Curio Efficacy White Paper

Bending the Curve of Maternal Mental Health with Products across Continuum of Care: Efficacy Summary of MamaLift and MamaLift Plus

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The following efficacy summary describes the Curio Platform offerings for maternal mental health. Curio Digital Therapeutics has developed an AI-driven predictive tool to identify and risk-stratify members at risk for developing postpartum depression. Combined with neurobehavioral interventions, the Curio Platform affords an opportunity for plans to reduce costs while improving the quality of care. Efficacy summaries for Curio's MamaLift and MamaLift Plus neurobehavioral interventions are described.

Bending the Curve: MamaLift and MamaLift Plus

Postpartum depression (PPD) is the most common and underdiagnosed obstetric complication, affecting as much as 20% of postpartum women.[1] Suicide accounts for 20% of postpartum deaths and is the second most common cause of maternal mortality.[2] In 2021, the March of Dimes gave a D+ score for maternity care in the US.[3]

Current Practices: Screening and Treatment

The American College of Obstetricians and Gynecologists (ACOG) notes that depression onset occurs prior to pregnancy in 27% of women, during pregnancy for 33%, and in the postpartum for 40%. In clinical practice, symptoms may appear as late as 12 months.[4] Accordingly, they recommend Obstetrician/Gynecologists (OBGYNs) screen women at the first obstetric visit, at 24-48 weeks gestation, and at the comprehensive postpartum visit.

Despite these recommendations, few women are screened or receive treatment. Analysis of Medicaid populations demonstrates that rates for screening and follow-up were less than 16% during pregnancy and 17% during postpartum. Commercially insured populations reported even lower screening and follow-up rates, with only 9% of pregnant women and 11% of postpartum women being screened.[5] Among those who screen positive, only 22% receive some treatment.[6] Evidence shows that even sub-clinical symptoms can cause harm, even though they are not screening positive.[7] Among those who are treated, about 20% are overtreated and incur excessive expenditure of about $10,000 each. Meanwhile, undertreated mothers, including those with subclinical symptoms, cost health plans $18,000 in direct costs annually.[8]

Bending the Curve

Curio Digital Therapeutics (“Curio”) leverages predictive analytics and evidence-based neurobehavioral interventions to divert 2 out of 3 cases of postpartum depression. The Curio Platform includes an AI-driven predictive algorithm that can identify women as early as the second trimester who would go on to develop PPD. This patent-pending technology is a breakthrough in risk identification. By stratifying PPD risk, limited therapist resources can be directed to the highest need. Curio couples risk stratification analytics with its suite of digital-forward neurobehavioral interventions that address a range of OB/gynecological and behavioral health needs. Curio’s neurobehavioral interventions are gamified and include nudge architecture to drive engagement and deliver outcomes that matter to health plans.

Curio’s flagship program is MamaLift. MamaLift is an FDA Class I General Wellness device intended to help women reduce their risk of anxiety and depression during pregnancy and after delivery. MamaLift Plus is a digital therapeutic device to treat women who have been diagnosed with PPD. MamaLift Plus has been submitted for premarket review as an FDA Class II digital therapeutic and is not for sale at this time.

The following summary describes efficacy analyses for MamaLift and MamaLift Plus digital behavioral interventions. Efficacy analyses are used to determine the capacity of a drug or therapy to produce a desired effect under controlled circumstances.

Methods

Clinical thresholds are measured by the Edinburgh Postnatal Depression Scale (EPDS). The EPDS is the most used validated screening tool for perinatal depression and anxiety. An improvement of four or more points is considered clinically meaningful. To assess the efficacy of MamaLift in women presenting with higher risk of PPD, two baseline thresholds of EPDS were chosen to create the subgroups of interest. The subgroups of interest were identified following discussions with mental health experts, Key Opinion Leaders (KOLs), and regulatory agencies (FDA). The first subgroup of women had baseline EPDS scores greater than or equal to 10 (≥ 10). This subgroup was defined based on the American College of Obstetricians and Gynecologists (ACOG) guidelines suggesting that women with EPDS scores greater than or equal to 10 should be initiated into treatment or referred to a mental health provider. The second subgroup was defined as women with baseline EPDS scores greater than or equal to 13 (≥ 13). This subgroup was defined based on regulatory feedback (FDA) indicating women with these baseline scores were the target group most likely to benefit from interventional therapy.

MamaLift was assessed in two ex-US studies, and MamaLift Plus was assessed in a single-arm Proof of Concept (POC) study in the US. In Curio's POC study, MamaLift Plus was assessed in a more severe group of women with baseline EPDS scores ≥ 10. Efficacy analysis results from the POC study are consistent with findings from the two ex- US clinical trials and demonstrate MamaLift Plus's potential for treating PPD in US populations.

Brief Description of ex-US Studies: MamaLift (Class I)

MamaLift's clinical effectiveness has been evaluated in two ex-US randomized controlled trials (RCTs), described in this summary as the 2017 Pilot RCT and 2019 Large RCT.

The 2017 Pilot RCT enrolled 194 subjects (n=194), of which n=68 had baseline EPDS scores ≥ 10 and n=31 had baseline EPDS scores ≥ 13. The 2019 Large RCT enrolled 1053 evaluable subjects (n=1053), of which 448 had baseline EPDS scores ≥ 10 and n=274 had baseline EPDS scores ≥ 13.

Efficacy analysis was conducted on the retrospectively defined subgroups described above (EPDS≥ 10 and EPDS≥ 13). The efficacy analysis was conducted for both the ex-US studies (Table 1a-b, 2a-b). The results of the ex-US studies suggest that MamaLift is safe and efficacious in reducing symptoms of depression and anxiety in women presenting as high and low risk for developing PPD.[9-13]

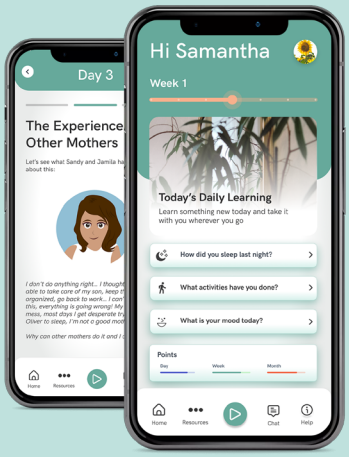


Table 1a: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 10 for 2017 Pilot RCT

	MamaLift (n=35)	Control (n=33)	P-Value
Change of 4+ points	23 (65.7%)	13 (39.4%)	.004
Change to <10 EPDS	27 (77.1%)	15 (45.5%)	.007

Table 1b: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 13 for 2017 Pilot RCT

	MamaLift (n=15)	Control (n=16)
Change of 4+ points	11 (73.3%)	11 (68.8%)
Change to <13 EPDS	13 (86.7%)	12 (75.0%)

Table 2a: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 10 for 2019 Large RCT.

	MamaLift (n=146)	Control (n=302)	P-Value
Change of 4+ points	74 (50.7%)	96 (31.8%)	<0.001
Change to <10 EPDS	27 (77.1%)	15 (45.5%)	.007

Table 2b: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 13 for 2019 Large RCT.

	MamaLift (n=96)	Control (n=178)	P-Value
Change of 4+ points	54 (56.3%)	70 (39.3%)	.007
Change to <13 EPDS	56 (58.3%)	72 (40.4%)	.005

Development of MamaLift Plus

Based on the efficacy findings from the ex-US studies, Curio further enhanced MamaLift. The enhanced program, MamaLift Plus, supports treatment for mild-to-moderate PPD. In developing MamaLift Plus, the original program was first translated from Portuguese to English. It was tested with native speakers to ensure translation quality and cultural relevance, and minor adjustments were made. Specifically, adjustments were made to the names of characters presented in MamaLift, and spelling was localized for US norms. In addition, trackers for mood, sleep, and activities were added to the program based on extensive evidence suggesting that self-tracking can improve mood, engagement with activities, and sleep. Finally, additional modules were added, focusing on Interpersonal Therapy (IPT), Dialectical Behavior Therapy (DBT), and Behavioral Activation Therapy (BAT) to support treatment in women with a diagnosis of mild-to-moderate PPD. The resulting version of MamaLift Plus was an 8- module intervention delivered via a digital app/platform. MamaLift Plus has also been evaluated for acceptability and usability in a Human Factors Trial, a POC trial, and an RCT.[14-16]

Brief Description of US Studies: MamaLift Plus

MamaLift Plus's clinical effectiveness has been evaluated in two US trials, described in this summary as the 2021 Single-Arm Proof-of-Concept (POC) study and Supporting Maternal Mental Health and Emotional Regulation (SuMMER) RCT. The POC trial enrolled 15 subjects (n=15), all of whom had baseline EPDS scores ≥ 10. The SuMMER RCT enrolled 141 subjects (n=141), all of whom had baseline EPDS scores ≥ 13. In the SuMMER RCT, subjects were randomized to the intervention arm (MamaLift Plus) or control arm (digital placebo).

MamaLift Plus has demonstrated promising evidence of effectiveness in its POC Study.[15] A responder analysis was conducted on the POC. The results are given alongside active arm (i.e., MamaLift arm) analyses for the 2017 Pilot RCT and 2019 Large RCT in Tables 3a and 3b.

Table 3a: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 10

	2017 Pilot RCT (n=35)	2019 Large RCT (n=146)	2021 Single-Arm POC (n=15)
Change of 4+ points	23 (65.7%)	74 (50.7%)	8 (53.3%)
Change to <10 EPDS	27 (77.1%)	82 (40.4%)	9 (60.0%)

Table 3b Responder Analysis for Evaluable Subjects (with Baseline EPDS ≥ 13)

	2017 Pilot RCT (n=15)	2019 Large RCT (n=96)	2021 Single-Arm POC (n=10)
Change of 4+ points	11 (73.3%)	54 (56.3%)	7 (70.0%)
Change to <13 EPDS	13 (86.7%)	56 (58.3%)	7 (70.0%)

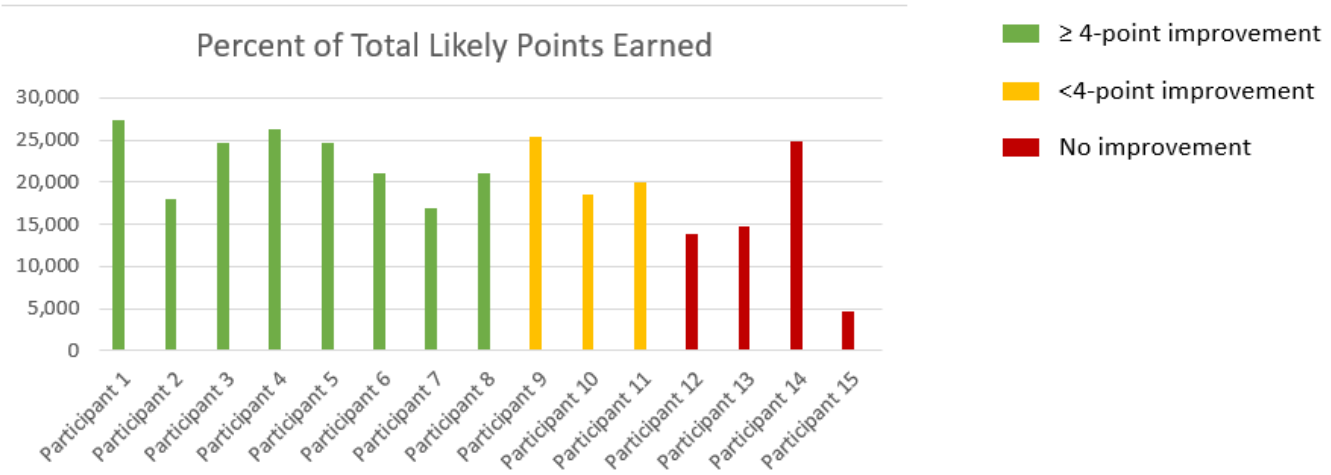
MamaLift Plus also generated positive data in its SuMMER RCT, meeting its primary endpoint of a ≥ 4-point improvement in EPDS score. A responder analysis was conducted on the Intent to Treat (ITT) population (n=141). Results for both the intervention and control arms are given in Table 4a.

Table 4a: Responder Analysis for Evaluable Subjects with Baseline EPDS ≥ 13

	MamaLift Plus (n=95)	Control (n=46)	P-value
Change of 4+ points	79 (83.2%)	10 (21.7%)	< 0.0001
Change to <13 EPDS	78 (82.1%)	14 (30.4%)	< 0.0001

Engagement Drives Outcomes

Engagement with the MamaLift Plus application is quantified using points. Subjects have the opportunity to earn up to 500 points per day for completing their behavioral therapy lesson and three trackers. Over the course of the eight-week long POC study, subjects could earn up to 28,000 points. 80% adherence, a benchmark for behavioral interventions, is equated to 22,400 points. Figure 1 below shows the total amount of points that each of the 15 subjects earned as percent of the total points that were available to them (28,000). The figure illustrates how engagement with MamaLift Plus drives improvement in clinical outcomes.



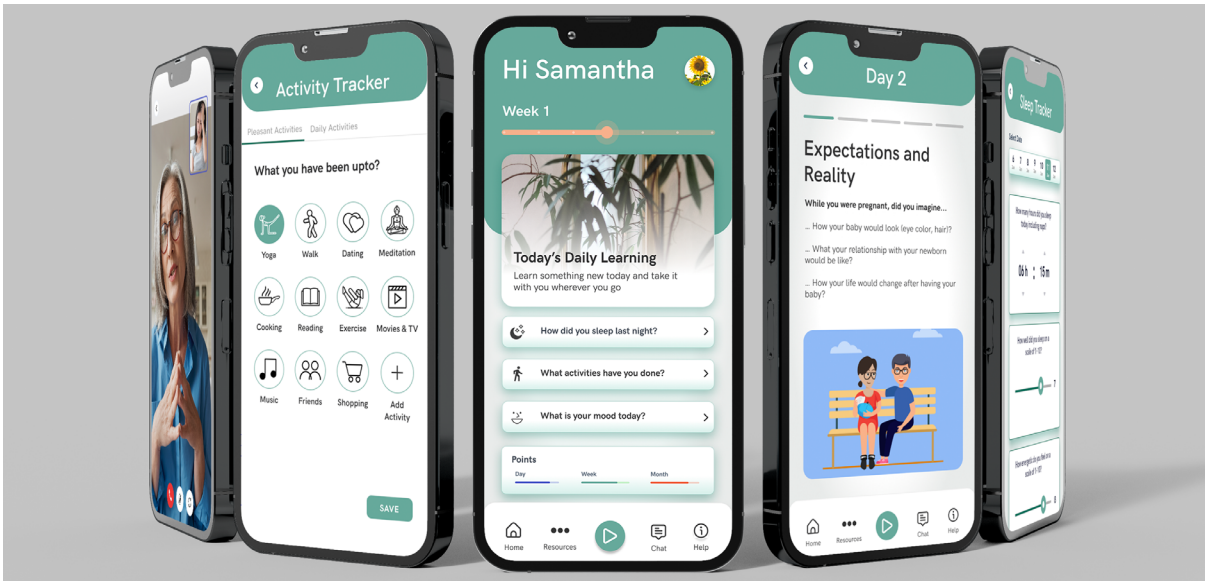
Conclusion

The efficacy summaries from the 2017 Pilot RCT and 2019 Large RCT are consistently in favor of MamaLift compared to the control treatment. Subjects who receive the digital intervention (MamaLift) demonstrate greater improvement in their depressive symptoms compared to control subjects as measured by EPDS. The results are statistically significant, and the improvements are clinically meaningful.

The 2021 Single-Arm POC of MamaLift Plus is of small sample size and has a single arm (all active). However, the endpoint is self-assessed and therefore not subjected to assessor bias due to treatment being known. Moreover, the efficacy estimates follow the same trend (greater %age improve if the baseline EPDS is higher) as observed in the 2017 and 2019 studies. In addition, the POC engagement data demonstrates that daily engagement with MamaLift Plus drives improvement in clinical outcomes. Hence, the totality of evidence is very positive. Although from a single-arm study, the results are very consistent with the 2 ex-US clinical trials and demonstrate potential efficacy in US populations.

The SuMMER RCT of MamaLift Plus also demonstrates positive findings in favor of MamaLift Plus compared to the control treatment. Subjects who receive the digital intervention (MamaLift Plus) demonstrate greater improvement in their depressive symptoms compared to control subjects as measured by EPDS. The results are statistically significant, and the improvements are clinically meaningful.

The Curio Platform provides an opportunity for health plans to realize cost savings while improving the quality of care. By leveraging the Curio Platform, plans can identify and risk stratify pregnant members as early as the second trimester. Early identification drives improvements in HEDIS scores, while timely intervention with Curio's suite of neurobehavioral interventions reduces cost and improves outcomes.



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8 Data on file

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15 Data on file

16 Data on file