The Effectiveness of Internet-Based Cognitive Behavioral Therapy for Depressive Symptoms During Pregnancy Using Real-World Data: A Retrospective Cohort Study

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Abstract

Background: While numerous internet-based cognitive behavioral therapy (iCBT) programs have been developed and tested through randomized controlled trials (RCTs) for various mental health conditions and specific populations, research on their effectiveness and real-world application remains limited.

Objective: This study aimed to examine the effectiveness of a previously developed iCBT program implemented in an existing app for improving depressive symptoms among pregnant women in a real-world setting.

Methods: The previously developed iCBT program for preventing perinatal depression was already implemented in an existing app that aims to provide information to pregnant women about pregnancy and babies. The log data stored in the app identified iCBT program users and non-users, allowing us to conduct this retrospective cohort study. The data from September 2022 to September 2024 was extracted from the app after anonymous processing. The primary outcome was the score on the self-reported Edinburgh Postnatal Depression Scale (EPDS), which participants input by themselves on the app. The exposure group was defined as completers of all 6 modules of the iCBT program. The non-exposure group was defined as non-users of the program who matched the baseline characteristics of the exposure group. The change in EPDS score before and after using the program was compared using effect size, and repeated two-way analysis of variance (repeated two-way ANOVA) was conducted to test the difference between the exposure and non-exposure groups.

Results: 119 women who completed the iCBT program and pair-matched 448 controls were selected. The average EPDS scores at the baseline were 7.24 in the exposure group and 7.25 in the non-exposure group. After using the iCBT program, the EPDS scores changed by -0.69 and +0.99 in the exposure and non-exposure groups, respectively (Cohen's d = 0.31, 95%CI 0.11 - 0.51). The repeated two-way ANOVA showed statistical significance in interaction terms between the groups and the measurement time points (P=.04).

Conclusions: The previously developed iCBT program showed a significant modest effect on decreased depressive symptoms among pregnant women in the real-world setting. Future research should attempt to minimize dropouts and increase participation in the program.

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Original Paper

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Conclusion: The previously developed iCBT program showed a significant modest effect on decreased depressive symptoms among pregnant women in the real-world setting. Future research should attempt to minimize dropouts and increase participation in the program.

Keywords

antenatal depressive symptom; prevention; internet-based cognitive behavioral therapy; real word data; digital mental health; mobile health

Introduction

Depression is common among pregnant women, with a global prevalence of antenatal depression estimated at 20.7%. In Japan, prevalence rates are 14.0% during mid-pregnancy and 16.3% in late-pregnancy

[1,2]. The brain experiences drastic structural changes during pregnancy, resulting in increasing mental health vulnerability even among healthy women [3]. In Japan, suicide is the most frequent cause of perinatal death, and depression is the major risk factor for suicide [4]. Depressive symptoms during pregnancy affect not only pregnant women themselves but also fetuses and babies. These can lead to adverse outcomes for fetuses and babies, such as impaired physical growth, preterm birth, low birth weight, decreased reactivity, changes in temperament, and behavioral disorders [5–7]. Therefore, it is essential to work on preventing depression among pregnant women.

Cognitive behavioral therapy (CBT) is one of the ways to prevent depression during pregnancy [8]. Internet-based CBT (iCBT) has recently increased accessibility and convenience. An iCBT program for preventing depression among pregnant women on the smartphone app has already been developed and investigated for its effectiveness in a randomized controlled trial (RCT) in Japan [9,10]. This RCT showed that the program was effective in preventing perinatal depression among people with mild psychological distress, though not among all participants. The program is now available as a free service on a popular Japanese app for anyone to use [11].

RCTs are conducted in a strictly controlled setting, which may be inconsistent with the real-world setting. Significant differences were reported between the study population from RCTs and the study population from real-world data, even using the same sampling criteria [12]. The engagement of the mobile mental health app was also lower in the real-world setting than in the clinical trial setting [13,14]. Therefore, it is necessary to confirm whether the developed iCBT program is effective not only in study settings but also in real-world settings to ensure the external validity of the program [15–17]. Even though several studies have evaluated the actual use of digital interventions and identified their effectiveness for the treatment of depression and anxiety [18–22], we found no such efforts for iCBT programs for prevention or among pregnant women.

The objective of this observational retrospective cohort study was to investigate the effectiveness of iCBT usage among pregnant women in improving depressive symptoms in a real-world setting.

Method

Study Design, Data setting

This observational study was conducted based on a previous RCT study [9]. This previous RCT showed that the newly developed iCBT program was effective in reducing the onset of perinatal depression only among women who had mild psychological distress [9]. The users' iCBT program evaluation was reported to be high in acceptability, appropriateness, fidelity, and satisfaction [23]. After the study, this developed iCBT program was implemented in the real world. The iCBT program was released in the existing app for perinatal women called "Luna Luna Baby" by MTI Ltd. as a free standard feature in September 2022 [11]. Luna Luna Baby is a smartphone app that aims to provide pregnant women with information about pregnancy and babies. The self-assessment service based on the Edinburgh Postnatal Depression Scale (EPDS) questionnaire was also implemented in the app at the same time, allowing pregnant women who use

this app to check their current mental status whenever they want. The app routinely logged the results of users' self-checked EPDS scores. This data included not only the result of the EPDS score and its measurement date but also basic information about the user at the time of EPDS measurement, such as age, weeks of pregnancy, and the number of times that users had read the iCBT modules. This study used the sample from September 2022 to September 2024 extracted from this EPDS service log data after anonymous processing. We also used information on the number of visitors to the app pages and app specifications during this period. These were all provided by MTI Ltd., the app developer.

Participants and Measurements

Participants selection

Pregnant women who used the Luna Luna Baby app were possible participants. Among them, those who were in their antenatal period were included. Those who were in their postnatal period or those with missing age data were excluded. The exposure group was identified as those who completed the iCBT program. The non-exposure group was identified as those who had never read the iCBT modules. To compare changes in depressive symptoms, participants were limited to those who had EPDS measurements at two time points, before and after exposure to the iCBT program. For the non-exposure group, participants were limited to those who had EPDS measurements at two time points, at least 5 weeks apart, based on the estimated iCBT program duration. The details of the selection are shown in Figure 1.

Exposure: iCBT program use

Exposure group

The iCBT program consists of a total of 6 modules. The details of the module contents were explained elsewhere [10]. After 16 weeks of pregnancy, app users can read the modules once a week, each within 5 minutes, at any time. Though the program can be completed within 5 weeks at minimum, it can be used at any time as long as the users continue to use the app. The program's progress is managed by clicking the "Read" button at the bottom of each module page, and the next module will be opened one week after clicking the button. The number of modules progressed is recorded when EPDS is measured, which enables us to identify the timing of the program use from EPDS log data.

Non-exposure group

The non-exposure group was identified by matching baseline variables with the exposure group: age (±2), weeks of pregnancy (±1), and total EPDS score (±1) [24–26]. The total EPDS score was added in the current study as a matching variable because it was suggested that the baseline severity of depressive symptoms affects the intervention effects [9,27]. We randomly selected up to 4 controls per iCBT program completer without replacement [28,29].

Outcome: Antenatal depressive symptoms

To evaluate the depressive symptoms during pregnancy, we used the Japanese version of the

Edinburgh Postnatal Depression Scale (EPDS) [30,31]. This scale consists of 10 questions about perinatal-specific depressive symptoms measured on a 4-point scale ranging from 0 to 3, with a total score ranging from 0 to 30. The higher score indicates a more severe mental health status. A cutoff of 12/13 is considered appropriate for antenatal depression[32]. In addition, a cutoff of 8/9 is often used clinically in Japan to screen for perinatal depression[30], so this cutoff was also considered. Though participants could answer the questionnaire only at given time points (e.g., 16 to 20 weeks of pregnancy, 32 weeks of pregnancy) in the previous RCT [9], app users can answer the EPDS whenever they want to check their mental status after the implementation. The app will display advice to the users depending on the measured score: “There seems to be no problem with your mental status. Let's continue with the self-check of your mental status.” when the score is 0-8, “You may not be feeling well. We recommend that you take extra care of yourself by getting enough sleep, taking time for yourself, and doing activities that will refresh you. Please also use our Pre-mother School modules.” when the score is 9-12, and “It is possible that your mental status is not at its best. We recommend that you take better care of yourself than usual and consult with a trusted family member, friend, supervisor, or colleague. If you continue to be in the wrong mood, please consider consulting your obstetrician-gynecologist or public consultation service.” when the score is 13 or over. These messages appeared automatically, and there was no tracking of what actions participants took afterward.

Process evaluation

To evaluate the implementation of the program, we reported two indicators: reach and completion rate. After the implementation, both the iCBT program and the EPDS questionnaire were stored on a higher-level page named “mental care.” The “mental care” page lists mental health-related functions, a hierarchy of two levels down from the homepage (Figure 2). In February 2023, the specifications were updated to include a banner that enables users to jump from the homepage to the “mental care” page with a single click. The banner shows the message, “For mothers who try too hard, let’s check your mental state.” Under these specifications, reach was defined as the proportion of those who had visited the “mental care” page, iCBT program page, and EPDS page at least once, each. The completion rate was defined as the proportion of those who had completed all six modules.

Covariates

Age and weeks of pregnancy at the time of the baseline EPDS score were measured and used as basic information. For service usage information, the observational period was defined as the period between the baseline and follow-up time points when EPDS scores were measured because the log data did not include date information about the iCBT program usage. The number of additional EPDS measurements during an observational period other than baseline and follow-up was also calculated.

Statistical analysis

First, the baseline characteristics of the exposure and the non-exposure groups were compared using standardized differences. Service usage information was also compared between groups using t-tests. We calculated changes in EPDS scores after the program use, 95% confidence intervals (CI), and effect size

of Cohen's d to assess the association between the iCBT program and depressive symptoms. Repeated measure analysis of variance (repeated measure ANOVA) was also conducted to identify the statistical significance of interaction terms between the groups and the measurement time points. As for the process evaluation, reach and completion rate were calculated using information on the number of users visiting the "mental care" page, iCBT program page, and EPDS questionnaire page per month. All analyses were performed using R version 4.4.1. and $p<0.05$ was set as statistically significant.

Ethical approval

This study was approved by the Research Ethics Committee of the Graduate School of Medicine/Faculty of Medicine, The University of Tokyo (Approval No. 2019150NI).

Result

Participants' characteristics

Of the 101,493 women (173,712 records) who answered the EPDS on the app from September 2022 to September 2024, 209 women (1,675 records) completed six iCBT modules, and 64,373 women (101,251 records) never read the iCBT modules. After excluding those without EPDS measurements before and after using the iCBT or those who failed to match, 119 women who completed the iCBT program and pair-matched 448 controls were identified.

All variables showed standardized differences of <0.1, which suggests that baseline characteristics were balanced between exposure and non-exposure groups after the matching (Table 1). The prevalence of antenatal depressive symptoms above the EPDS cutoff of 12/13 was 16.0% and 17.4% among the exposure and non-exposure groups, respectively. The descriptive analysis of service usage information is shown in Table 2. The mean observational period was 11.67 weeks in the exposure group and 13.61 weeks in the non-exposure group. The mean number of additional EPDS measurements during the observational period was 3.17 times in the exposure group and 0.51 times in the non-exposure group.

[Table 1] Baseline characteristics after matching

Variables	**Exposure group** N=119 Mean (SD); n(%)		**Non-exposure group** N=448 Mean (SD); n(%)		Standardized differences
Age(years)	33.31	(4.12)	33.04	(3.85)	0.068
Weeks of pregnancy(weeks)	18.00	(5.01)	17.63	(4.85)	0.075
EPDS score	7.24	(5.30)	7.25	(5.18)	0.002
EPDS≧9	40	(33.6%)	147	(32.8%)	0.017
EPDS≧13	19	(16.0%)	78	(17.4%)	0.039

SD: standard deviation, iCBT: internet-based cognitive behavioral therapy, EPDS: Edinburgh Postnatal Depression Scale

[Table 2] Descriptive analysis of service usage information

Variables	Exposure group N=119 Mean (SD); n(%)		Non-exposure group N=448 Mean (SD); n(%)		*P* value
Observational period [a]	11.67	(5.80)	13.61	(6.13)	.002
Number of additional EPDS measurement [b]	3.17	(1.70)	0.51	(0.95)	<.001

iCBT: internet-based cognitive behavioral therapy, EPDS: Edinburgh Postnatal Depression Scale

[a] observational period was defined as the period between the baseline and follow-up time points when EPDS scores were measured.

[b] Number of additional EPDS measurements during observational period other than baseline and follow-up.

Antenatal depressive symptoms before and after using the iCBT program

Table 3 and Figure 3 show the EPDS scores and the differences before and after using the program. The average EPDS scores at the baseline were 7.24 in the exposure group and 7.25 in the non-exposure group. Compared to before using the program, the EPDS scores changed by -0.69 and +0.99 in the exposure and non-exposure groups, respectively (Cohen's d = 0.31, 95%CI 0.11 - 0.51). The repeated measure ANOVA showed statistical significance in interaction terms between the groups and the measurement time points (*P*=.04).

[Table 3] Change in depressive symptoms after iCBT intervention

Variables	Exposure group N=119			Non-exposure group N=448			Effect size (Cohen's d)
	Mean	(SD)	95%CI	Mean	(SD)	95%CI	
EPDS at baseline	7.24	(5.30)	6.27 - 8.20	7.25	(5.18)	6.76 - 7.73	
EPDS at follow-up	6.55	(5.19)	5.60 - 7.49	8.24	(6.16)	7.66 - 8.81	
change difference of EPDS	-0.69	(4.92)	-1.58 - 0.20	0.99	(5.56)	0.47 - 1.51	0.31

iCBT: internet-based cognitive behavioral therapy, EPDS: Edinburgh Postnatal Depression Scale,

CI: confidence interval

Process evaluation

As for reach, 5.4% of overall app users visited the “mental care” page. Of these, 26.5% visited the iCBT program page, and 67.5% visited the EPDS page. As for the completion rate, 2.6% of those who visited the iCBT program page at least once completed all six modules. When the population was limited to those who visited the program page and clicked the “read” button at least once, 32.3% completed six modules.

Discussion

Principal findings

This study examined the effectiveness of the iCBT program for pregnant women in preventing depressive symptoms during pregnancy in a real-world setting. The study found a statistically significant trend in the reduction of depressive symptoms after using the iCBT program in the exposure group compared with the non-exposure group. The effect size of the program for reducing depressive symptoms was 0.31. This is similar to a previous meta-analysis that reported an effect size of 0.28 for smartphone app interventions aimed at treating depressive symptoms [17], suggesting that this iCBT program also had a mild effect on preventing depressive symptoms among pregnant women.

This study showed that the average EPDS score at the baseline was 7.24 in the exposure group and 7.25 in the non-exposure group. These scores were higher than the baseline EPDS scores reported in a previous RCT study that evaluated the effectiveness of this iCBT program [9]. In that study, individuals with mild psychological distress at baseline had EPDS scores of 5.66 and 5.45, respectively. The differences might be due to the participants’ characteristics. The current study needed to limit the participants to those who voluntarily measured EPDS scores twice to investigate the change in depressive symptoms. A previous study showed that women with antenatal depression symptoms at baseline were more likely to use the screening features of pregnancy-related apps and to spend more time using the apps [33]. It may be possible that the participants in this current study were those who had mild to severe mental health issues and greater motivation to learn about mental health.

The number of additional EPDS measurements during the observational period was more frequent in the exposure group than in the non-exposure group. It has been pointed out that repeated scale measurements themselves may have a transformative effect on cognition and behavior [34]. It has also been reported that repeated measurements of self-reported questionnaires have little impact that would raise serious concerns [35]. A study examining the effects of stress screening in the workplace and the efforts to improve the work environment found that stress screening alone did not improve workers’ psychological distress. Significant improvements were observed only when both the stress screening and the effort to improve the work environment were implemented together [36]. Considering these studies, it may be

reasonable to assume that the EPDS measurement itself in the present study had little effect on depressive symptoms.

The average proportion of visitors to the “mental care” page among app users was 5.4%. This was similar to the previous study, which reported a 4.0% open rate by daily active users of popular mental health apps in the real world [14]. Even though the iCBT program and the EPDS questionnaire were stored on the same “mental care” page, the visit rates were more than double, at 26.5% and 67.5%, respectively. This may suggest that many users who visited the “mental care” page were aiming to self-check their mental health using the EPDS questionnaire, not to use the iCBT program. Furthermore, the completion rate of the iCBT program was 2.6%. This result is consistent with previous reports that a digital mental health intervention could attract only to the first module, and many people dropped out before reaching the final module [14,18,37]. However, when the population was limited to those who clicked the “read” button at the bottom of the module page at least once, the completion rate was 32.3%. This was close to the completion rate of 37.2% in the previous RCT intervention [9]. This might suggest that the requirement to click the “read” button after reading the module contents hindered the program's progress.

Limitations

This study has several limitations. First, the population selected for effectiveness evaluation didn’t represent all the app users, as only 5.4% of app users visited the “mental care” page, and 26.5% of these visitors visited the iCBT program page. Furthermore, only 2.6% completed all 6 modules among those who visited the iCBT program page. To evaluate the effectiveness of the iCBT program with more app users in the future, it may be necessary to improve the program’s delivery environment. Although the number of participants was small, we still were able to evaluate the effectiveness of the iCBT program on those who completed the program in a real-world environment. Second, there was a difference in the baseline and follow-up time points between each person because they could measure EPDS whenever they wanted. Although the observational period was two weeks longer in the non-exposure group, it is unlikely that this gap would cause a significant change in depressive symptoms at the follow-up, considering that the baseline time points were matched between the two groups. Third, there was a possibility of unmeasured confounding. The log data used in this study only included EPDS scores and related information; no socioeconomic factors such as educational history and employment status could be considered. Lastly, despite this iCBT program targeting perinatal depression prevention, only the effect on antenatal depressive symptoms could be evaluated because few app users continued to use the EPDS measurement service after delivery.

Conclusion

A developed internet-based cognitive behavioral therapy targeting the prevention of perinatal depression was significantly effective in decreasing depressive symptoms among pregnant women in a real-world setting. Future studies should explore efforts to reduce dropouts and increase participation in the program to help more pregnant women reduce their depressive symptoms.

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Authors' contributions

DN was in charge of this study, supervising the process and providing his expert opinion. AT and DN designed the study and analyzed the data. AT wrote the first draft of the manuscript. NS and KI ensured that questions related to the accuracy or integrity of all parts of the work were appropriately investigated and resolved. All authors approved the final version of the manuscript.

Conflicts of interest

DN received personal fees outside the submitted work from Startia, Inc., MD.net, and an honorarium from Takeda Pharmaceutical Co. and Otsuka Medical Devices Co., Ltd. NS reports personal fees from Medilio Inc., outside the submitted work. KI is employed at the Department of Digital Mental Health, an endowment department supported with an unrestricted grant from 15 enterprises (https://dmh.m.u-tokyo.ac.jp/c), outside the submitted work. The other authors declare no conflicts of interest.

Abbreviations

ANOVA: analysis of variance
EPDS: Edinburgh Postnatal Depression Scale
iCBT: internet-based Cognitive Behavioral Therapy
RCT: randomized controlled trial

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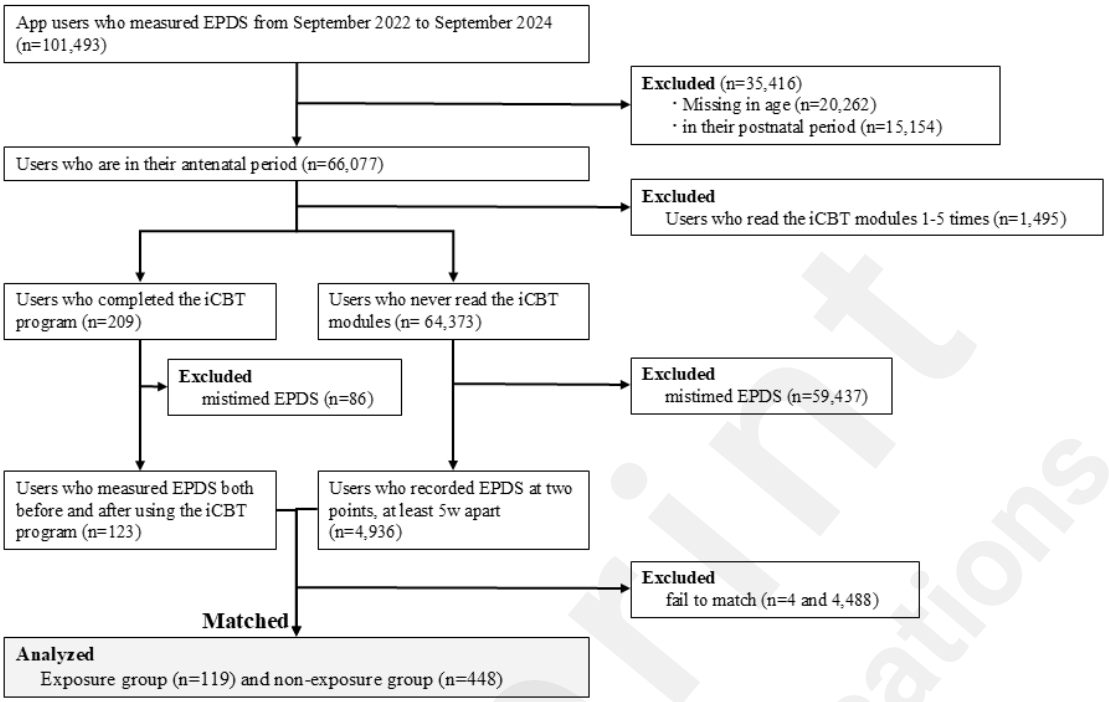
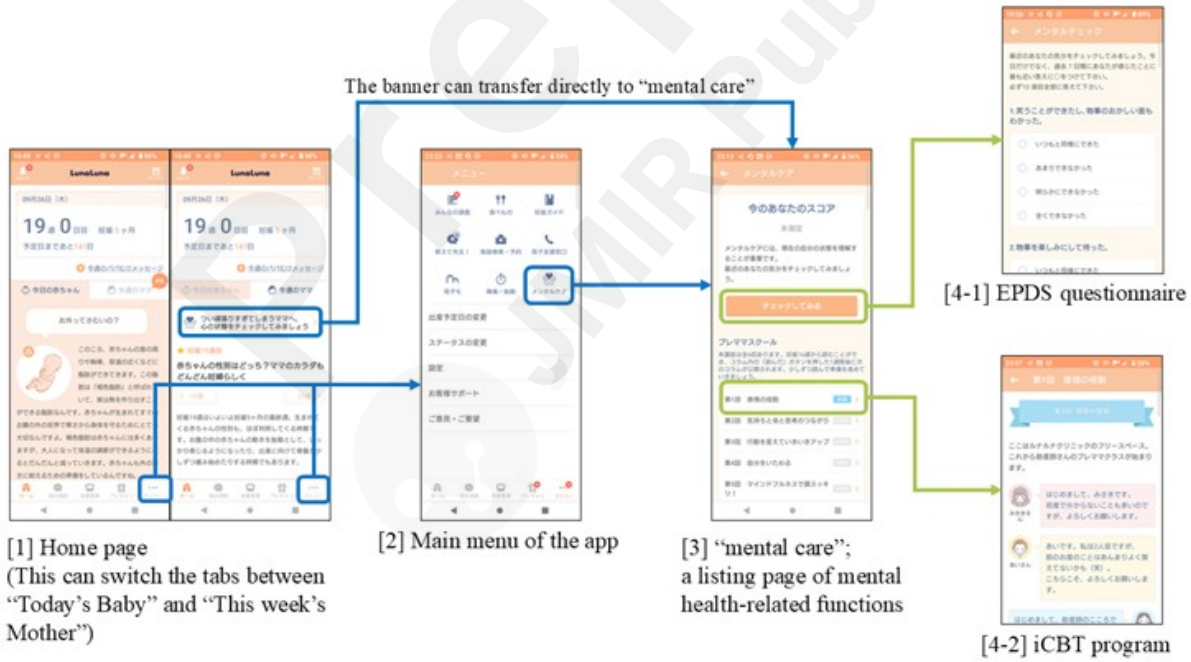
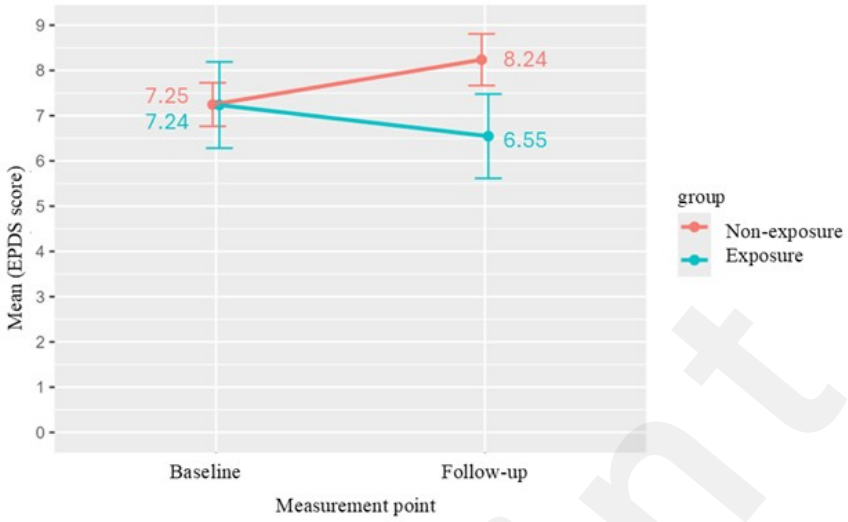
Figures



[Figure1] Participants selection flowchart.



[Figure 2] Structure of the Luna Luna Baby app.

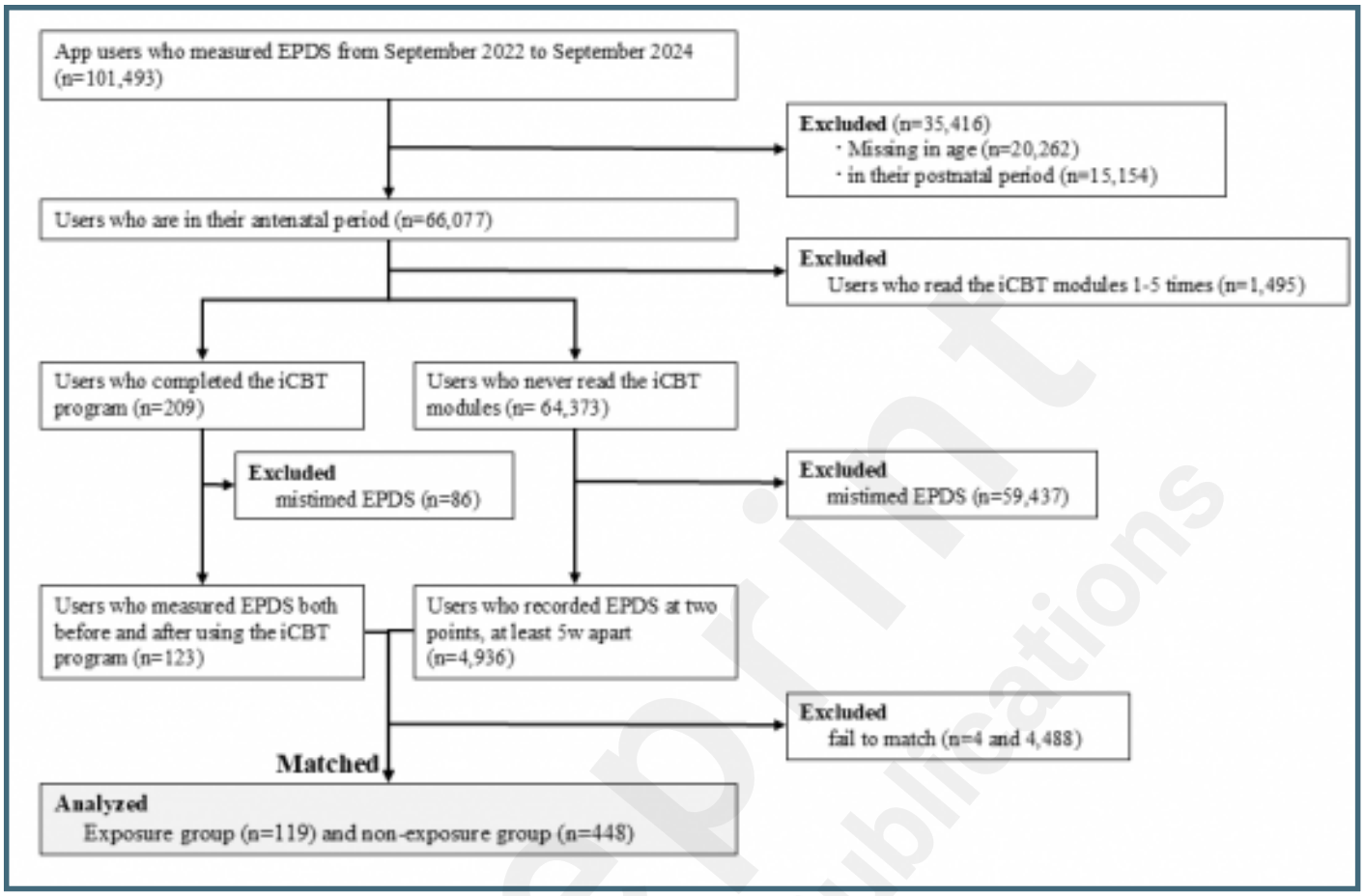


[Figure 3] Change in EPDS score after the iCBT program use.

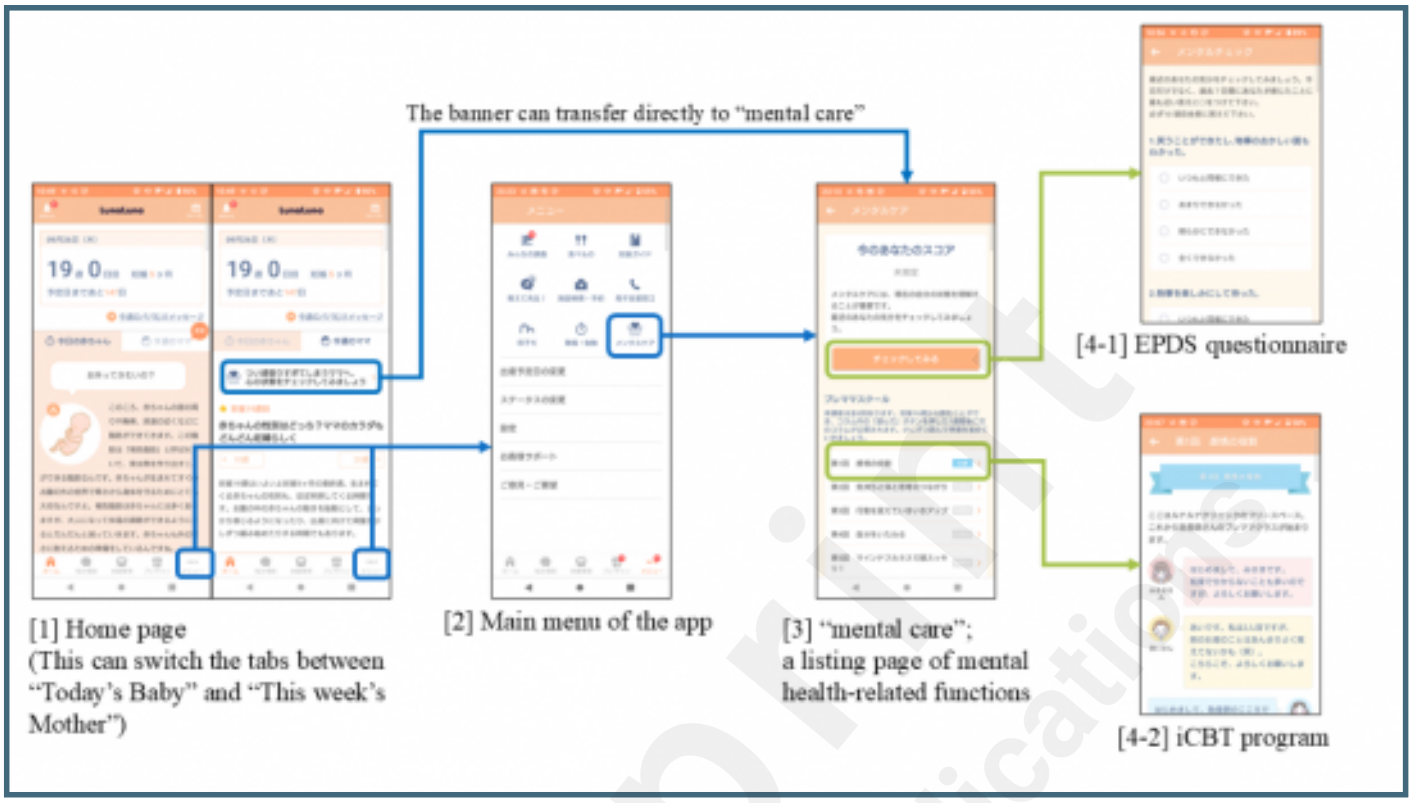
Supplementary Files

Figures

Participants selection flowchart.



Structure of the Luna Luna Baby app.



Change in EPDS score after the iCBT program use.