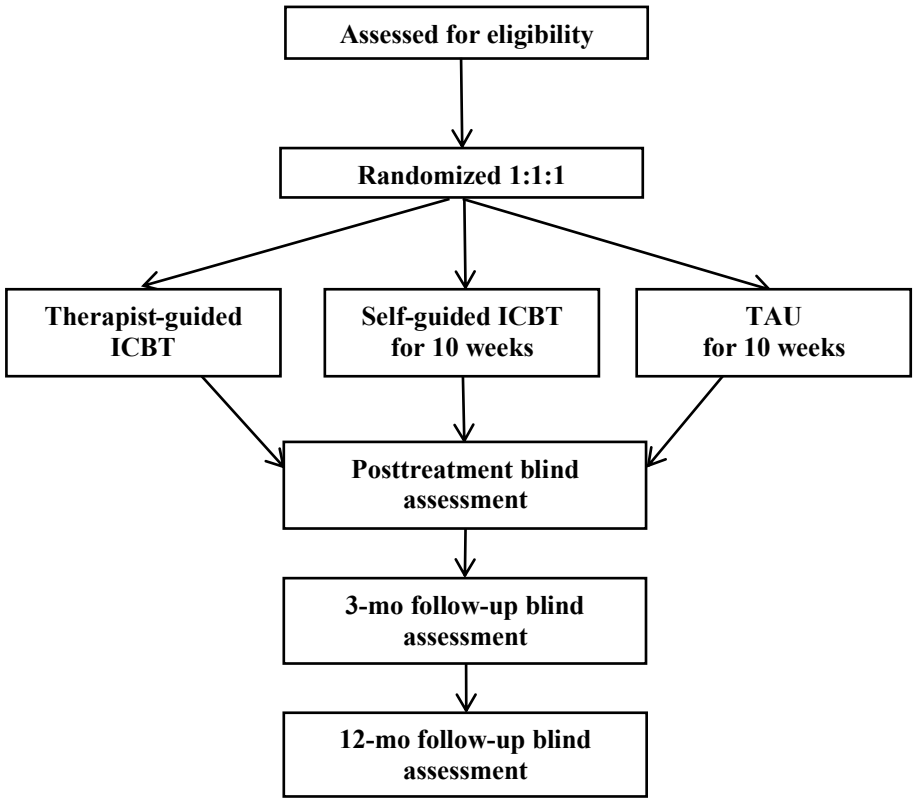
2. Feasibility and acceptability randomized pilot study. This step is designed to establish the feasibility and acceptability of the guided and unguided ICBT interventions as well as to establish and optimize study and clinical routines. The trial will include between 30 and 45 adolescents and their caregivers from all over Sweden who will be randomized to guided ICBT, unguided ICBT or TAU. This study will inform us regarding necessary iterations of the ICBT interventions, patient safety aspects and help us with practical preparations for the full-scale RCT. We expect that the data collection of this step will be completed within one year.

3. Evaluation of efficacy and cost-effectiveness of ICBT in a full-scale RCT. A full-scale RCT will be conducted to evaluate the relative efficacy of guided and unguided ICBT vs TAU for mild to moderate MDD. The study will include N=300 adolescents and their caregivers, recruited through self-referral or referral from general CAMHS clinics from all over Sweden. Participants will be randomized to one of three arms: a) guided ICBT, b) unguided ICBT, or c) TAU. Patients in the TAU arm will be referred to the their local CAMHS outpatient service. Cost data will be collected alongside with the RCT, analyzed from a healthcare and societal perspective and expressed as the incremental cost-effectiveness ratio (ICER). The ICER is a measure of the relationship between the additional cost of the more effective treatment and the additional health benefit it provides, compared to the less effective treatment.

4. Long term effects of the interventions. Participants from all three arms of the RCT will be assessed twelve months after treatment completion using both clinician and self-report measures.

Study design. The objectives will be investigated in a single-blind parallel-group randomized controlled trial for adolescents with mild to moderate depression. Data will be analyzed according to intention-to-treat principles. The study design for the RCT is shown in the Figure below. The study is approved by the Swedish Ethical Review Authority, Sweden, and preregistered at ClinicalTrials.gov. The participants and their caregivers will receive verbal and written information about the study, including an informed consent form and an information brochure specifically designed for the adolescents.

Figure 1. Flow chart of study design for the RCT



Study setting. The study will be conducted at the Child and Adolescent Psychiatry Research Center, within Region Stockholm in collaboration with Karolinska Institutet. The members of the research group have extensive experience from clinical work with depression, anxiety and other common mental health disorders in children and adolescents as well as research and clinical implementation of ICBT. Previous research of ICBT for anxiety in small children (8), obsessive compulsive disorder in adolescents (9), and functional abdominal pain (10) have showed high acceptability, safety and promising results.

Participants. For both the pilot RCT and the full-scale RCT participants will be adolescents aged 13 – 17 years with a diagnosis of major depressive disorder, recruited through referral and online self-referral. Exclusion criteria include acute problems, such as severe major depressive disorder, suicidal risk or another severe psychiatric disorder; ongoing maltreatment or abuse within the family; receiving CBT within the past 12 months and recent changes in psychotropic medication. Participants will complete self- and parent-administered measures of depressive symptom severity, function, and quality of life at baseline, mid-treatment, post-treatment, and at follow-up assessments at 3- and 12-months post treatment. Depressive symptoms and suicidality will be monitored weekly. The primary clinical outcome variable is clinician-rated depressive symptoms, and the primary endpoint is the follow-up 3-months post treatment. Blind evaluations will be conducted by independent assessors after treatment and at 3-month follow-up at the clinic, both times complemented with online questionnaires. To ensure blinding, participants are instructed not to disclose which treatment they have received. Also, after the evaluation the blind assessors guess the participant's group allocation and record whether the family has unintentionally disclosed their group allocation. If unblinding occurs, another blind assessor will rerate the participant's score on the primary clinical outcome measure based on a recording from the interview.

Interventions. Two of the treatment arms consist of ICBT, therapist and self-guided, and involve both the adolescent and the caregiver. Each consists of eight chapters, delivered over a maximum of ten weeks. During the therapist-guided ICBT, participants have regular contact with a trained therapist. The therapist provides feedback, answer questions, and reminds to complete the next module if required. The treatment manual, developed by our research team, consists of evidence-based interventions adapted to an online format inspired by previously published treatment manuals on behavioral activation for adolescents (11). The main goal of behavioral activation is to increase engagement in value-based activities and decrease avoidant behaviors that serve to maintain depression.

The self-guided ICBT is identical to therapist-guided ICBT, however without the therapist support. To ensure patient-safety, there will be clear instructions to the patients and primary caregivers on how to get in contact with the Child and adolescent mental health services' emergency unit in case of acute problems, and there will be clinical routines to detect and manage deterioration or suicidal tendencies.

Participants randomized to TAU, will be referred to the local Child and adolescent mental health services or primary care unit for children and youths and will be free to receive any treatment, either psychosocial, medical or the combination of both.

Significance

Our research on ICBT for adolescents with depression could, if effective, dramatically increase the availability of evidence-based treatments and decrease the risk of future mental and physical illness and disability for a substantial number of patients. The cost-effectiveness evaluation will answer the question as to whether therapist- and/or self-guided ICBT could generate additional health effects at a justifiable cost, compared to what patients currently are offered. The results of our study has the potential to aid decision-makers in allocation of scarce resources and contribute to the development of new policies and guidelines.

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