Clinical Research Summary

Background

Depression is one of the most common mental health disorders among adolescents with continued increases in prevalence[1]. Pediatric primary care guidelines recommend that all adolescents be screened for depression annually[2], but effective treatment options and immediate access to specialized mental healthcare are often limited. SparkRx by Limbix[a] is a 5-week, self-guided, cognitive behavioral therapy (CBT)-based, digital therapeutic mobile application designed to adjunctively treat depressive symptoms in adolescents. To evaluate the clinical effectiveness of SparkRx as a treatment for depressive symptoms during the COVID-19 pandemic, a virtual, randomized controlled trial (RCT; NCT04524598) was conducted to compare SparkRx to an active control mobile app.

Methods

A community sample of 121 eligible adolescents (81 female; 26 male; 14 non-binary), aged 13-21, with self-reported moderate to severe symptoms of depression at baseline (PHQ-8 ≥ 10) were recruited nationwide to participate in the virtual RCT[b]. Participants were randomly assigned to use either the SparkRx (n = 63) or the control app (n = 58) for the five-week intervention period. Participants completed weekly in-app PHQ-8 assessments. Intervention-related changes in depression symptoms (PHQ-8) and app usage were evaluated. Follow-up analyses included teens with self-reported mild to moderate symptoms of depression at baseline (PHQ-8 ≥ 5; SparkRx n = 75, Control n = 79).

Clinical Research Summary (cont.)

Results

Efficacy:

Pre-Planned Analyses: Participants who received SparkRx showed a clinically meaningful reduction[3,4] in depression symptoms, meaning it was enough to have a notable impact on daily life (≥ 5 point symptom reduction across the five-week intervention; Figure 1a). At the end of the study, the SparkRx group had a significantly lower remission[d] rate than the Control group (SparkRx = 17%; Control = 3%; p = .01; FDR adj p = .027). At the end of treatment, 24% of SparkRx participants had a treatment response compared to 14% of Control group participants, but this difference was not statistically significant (p = .07; FDR adj. p = .16). The modified intention-to-treat analysis comparing SparkRx to Control across the 5 weeks was not significant (p = .06; FDR adj. p = .06).

For participants who consistently engaged[e] with the research protocol (n = 86), SparkRx led to a statistically significant reduction in depression symptoms compared to Control (p = 0.01; FDR adj. p = .02; Figure 1b)). Statistical significance was retained for all analyses after controlling for multiple comparisons. At the end of treatment, 21% of SparkRx participants had depressive symptoms in the remission range and 29% had a treatment response (Control = 4%, 15%, respectively).

Follow-Up Analyses: Follow-up analyses that included teens with mild to severe depression symptoms (PHQ ≥ 5) suggested that participants who received SparkRx showed a statistically significant change in depression symptoms when compared to participants who received the control (p = .003; FDR adj. p = .005 Figure 2a). At the end of the study, SparkRx participants showed a significantly lower remission rate (SparkRx = 27%; Control = 11%; p = .01; FDR adj. p = .03) and a statistically greater treatment response (SparkRx = 30%; Control = 15%; p = .03; FDR adj. p = .04) compared to Control.

For participants that consistently engaged with the research protocol (n = 101), SparkRx continued to have a statistically significant reduction in depression symptoms compared to Control (p < .001; FDR adj. p = .002; Figure 2b). Statistical significance was retained for all follow-up analyses after controlling for multiple comparisons. At the end of treatment, 30% had depressive symptoms in the remission range, and 39% of SparkRx participants had a treatment response (Control = 10%, 14%, respectively).

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Adherence- SparkRx participants only: There was high engagement with SparkRx compared to depression apps evaluated in research and real-world settings (Figure 3). Mean participant adherence was 3.17 (63.5%) of 5 expected program modules.

Safety - SparkRx participants only: No participants experienced a serious adverse event or unanticipated adverse device effect.

Conclusion

SparkRx showing promising evidence of reducing depression symptoms in adolescents more than psychoeducation alone. This symptom reduction was clinically meaningful. Furthermore, SparkRx was shown to be a safe and engaging means of treating depression. As adjunct treatment, SparkRx can serve as an immediate and readily available treatment for depression symptoms and increase critical early access to mental health care for adolescents.

[a] These claims have not been validated by the US FDA with regard to the safety or efficacy of SparkRx. Limbix released the initial version of SparkRx per https://www.fda.gov/media/136939/download in 2021

[b] 39 additional participants with subthreshold depression symptoms were enrolled to provide access to mental health resources during COVID-19 but were not a part of the pre-specified target population and therefore not included in analyses.

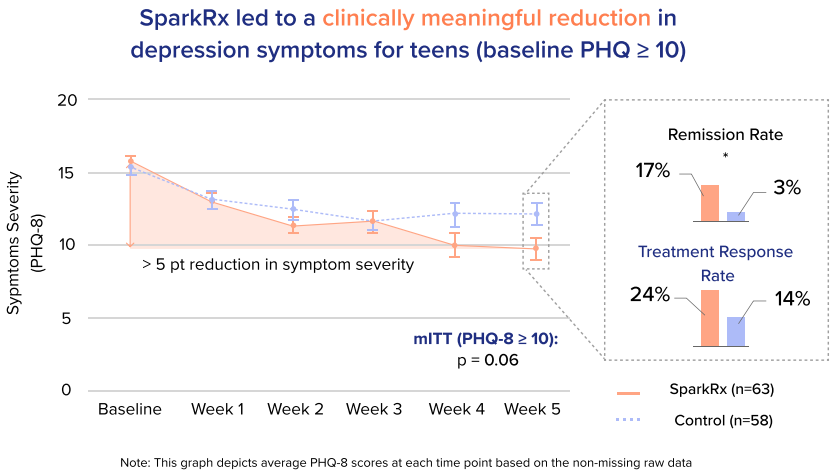
[c] Treatment response defined as a post-intervention 50% less than baseline PHQ score[5,6].

[d] Remission defined as a post-intervention PHQ-8 score < 5.[5,7]

[e] Consistently engaged defined as completed all PHQ assessments

Clinical Research Summary (cont.)

Figure 1. Clinical Outcomes: Treatment related change in depression symptoms (PHQ-8)



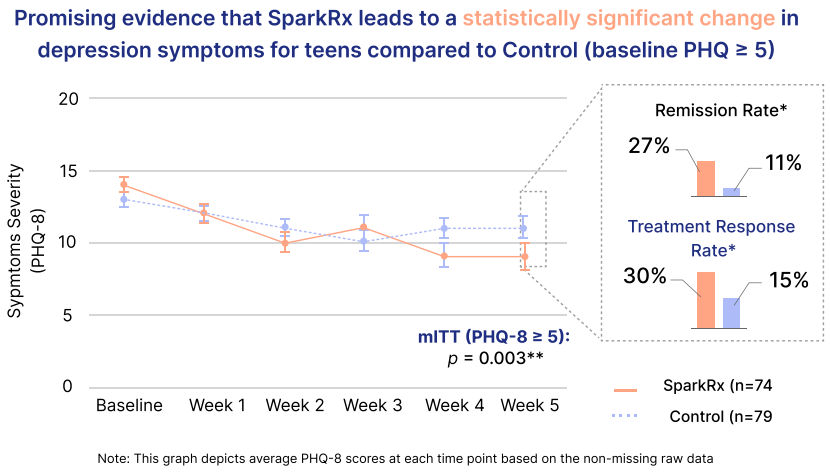
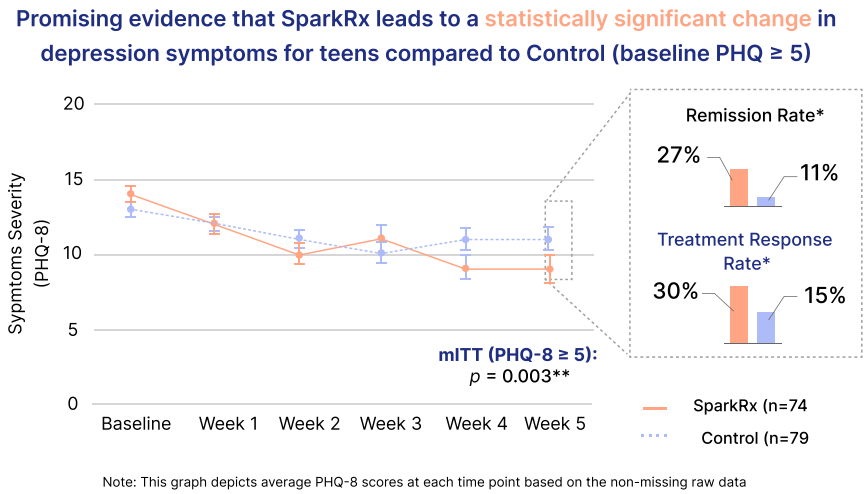


Figure 1a: Participants who received SparkRx showed a clinically meaningful reduction in depression symptoms. At the end of the study, 24% of SparkRx participants had a treatment response and 17% were in remission. (modified intention-to-treat analysis; PHQ ≥ 10)

Figure 1b: For participants that consistently engaged, SparkRx led to a statistically significant reduction in depression symptoms compared to Control (p = .01) and a 21% remission rate compared to a 4% remission rate for Control at the end of treatment. (Per-protocol analysis; PHQ ≥ 10)

Clinical Research Summary (cont.)

Figure 2. Clinical Outcomes: Treatment related change in depression symptoms (PHQ-8 ≥ 5)



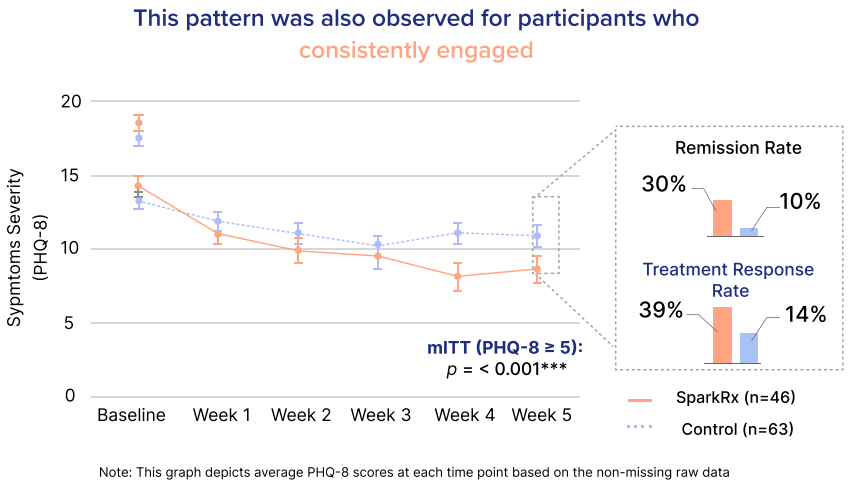


Figure 2a: Participants who received SparkRx showed a statistically significant reduction in depression symptoms ($p < 0.003$). At the end of the study, 30% of SparkRx participants had a treatment response and 27% were in remission. (modified intention-to-treat analysis; PHQ ≥ 5)

Figure 2b: For participants that consistently engaged, SparkRx led to a statistically significant reduction in depression symptoms compared to Control ($p < 0.001$) . At the end of treatment, 39% of SparkRx participants had a treatment response, and 30% were in remission. (Per-protocol analysis; PHQ ≥ 5)

Clinical Research Summary (cont.)

Figure 3. SparkRx engagement and adherence

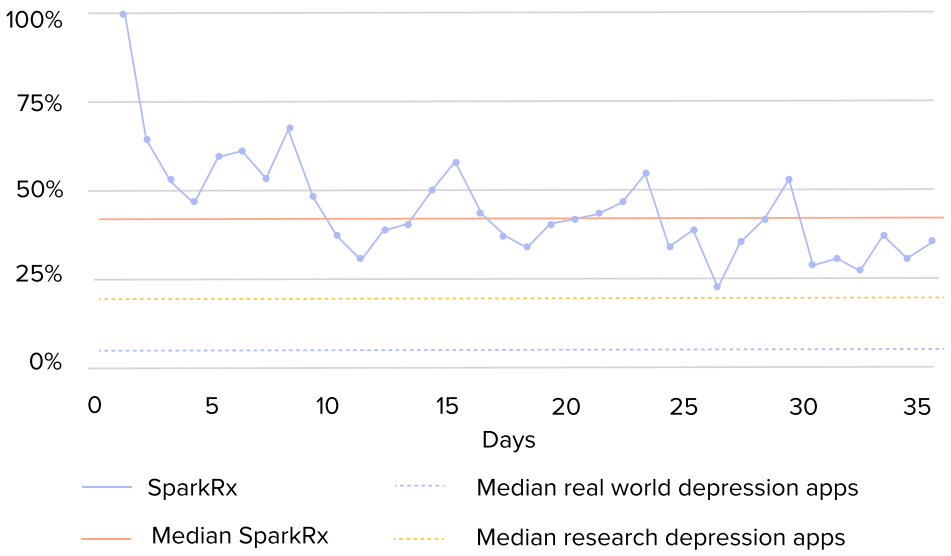


Figure 3: Percent Daily Usage. SparkRx app usage was higher than depression apps both in research and real-world.

References

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SparkRx Important Safety Information

Intended Use: SparkRx is a digital therapeutic intended to provide a neurobehavioral intervention (Cognitive Behavioral Therapy - Behavioral Activation) in patients 13 to 22 years of age as adjunct treatment for symptoms of depression.

SparkRx has not been cleared or approved by the U.S. Food and Drug Administration. During the COVID-19 public health emergency, SparkRx is being made available without a prescription under the FDA's enforcement policy for digital health devices treating psychiatric disorders.

Warnings: This app is not an emergency service provider. Patients experiencing a mental health emergency or having thoughts of self harm and suicide, should call 911 or go to the nearest emergency room.

Patients can also call or text 988, a 24/7 suicide and crisis lifeline. Patients will be connected to a trained crisis worker who can help them find support right away.

Patients should be clearly instructed not to use SparkRx to communicate severe, critical, or urgent information to their health care provider. Patients should also be informed that text they enter into SparkRx will not be monitored or reviewed by a health care provider.

SparkRx is not meant to be used as treatment without supervision of a health care provider. Please instruct your patients to contact you should they notice a worsening of symptoms or an increase in thoughts of suicide or self-harm.

SparkRx is not meant to be a substitution for any treatment or medication.

SparkRx is intended for patients whose primary language is English with a reading level of 5th grade or above, and who have access to an Android/iOS smartphone or tablet. SparkRx is intended only for patients who own a smartphone or tablet and are familiar with use of smartphone or tablet apps (applications).

SparkRx contains sensitive medical information. Please instruct patients to protect their information by password protecting their smartphone or tablet, and ensuring no one else may access their device.

SparkRx does not address concerns of active suicidal ideation with intent. SparkRx is not intended for the prevention of suicide attempts or self-harm behaviors. Patients with active suicidal ideation with intent or those who have had a past suicide attempt may still be given SparkRx to help treat depression but should not be given SparkRx to prevent, treat or mitigate active suicidal ideation with intent.

Patients with posttraumatic stress disorder (PTSD) who are currently experiencing marked alterations in arousal or reactivity associated with traumatic events may find that the level of exposure related to guided behavioral activation exacerbates symptoms.

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