Peer Review File

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Reviewer A

The study addressed the feasibility of an intervention for adolescents with type 1 diabetes and depressive symptoms. Due to the heavy burden of the target group, it is very important to provide a low-threshold offer to those affected. The study could make an important contribution. However, the evaluated n is very small with 7 and no conclusions can be drawn. The qualitative feedback makes an important contribution to the further optimization of the study. If the possibility existed, more participants should be recruited from my point of view for this publication, in order to achieve at least the calculated target n. It would be very important to conduct a RCT with a control group in order to be able to make confirmatory statements in a next step. In general, the manuscript should go into more detail on several aspects. I recommend conducting another extensive literature review to better justify your own research questions and compare your findings with existing publications on iCBT in this target population.

Reply: We thank the Reviewer for their careful review of the previous manuscript and their many constructive comments. We have extensively revised the manuscript based on Reviewer feedback. We clarified in the Discussion section that an RCT would be a necessary future step.

Changes in text:

"*To better determine benefit of such an intervention, a randomized control trial with a control group would be important*."

Reply: Additional articles utilizing CBT and online interventions were added to the Introduction section, however, the literature is lacking in articles using internet-based CBT in this population.

Changes in text:

"An integrative review of CBT in adolescents with T1DM found improvements in anxiety, coping, quality of life, and depressive symptoms in several studies, [25]. … A recent systematic review assessing the effectiveness of digital interventions in youth with T1DM showed modest but inconsistent improvements in patients' self-efficacy, adherence to diabetes self-management tasks and glycemic control [23]. … [9]. One study in adults with T1DM using a diabetes-focused online CBT showed improvements in glycemic control [24]. (Lines 72-80)

"These data suggest that engagement in a computer-based CBT program can lead to improved depressive symptoms in adolescents with T1DM and warrant future randomized controlled trials to accurately determine benefit." (Lines 239-241)

Major comments:

Introduction

I think it would be useful to provide more information about the effectiveness of

CBT in depression and diabetes and also to describe in more detail why it is useful to make an internet-based offer (e.g. location and time independence). I also lack information on the current state of studies on Internet-based interventions for adolescents with diabetes or chronic diseases in general. There are meta-analytic findings on this that should be considered.

Reply: We have included this additional information regarding effectiveness of CBT and usefulness of internet-based options in the Introduction.

Changes in text:

"*An integrative review of CBT in adolescents with T1DM found improvements in anxiety, coping, quality of life, and depressive symptoms in several studies, [25]. However, in-person CBT may be burdensome to patients and may not be cost effective [8]. A recent systematic review assessing the effectiveness of digital interventions in youth with T1DM showed modest but inconsistent improvements in patients' self-efficacy, adherence to diabetes self-management tasks and glycemic control [23]. Computerized interventions can be an efficacious and cost-effective first line intervention and offers flexibility with time and location [9]. One study in adults with T1DM using a diabetes-focused online CBT showed improvements in glycemic control [24]"* (Lines 72-80)

Materials and Methods:

Please provide more information on the intervention content. For example, what were the exact contents of the modules? What was the duration of a module? How were the information presented? With texts or videos? Did the participants receive feedback? Were they reminded to complete the modules.

Reply: We have included details on the intervention content in the Materials and Methods section.

Changes in text:

"Participants were given access to the CATCH-IT program, which includes a brief practitioner-provided motivation enhancement component (in-person at time of enrollment and through phone calls), fourteen online self-directed modules, and information for parents to support the adolescent (five printed modules that described the CATCH-IT modules). The content of the modules targets multiple etiological elements by teaching skills from empirically supported, face-to-face interventions including Behavioral Activation, Cognitive Behavioral Therapy, and Interpersonal Psychotherapy. CATCH-IT targets mechanisms that are associated with increased risk for depression in adolescents. The modules are grouped into six sections: introduction, how do you act, how do you think, how do you socialize, how resilient are you, and wrap up. There are one to four modules in each section, and teens spend approximately 15 to 20 minutes per module [10, 26]. Information is presented as slides and videos showing adolescent stories [10, 26]. Additionally in this pilot study, participants were given a journal with activities based on best practices of depression prevention. Participants had clinic visits at screening (baseline) and three months later (exit), and safety phone calls or text messages from the research team to monitor for adverse events (weeks 1 – 6) as well as reminders

to complete modules" (Lines 125-139)

Results:
L131: Why were the three participants who did not complete the whole intervention excluded? What is the added value of doing a per-protocol analysis? Wouldn't it make sense to evaluate based on intention-to-treat sample?
Reply: While we agree that an intention to treat analysis would be appropriate, it was not possible because follow-up information was not obtained from the three participants who discontinued the intervention, so we had to do a per-protocol analysis. Future studies will be evaluated based on an intention-to-treat sample.
Changes in text:
"... and three discontinued the intervention (one participant was enrolled in a therapeutic program, and two participants withdrew due to time constraints)" (lines 167-168)

Discussion:
I would focus the discussion on the qualitative surveys. Please discuss them in the light of other findings on qualitative studies in adolescents with chronic conditions. It is not possible to make any statements regarding the quantitative evaluations with such a small number of participants. I would strongly recommend to not make any conclusions about the effectiveness.
Reply: We agree with the Reviewers recommendations and have revised the Discussion section to incorporate the suggestions.
Changes in text:
" The results from this study were difficult to interpret given limitation of small sample size." (Lines 208-209)
"Participation in other diabetes-focused web-delivered systems yielded improvements in self-efficacy, quality of life, improved self-monitoring of blood glucoses, and other behavioral outcomes highlighting the potential beneficial utility of online modules in adolescents with T1DM [22,27]. Similar themes were seen in the qualitative feedback from participants in this study, such as participants learning coping skills to help with stress and anxiety, recognizing proactive diabetes management can prevent negative outcomes, and countering negative thoughts. There are promising results regarding feasibility and high satisfaction with an internet-based CBT model in adolescents with chronic health conditions (Cystic Fibrosis, Juvenile Idiopathic arthritis, and T1DM) and comorbid depression, though studies are ongoing to assess effectiveness [28]." (Lines 216-224)

Minor comments:
Abstract:
L26: Please provide range of age of included adolescents and cut-off values for mild and moderate depressive symptoms in the PHQ-A
Reply: Manuscript has been revised to include requested information
Changes in text: *"Adolescents (13 to 17 years old) with T1DM and mild (score 5-9)*

or moderate (score 10-14) depressive symptoms…" (Line 32)

L35: Please provide concrete results. What did the participants tell in the qualitative feedback?
Reply: Manuscript has been revised to include requested information
Changes in text: "*Participants provided robust qualitative feedback on the modules and areas for improvement in subsequent iterations, such as inclusion of diabetes-related content*." (Line 41)

Introduction:
L45/48: Does "diabetes" refer to Type 1 diabetes only?
Reply: The studies cited included youth with Type 1 or Type 2 diabetes. The manuscript has been adjusted to reflect this recommendation.
Changes in text: Lines 63, 64, 66

L50: Please define T1DM at the first time?
Reply: The manuscript has been adjusted to reflect this recommendation.
Changes in text: Line 69

L54: Is CBT the abbreviation for cognitive behavioral therapy or for group-based cognitive behavioral therapy?
Reply: Yes, CBT is abbreviation for cognitive behavioral therapy, revised.
Changes in text: Line 71 removed the word "group", as CBT is abbreviation for cognitive behavioral therapy.

L63: Who were the target groups in these studies?
Reply: The target group is adolescents (ages 14-21) at risk for depression in primary care setting. The manuscript has been revised to reflect this recommendation.
Changes in text: Lines 84-85 describe the target group.

L62-64: I would recommend to put the intervention description to the method section.
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Lines 131-134 moved to Methods section.

L67: In your title you talk about depressive symptoms. I think this is more adequate than "risk for developing depression"
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Lines 87-88

Materials and Methods:
L72: Please provide the applied cut-off values for mild and moderate depressive symptoms

Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Line 101, “*mild depression score 5-9, moderate score 10-14.*”

L73: “During their clinic visit”: was it an in-patient stay?
Reply: This was an outpatient clinic visit.
Changes in text: none

L75: What does “CES-D is not standard of care” mean?
Reply: CES-D is not something that patients in our diabetes clinic complete as part of clinic flow, whereas all patients with diabetes complete PHQ-A. Therefore, in order to have patients fill out CES-D, patients had to consent to complete. Added clarification “in the clinic workflow”
Changes in text: Lines 103 to 110 describe typical clinical practice and added that CES-D is not part of standard clinic workflow.

L78: “PHQ-A<20”: This would mean that adolescents were included who did not have evidence of depressive symptoms in the PHQ-A. Is this correct? If so, I would find a rationale helpful.
Reply: PHQ-A < 20 as that is cut-off for severe depression, but participants still needed to meet mild or moderate depression cut off values, so PHQ-A greater than or equal to 5. Clarified the criteria."
Changes in text: Line 113 clarified PHQ-A criteria as PHQ-A ≥ 5 but <20

L93: Since there was no comparison group, I would not speak of "effectiveness". I recommend specificity: assessing the within-group effect.
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Line 126 changed to read “within group effect”

L80: How was dealt with young people with severe depression scores? Did they receive alternative offers? Why was it a criterion for exclusion?
Reply: Severe depression scores was exclusion criteria because it was a similar exclusion in other studies of CATCH-IT for adolescents in primary care setting, and an internet-based program would not be an advised intervention as mentioned (line 115 in track changes version of manuscript).
If patient has score consistent with severe depression, typical protocol is to consult the clinic social worker for further mental health support and guidance. Added clarification to current clinic practice to methods: “Setting and Participants” section.
Changes in text: lines 104-107 describe practice for severe depression scores.

L101: What was done in case of an adverse event? Who made the safety calls?
Reply: A member of our research team made the safety calls. We did not have any adverse events, but we would have followed our IRB protocol if we had encountered an adverse event.

Changes in text: line 155 in track changes manuscript

L114: What do you mean by "task"? Did the participants get money for each completed module? If so, please explain why.
Reply: "Task" means baseline questionnaires, weekly safety phone calls, 12-week follow up questionnaires), added to text. Money was provided in the form of a ClinCard which is a reloadable debit card used as a method to reimburse research participants.
Changes in text: Lines 168 to 171 discuss compensation and details of tasks.

Discussion:
L164: You should not speak about assessing the "effectiveness" without a control condition.
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Line 225.

L166: Based on your small n you should not make this conclusion.
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Lines 227-229.

L169: Due to the small n, you should not compare your results.
Reply: The manuscript has been revised to reflect this recommendation
Changes in text: Lines 229-230

Reviewer B

1. Informed consent should be obtained from the patients' parents or legal guardians, not the minor patients themselves.

Reply: We have updated the informed consent to read as suggested.

2. In the sentences below, you refer to "studies" but have only one citation. Please check and revise.

adolescents with chronic health conditions (Cystic Fibrosis, Juvenile Idiopathic arthritis, and T1DM) and comorbid depression, though studies are ongoing to assess effectiveness [28].

post ΔCES-D of 4.7, (consistent with previous studies about the efficacy of CBT in reducing depressive symptoms [18]) using paired t-tests assuming a standard deviation of 5.7 and $\alpha=0.05$.

Reply: The text has been updated.

3. Please add the measure unit in Table 1-3.
Reply: The HbA1c unit (%) has been added. Full names of the abbreviations have been clarified in the tables. The questionnaires PHQ-A, CES-D, and PAID-T provide a raw score, there are no units for this.

4. There are 10 items related to diabetes in Table 4. Please check and revise.

197 of the CATCH-IT program and some universal themes. Thirteen common themes were
198 identified within the field notes, nine related to having diabetes and four unrelated to
199 diabetes (Table 4). There were mixed views on inclusion of diabetes-related goals in

Reply: Thank you for highlighting this revision. In fact, there are 12 common themes, 8 are diabetes related, and 4 unrelated to diabetes. The eight diabetes related themes are: negative thoughts, video content, social network (support and opposition), time givers and breakers, goal setting (support and opposition), diabetes and depression, stressful events, new situations.

5. Table headers are missing in Table 2-4.

Reply: Tables 1, 2 and 3 have updated. The table header is now titled "Measured Value."

The n or sample size clarifies that this is number of participants.

The table cells for "Goal Setting" and "Social Network" have been merged, to show that they are a shared diabetes related theme, with statements of support and opposition from participants

6. Please indicate the full name of the abbreviations that are marked yellow in the attached manuscript. And please check whether the full name of T1DM in the manuscript is correct.

Reply: The full name of abbreviations is adjusted. Both T1DM and T1D are accepted abbreviations for Type 1 Diabetes Mellitus. For consistency, abbreviation adjusted to T1D throughout manuscript.

7. Please add the age unit here.

106 functional status and self-esteem in adolescents (ages 14-21) without diabetes who
107 were at risk for depression in primary care setting (13–17).

Revised as suggested to read as "ages 14-21 years". The (13-17) is referring to the citations/references, not age.