

Mobile Device-Based Health Management Applications

Policy # 00756

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

Note: Drug Testing in Pain Management and Substance Use Disorder Treatment addressed separately in medical policy 00387.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider mobile health management software applications (MSA) to be **eligible for coverage**** when **ALL** of the following criteria are met: (see Policy Guidelines)

- The MSA has been approved or cleared by the Food and Drug Administration (FDA); **AND**
- There is credible scientific evidence which permits reasonable conclusions regarding the impact of the MSA on health outcomes; **AND**
- The MSA has been proven materially to improve the net health outcome or be as beneficial as any established alternative; **AND**
- The MSA has been prescribed by a healthcare practitioner; **AND**
- There is documentation supporting that the MSA was ordered for a covered purpose such as preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and in accordance with generally accepted standards of medical practice*; **AND**
- The requested MSA is not primarily for the convenience of the individual, prescribing clinician, caregiver, or other healthcare provider.

*Generally accepted standards of medical practice means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, physician specialty society recommendations and the views of physicians practicing in relevant clinical areas, and any other relevant factors.

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When Services Are Considered Not Medically Necessary

The use of mobile-based health management applications when the coverage eligibility criteria have not been met is considered to be **not medically necessary****, including when the requested application constitutes duplication of services (e.g., the requested service duplicates another service or intervention that provides the same clinical function or therapeutic intent, or provides substantially similar clinical function or therapeutic effect as another covered or available intervention without evidence of incremental clinical benefit).

***Note:** Please see Table 1. in Policy Guidelines for additional information about reviewed mobile-based health management applications, including whether they may be considered medically necessary.*

Policy Guidelines

Table 1. Examples of Practitioner-prescribed, FDA cleared or approved, MSAs (not an all-inclusive list)

Device Name	Software Developer	May Be Considered Medically Necessary
<i>See Rationale/Source section for more information</i>		
AspyreRx ^{TM†}	Better Therapeutics, Inc	No
BlueStar ^{®†} Rx	WellDoc ^{®†}	No
Canvas Dx ^{TM†}	Cognoa, Inc	No
CT-132	Click Therapeutics, Inc	No
DaylightRx	Big Health, Inc	No
d-Nav Insulin Guidance System ^{®†}	Hygieia	No
Drowzle ^{TM†}	Resonea	No
EndeavorRx ^{TM†}	Akili Interactive	No
FibriCheck ^{®†}	Qompium, NV	No
Freespira ^{®†}	PaloAlto Health Sciences, Inc	No
Halo ^{TM†} AF Detection System	LIVMOR, Inc	No

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Home Vision Monitor ^{®†} (HVM),	Vital Art and Science, LLC	No
Insulia ^{®†}	Voluntis, Inc	No
iSageRx	Amalgam Rx, Inc.	No
LumosityRx	Lumos Labs, Inc.	No
MamaLift Plus ^{TM†}	Curio Digital Therapeutics Inc,	No
Mobile Insulin Dosing System	Glooko, Inc.	No
My Dose Coach	Sanofi, Inc	No
NightWare ^{TM†}	Apple Watch ^{®†}	No
Oleena ^{®†}	Voluntis, Inc	No
Parallel ^{TM†}	Mahana Therapeutics, Inc	No
Regulora ^{®†}	metaMe Health Inc	No
Rejoyn	Otsuka America Pharmaceutical, Inc.	No
reSET ^{®†} and reSET-O ^{®†}	PursueCare, LLC	No
SleepCheckRx	ResApp Health, Inc	No
Sleepio ^{®†} Rx	Big Health, Inc	No
Stanza ^{TM†}	Swing Therapeutics, Inc	No

Background/Overview

This document addresses the use of practitioner-prescribed software applications for health management purposes when used on a mobile device (e.g., mobile phone, laptop, smartwatch, or tablet) with the intent to evaluate, diagnose or treat an illness, injury, disease or its symptoms. This document does not address mobile-based software applications (MSAs) that are used in the function or control of another FDA-cleared or approved stand-alone hardware medical device. This document also does not address MSAs accessible to the general public for download (including direct-to-consumer [DTC] or over-the-counter [OTC] applications), applications that promote general wellness, or applications operated by a healthcare practitioner in a clinical setting for remote health monitoring.

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Note: Over-the-counter (OTC) and consumer wearable devices may be excluded from benefit plan coverage. This may include smart phone, smart watch, or other personal tracking devices, including any software or applications.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Estimates report over 85% of adults living in the United States (US) own a smartphone (Pew Research Center, 2021). “Health-related mobile applications available to consumers on top app stores worldwide now surpass 350,000, with more than 90,000 digital health apps added in 2020 — an average of more than 250 apps per day.” (Institute for Human Data Science [IQVIA], 2021, 2024). Examples of medical mobile device software applications (MSAs) currently available include applications that purport to perform cognitive behavior therapy, augment weight loss goals, identify a suspicious nevi (mole), or even distinguish between normal cardiac sinus rhythm and potentially dangerous arrhythmias. Transforming a personal mobile device, such as a smartphone, into a medical device has the potential for far-reaching implications on the diagnosis and management of many diseases and disorders in addition to promoting general health and wellness. Despite the enormous effort to develop and disseminate digital health innovations, evidence of efficacy, or even a widely accepted framework for evaluation of efficacy, currently remains lacking. According to IQVIA (2021), independent organizations continue to highlight the need for larger and more robust randomized controlled trials (RCTs) that follow patients for longer times and report between-group differences in benefit, assessments of usability, and user-retention to determine the durability of their clinical effect, and evidence of cost-effectiveness that can be analyzed versus standard of care.

The US Food and Drug Administration (FDA) Center for Devices and Radiologic Health (CDRH) is among one of several groups leading development of a framework for evaluating the burgeoning number of MSAs anticipated to reach market as part of the expanding digital health innovation arena. The framework is detailed in their guideline entitled, “Policy for device software functions and mobile medical applications” (FDA, 2019).

The FDA’s regulatory oversight of software functions includes the following subsets:

1. **Software functions that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s) or analyzing medical device data.**

Examples of software functions that control medical devices include: software that provides the ability to control inflation and deflation of a blood pressure cuff through a mobile platform and mobile apps that control the delivery of insulin on an insulin pump by transmitting control signals to the pumps from the mobile platform.

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Device software functions of these types are considered accessories to the connected device and not addressed by this document.

2. **Software functions (typically, mobile apps) that transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices.** Examples of these types of software functions include: a software function that uses a mobile platform for medical device functions, such as attachment of a blood glucose strip reader to a mobile platform to function as a glucose meter; or attachment of electrocardiograph (ECG) electrodes to a mobile platform to measure, store, and display ECG signals; a software function that uses the built-in accelerometer on a mobile platform to collect motion information for monitoring sleep apnea; a software function that uses sensors (internal or external) on a mobile platform for creating electronic stethoscope function is considered to transform the mobile platform into an electronic stethoscope.

Mobile software functions of this type are addressed by this document when the ancillary hardware device is intended to function solely in conjunction with the mobile device application.

3. **Software functions that become a regulated medical device by performing patient-specific analysis and providing patient-specific diagnosis, or treatment recommendations. These types of functions are similar to or perform the same function as those types of software devices that have been previously cleared or approved.**

Examples of software functions that perform sophisticated analysis or interpret data (electronically collected or manually entered) from another medical device include: software functions that use patient-specific parameters and calculate dosage or create a dosage plan for radiation therapy; Computer Aided Detection software (CAD) image processing software; and radiation therapy treatment planning software.

The FDA's 2024 *Report on Risks and Benefits to Health of Non-Device Software Functions*, outlines categories of software that fall under the statutory exemptions outlined in Section 520(o)(1) of the FD&C Act. These include general wellness tools, software limited to administrative or data transfer functions, and certain clinical decision support tools that do not provide automated diagnostic or treatment output. Applications in these exempt categories are not regulated as medical devices by the FDA (FDA, 2024). This document addresses software applications only when they operate on a mobile device, have received FDA clearance or approval, are clinician-prescribed, and the intent of the MSA is to evaluate, diagnose or treat an illness, injury, disease or its symptoms.

In 2025, Lakhan conducted a cross-sectional study, which systematically reviewed all FDA-cleared, prescription-only digital therapeutics (PDTs [e.g., MSAs]) as of May 2025 to characterize patterns in regulatory pathways, sponsor geography, labeled indications, and therapeutic language. In total, 13 PDTs were identified, 8 of which were cleared via the 510(k) pathway and 5 via the De Novo classification pathway. All products were cleared under the CDRH, and sponsors were exclusively U.S.-based. The study found that FDA labeling varied meaningfully in terms of therapeutic claims. Although 11 of 13 PDTs included the word “treat” in their indication for use, many were accompanied by qualifiers such as “aid in the management” or “help improve symptoms.” Only 1

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product, CT-132 for migraine, received a treatment indication without modifiers, representing a “clean” treatment label and 2 products, EndeavorRx and reSET-O, were labeled not as treatments but as tools to improve attention function or retention in treatment, respectively. These distinctions in language may impact how PDTs are interpreted. The study concluded that labeling language plays a central role in determining therapeutic scope and regulatory positioning and has direct implications for adoption and use in clinical care.

Practitioner-prescribed, FDA cleared or approved, MSAs (not an all-inclusive list)

AspyreRxTM, Better Therapeutics, Inc.

AspyreRx is a prescription-only digital therapeutic device intended to provide cognitive behavioral therapy to individuals 18 years or older with type 2 diabetes. The device targets behavior to aid in the management of type 2 diabetes in individuals who are under the care of a healthcare provider. The application provides cognitive behavioral therapy intended as a treatment for adjunctive use with standard of care.

AspyreRx was evaluated in an RCT which enrolled 669 adults with type 2 diabetes and an HbA1c of 7 to < 11% (Hsia, 2022). Study participants were randomly assigned to receive access to AspyreRx (n=326) or a control application (n=343), both were adjunct to standard of care. After 90 days of access to AspyreRx, change in HbA1c was -0.28% (95% confidence interval [CI], -0.41 to -0.15) in the intervention group and +0.11% (95% CI, -0.02 to 0.23) in the control group (treatment group difference 0.39%; p<0.0001). Though statistically significant, the minimal clinically important difference (MCID) in HbA1c established in the peer-reviewed literature is 0.5%, this study did not attain that difference (Santos, 2023). Hypoglycemia was reported by 2 participants in the AspyreRx group and none in the control group. No adverse events in either group were attributed to AspyreRx use. Further study is warranted.

BlueStar[®]Rx, WellDoc[®]

BlueStar is a digital health platform for type 2 diabetes that provides tailored guidance driven by artificial intelligence and is focused on six critical dimensions of chronic disease care, which apply to diabetes as well as many other conditions like high blood pressure, pre-diabetes, and heart failure. BlueStar was evaluated in a randomized controlled trial (RCT) which enrolled 163 individuals with type 2 diabetes whose HbA1c levels were poorly controlled or abnormal at the time of enrollment. Enrolled primary care practices (PCP) were randomized to one of four study groups: control-usual care (n=56), coach-only (n=23), coach PCP portal (n=22), and coach PCP portal with decision support (n=62). Participants who were randomized to use an MSA to help manage their diabetes in addition to usual care, improved HbA1c by an average 1.9%, compared with a 0.7% improvement in those randomized to usual care alone, a difference of 1.2% (p<0.001) over the 12-month study period (Quinn, 2011). The study’s limitations include a small sample size in the study arms and an acknowledged randomization failure (“[coach portal with decision support] patients had higher baseline glycated hemoglobin than [usual care] (9.9 vs. 9.2%, p=0.04”) that may have inflated the observed effect size.

Agarwal and colleagues (2020) conducted a multicenter, pragmatic RCT to determine if BlueStar application usage leads to improved HbA1c levels among diverse participants across diverse clinical

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scenarios. In total, 223 study participants were randomized to either the ‘immediate treatment group’ (ITG; n=110 [received the BlueStar intervention for 6 months]) or the wait-list control group (WLC; n=113 [received usual care for the first 3 months and then received the intervention for 3 months]). The primary outcome was HbA1c levels at 3-month follow-up. Secondary outcomes assessed disease self-management, experience of care, and self-reported health utilization. At 3 months, the mean difference in HbA1c levels between the ITG and WLC groups was not statistically significant (mean difference = -0.42; 95% CI, -1.05 to 0.21; p=0.19). Similarly, there was no effect on secondary outcomes and BlueStar usage was found to vary significantly across clinical sites (median of 9 versus 36 log-ins over 14 weeks at the lowest, versus highest usage sites, respectively). Evidence of BlueStar’s clinical efficacy remains to be established in addition to defining factors that may affect individual and site-specific variations that impact the application’s usage as recommended.

Canvas DxTM, Cognoa, Inc.

Canvas Dx is used by healthcare providers as an aid in the diagnosis of Autism Spectrum Disorder (ASD) for individuals ages 18 months through 72 months who are at risk for developmental delay. The device is not intended for use as a stand-alone diagnostic device but as an adjunct to the diagnostic process. In 2022, Megerian and colleagues conducted a double-blinded, cohort study which tested the accuracy of CanvasDx. This study compared the diagnostic agreement of the device to two or more independent specialists in a cohort of 425 children (aged 18-72 months) who had developmental delay concerns (425 study completers, 36% female, 29% ASD prevalence). The PPV was determined to be 80.8% (95% CI, 70.3%-88.8%) and NPV was 98.3% (95% CI, 90.6%-100%). Of those who received a determinate output (ASD positive or negative [31.8%]) sensitivity was 98.4% (95% CI, 91.6%-100%) and specificity was 78.9% (95% CI, 67.6%-87.7%). Of 711 children originally consented to participate in the study, 286 (40%) dropped out. There is insufficient data to help us understand whether use of the Canvas Dx application decreases time to diagnosis in a real-world setting, in a manner that is likely to improve clinically relevant ASD outcomes.

In 2025, Salomon and colleagues published a retrospective, post-marketing analysis of 254 children evaluated with Canvas Dx. The device provided a determinate result in 63% of cases and demonstrated reported sensitivity of 99.1%, specificity of 81.6%, positive predictive value of 92.4%, and negative predictive value of 97.6% based on concordance with clinician diagnosis. Median age at diagnosis was 37.2 months, earlier than published U.S. averages. However, the study lacked a comparator group or independent diagnostic gold standard, did not evaluate downstream clinical outcomes such as time to intervention or functional improvement, and reported an abstention rate of 37%. Long-term diagnostic stability and post-diagnostic care patterns were not assessed.

In 2025, a prospective feasibility study was published by Sohl and colleagues evaluating the integration of Canvas Dx within a primary care ECHO Autism model (n=80). Median time from concern to diagnosis was 39 days; however, comparison to 180- to 264-day specialty center wait times was based on historical data rather than within-study controls. Canvas Dx returned a determinate result in 52.5% of cases, with full concordance between device output and clinician diagnosis among those determinate cases. No clinical outcomes were reported, and nearly half of children received indeterminate results requiring standard evaluation. This study suggests feasibility and high diagnostic concordance when a determinate result is generated, but does not demonstrate

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improvement in net health outcomes, earlier access to intervention compared with standard care, or comparative effectiveness.

CT-132, Click Therapeutics, Inc.

CT-132 is a prescription digital therapeutic developed by Click Therapeutics, Inc. for the preventive treatment of episodic migraine in adults. In April 2025, the FDA granted De Novo marketing authorization for CT-132 as the first prescription digital therapeutic specifically indicated for the adjunctive prevention of episodic migraine (FDA, 2025).

The pivotal evidence supporting this authorization came from the ReMMi-D trial, a Phase 3, double-blind, RCT. The trial enrolled 570 adults with 4-14 monthly migraine days (MMDs), who were randomized 1:1 to receive either CT-132 (n=286) or a sham digital therapeutic (n=284) over a 12-week treatment period. The primary endpoint was change in MMDs from baseline to the final 4 weeks of the intervention. Secondary outcomes included monthly headache days, quality of life, disability, and safety. At 12 weeks, the CT-132 arm demonstrated a statistically significant reduction in MMDs compared to the control arm (least squares mean [LSM] difference: -0.90 MMDs; 95% CI, -1.53 to -0.27; p=0.005). Monthly headache days were also significantly reduced (LSM difference: -0.85; 95% CI, -1.53 to -0.16; p=0.015). Participants receiving CT-132 reported greater improvements in disability and quality of life relative to control. No adverse events were attributed to treatment. These findings were presented in abstract form at the 2025 American Academy of Neurology Annual Meeting and have not yet been published in the peer-reviewed literature (Snipes, 2025).

DaylightRx

DaylightRx is a digital therapeutic intended to treat generalized anxiety disorder (GAD) using cognitive behavioral therapy (CBT) by improving GAD symptoms as an adjunct to usual care in individuals aged 22 years and older.

In 2020, Carl and colleagues conducted an RCT to evaluate the efficacy of Daylight for treating moderate-to-severe symptoms of GAD. A total of 256 adult participants (18-67 years; mean age=30.9) were enrolled and completed assessments at baseline, mid-intervention (3 weeks), post-intervention (6 weeks), and follow-up (10 weeks); the majority of the sample self-identified as female (68%), White (84%) and having at least some college education (83%). Study participants were randomized to either digital CBT (n=128) or waitlist control (n=128). The primary outcome, anxiety symptoms, was measured using the GAD-7 scale. Authors reported a significant reduction in GAD-7 anxiety scores in the digital CBT group compared with the waitlist control group at all assessment time points. At the 6-week follow-up, participants in the digital CBT group were more likely to experience remission of anxiety (65/107 [61%]) compared with waitlist control (38/122 [31%]) (odds ratio [OR], 3.99; 95% CI, 2.21, 7.21; p<0.001). At final follow-up (Week 10), 73/103 (71%) in the digital CBT group experienced remission compared with 41/124 (33%) in the waitlist control (OR, 5.84; 95% CI, 3.15, 10.82; p<0.001). The control group, which was unblinded, experienced a similar trend in significant reduction of symptoms from baseline, albeit less pronounced. While the reduction in self-reported GAD symptoms in this RCT is promising, a trial design including objective measures, in a more diverse sample is warranted.

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In 2025, Parsons and colleagues published results from a large, single-blind RCT evaluating DaylightRx against an active psychoeducation control in 351 U.S. adults with interview-confirmed GAD and a baseline GAD-7 score of 15 or higher. Participants were randomized 1:1 to DaylightRx or self-guided psychoeducation and followed through 24 weeks. The primary endpoints were remission by blinded clinician rating and self-reported GAD-7 scores. At 10 weeks, 71.0% of DaylightRx participants were rated in remission compared to 34.6% of controls (OR, 4.63; 95% CI, 2.85-7.54; $p<0.001$), and this advantage persisted at 24 weeks (77.7% vs. 52.0%; OR, 3.22; $p<0.001$). GAD-7 scores favored DaylightRx at all time points with large between-group effects (Cohen's $d=1.09$ at 10 weeks, 0.96 at 24 weeks). Statistically significant improvements in sleep, depressive symptoms, and clinician-rated anxiety severity were also observed. Completion of a greater number of CBT techniques was associated with stronger outcomes, supporting a dose-response relationship. Strengths of the trial include the use of blinded independent evaluators, conservative missing data assumptions, and broad inclusion criteria that allowed for stable medication use. However, limitations include modest racial/ethnic diversity (72% White, 6% Hispanic/Latino), exclusion of individuals with GAD-7 scores <15 , and absence of long-term follow-up beyond 24 weeks. Although the psychoeducation comparator exceeds a waitlist in rigor, it does not represent best-practice therapist-delivered CBT, limiting conclusions about DaylightRx's comparative effectiveness against standard of care.

d-Nav Insulin Guidance System[®], Hygieia

The d-Nav Insulin Guidance System was evaluated in a multicenter RCT of 181 individuals with uncontrolled type 2 diabetes. Participants were randomized to either d-Nav and healthcare professional support (intervention group; $n=93$) or healthcare professional support alone (control group; $n=88$). The primary outcome of interest was to compare average change in HbA1c from baseline to 6 months. Safety was assessed by the frequency of hypoglycemic events. The mean decrease in HbA1c from baseline to 6 months was 1.0% in the intervention group, and 0.3% in the control group ($p<0.0001$). The difference in frequency of hypoglycemic events between the groups was not statistically significant (Bergenstal, 2019). Current data is limited to a single study of small sample size and long-term data of net health outcomes is lacking.

Drowzle[®] Pro, Resonea

Drowzle Pro is a mobile software system that records and analyzes respiratory patterns during sleep to facilitate the in-home screening of obstructive sleep apnea (OSA).

Drowzle was evaluated in a longitudinal cohort study of 59 individuals who were administered a clinically indicated polysomnography (PSG) in a sleep lab where investigators compared the DROWZLE algorithm to PSG results. Investigators found the algorithm provided a sensitivity of 93.7%, specificity of 63.0%, negative predictive value of 89.5%, and positive predictive value of 75.0%, in the detection of moderate and severe OSA among individuals compared to PSG scores (Narayan, 2019). Studies evaluating real-world application are lacking, as is data describing how screening results impact diagnosis and management of OSA as compared to generally accepted standards of medical practice.

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EndeavorRx™, Akili Interactive

EndeavorRx is a game-based therapeutic intervention designed to improve cognitive function in children aged 8-12 who have been diagnosed with ADHD through a video game-like interface via at-home play for 25 min per day, 5 days per week for 4 weeks.

EndeavorRx was evaluated in an RCT which enrolled 348 children (8-12 years old) diagnosed with ADHD to receive treatment with either EndeavorRx (n=108) or a digital control intervention (n=168). Enrolled children were ineligible if they were already receiving medical therapy for ADHD. The mean change from baseline on the Test of Variables of Attention (TOVA) Attention Performance Index (API) was 0.93 in the EndeavorRx group and 0.03 in the control group (Adjusted $p < 0.050$); there were no differences between groups on secondary measures. There were no serious adverse events or discontinuations. Treatment-related adverse events were mild and included frustration (3%) and headache (2%). Compliance averaged 83% of expected sessions played (Kollins, 2020). Study limitations included the enrollment of only children with an objective baseline deficit in attentional function and those not currently receiving medical treatment for ADHD, thus representing a small subset of the ADHD population. In addition, the study-period was limited to 28 days of follow-up. It is unclear whether the treatment resulted in the improvement of clinically meaningful outcomes or benefits commensurate to generally accepted standards of medical practice. In 2021, Kollins and colleagues conducted a multi-center, open-label study of EndeavorRx as an adjunct to pharmacotherapy in a cohort of 8-14-year-old study participants with ADHD on stimulant medication (n=130) and not on any medication for ADHD (n=76). The enrolled participants used EndeavorRx for 4 weeks, followed by a 4-week pause and another 4-week treatment. The primary outcome of interest was change in ADHD-related impairment after 4 weeks as measured by the Impairment Rating Scale (IRS). IRS showed a statistically significant improvement in both cohorts ($p < 0.001$) after 4 weeks. However, it is unclear whether treatment with EndeavorRx generates a clinically meaningful benefit as the minimum clinically important difference (MCID) in childhood ADHD symptoms for the IRS has not been established. Durability of effect also remains to be determined.

FibriCheck®, Qompium, NV

FibriCheck is indicated for self-testing by individuals who have been diagnosed with, or are susceptible to developing, atrial fibrillation and who would like to monitor and record their heart rhythms on an intermittent basis. At present, only a pilot study with limited study participant numbers is published in the peer-reviewed literature (Beerten, 2021). While additional peer-reviewed evidence is available addressing diagnostic validity and performance, there is limited evidence to determine a meaningful impact on clinical outcomes.

Freestira®, Palo Alto Health Sciences, Inc.

Freestira is intended for the treatment of post-traumatic stress disorder (PTSD), panic disorder, panic attacks and other panic symptoms. Treatment entails two 17-minute in-home sessions daily for 4 weeks under the supervision of a licensed healthcare provider.

Freestira was evaluated in a multicenter, single arm trial of 69 adults with panic disorder who received 4 weeks of Capnometry Guided Respiratory Intervention (CGRI) using Freestira, which

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provides feedback of end-tidal CO₂ (PETCO₂) and respiration rate (RR) via a custom sensor device. This intervention is delivered via home use following initial training by a clinician and provides remote monitoring of client adherence and progress by the clinician. Outcomes were assessed immediately post-treatment and at 2- and 12-month follow-up. CGRI was associated with a response rate of 83% and a remission rate of 54%, in addition to large decreases in panic severity. Similar decreases were found in functional impairment and in global illness severity. Gains were largely sustained at follow-up. PETCO₂ moved from the slightly hypocapnic range to the normocapnic range (Tolin, 2017).

In 2020, Kaplan and colleagues evaluated the impact of Freespira over a 12-month period in a cohort of 51 individuals enrolled at a single center. In total, 45 (87%) completed the 4-week, twice-daily Freespira home device treatments and at least 15 of the 56 protocol-specified therapy sessions. By study-end (12 months) just 22 participants were available for complete analysis. Overall, the cohort's Panic Disorder Severity Scale (PDSS) score fell from a baseline median of 14.4 (standard deviation [SD]=3.8) to 4.4 (SD=4.5) at 12 months, and 82% of the cohort reported a PDSS decrease of $\geq 40\%$ (clinically significant) whereas 86% were free from panic attacks.

In 2025, the FDA expanded Freespira's 510(k) clearance to include the treatment of adolescents aged 13-17. This decision was supported by data from the 'Use of a FDA Cleared, Drug-free, Breathing System for Anxiety and Panic Disorders in Children and Teens' clinical trial (NCT02998502). Results from this trial have not been published in a peer-reviewed journal nor presented at a scientific conference.

Currently available evidence evaluation of Freespira lacks comparison to generally accepted standards of medical practice, is limited by sample sizes that do not reflect the prevalence of panic disorder in the general population and is subject to bias from loss to follow-up (Ostacher, 2021).

Halo™ AF Detection System, LIVMOR, Inc.

Halo is a wearable smartwatch device for intermittently monitoring pulse rhythms to detect atrial fibrillation (AF).

While there is no published peer-reviewed evidence at this time evaluating the Halo device, a retrospective propensity-matched cohort study was published in 2021 (Wang) which included 125 individuals with AF using wearables to monitor heart rate and rhythm and 500 with AF who did not use wearables. Study participants were followed for 90 days to compare pulse rate and healthcare use between individuals who wore wearables and those who did not. The study found that prior to propensity matching, those who use wearables were, on average, significantly younger ($p<0.001$) and healthier (composite score of congestive heart failure, hypertension, diabetes, prior ischemic event, vascular disease, age, and gender ($p<0.001$)). After matching, study participants using wearables were found to have similar pulse rates, to those who did not, but utilized significantly more healthcare. In particular, there was a significant difference in receipt of a cardiac ablation, with 17.6% ($n=22$) in the wearables group compared to 7.4% ($n=37$; $p=0.001$) having received an ablation. The study authors conclude, "Given the increasing use of wearables by patients with AF,

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prospective, randomized, long-term evaluation of the associations of wearable technology with health outcomes and health care use is needed.”

Home Vision Monitor®* (HVM; previously myVisionTrack), Vital Art and Science, LLC

Home Vision Monitor is intended for the detection and characterization of central 3 degrees metamorphopsia (visual distortion) in individuals with maculopathy, including age-related macular degeneration and diabetic retinopathy, and as an aid in monitoring progression of disease factors causing metamorphopsia.

Korot and colleagues (2021) studied the Home Vision Monitor in a cohort study of 417 individuals to evaluate uptake and engagement of the application but no published studies have evaluated clinically meaningful outcomes related to use of the software.

Insulia®*, Voluntis, Inc.

Insulia (formerly called Diabeo-Basal, Franc, 2019) is a Software program that recommends basal insulin doses for adults with Type 2 diabetes treated with long-acting insulin analogs as an aid in the management of diabetes based on the treatment plan created by a healthcare provider.

Insulia was evaluated in a 13-month RCT which enrolled a total of 191 participants with inadequately controlled type 2 diabetes who were randomized into three groups: group 1 (standard care, n=63), group 2 (interactive voice response system, n=64) and group 3 (Diabeo-BI app software, n=64). At 4 months follow-up, HbA1c reduction was significantly higher in the telemonitoring groups ($p<0.002$). Fasting blood glucose was reached by twice as many participants in the telemonitoring groups as in the control group, and insulin doses were also titrated to higher levels. No severe hypoglycemia was observed in the telemonitoring groups and mild hypoglycemia frequency was similar in all groups (Franc, 2019). Current data is limited to a short period of evaluation, and the comparison arm’s sample sizes were limited.

In 2020, Franc and colleagues published results of a multicenter RCT to investigate the efficacy of the Diabeo app software (Insulia) in a real word study (TELESAGE study). This open-label trial enrolled 665 individuals who were randomized into one of three parallel study arms: standard of care, Diabeo alone, or Diabeo+telemonitoring. The primary outcome was reduction in HbA1c levels at 12-month follow-up. Participants who used Diabeo one or more times a day demonstrated a significant and meaningful reduction in HbA1c levels compared to the standard of care arm after a 12-month follow-up (mean difference -0.41% in Diabeo alone arm [$p=0.001$] and -0.51% for Diabeo+telemonitoring arm [$p\leq 0.001$]). Adherence rates across all three study arms were very low. In the intention-to-treat population, HbA1c changes and incidence of hypoglycemia were comparable between arms. In this trial, intention-to-treat analyses showed no meaningful benefit, despite post-hoc exploratory analyses demonstrating statistical significance.

iSageRx, AmalgamRx, Inc.

iSageRx is indicated for the management of type 2 diabetes by calculating appropriate long-acting basal insulin doses for titrating insulin levels based on a clinician-prescribed, individualized titration plan. Currently, there is no published peer-reviewed evidence evaluating iSageRx, beyond an

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abstract, which permits reasonable conclusions regarding impact on health outcomes (Grdinovac, 2019).

LumosityRx

LumosityRx is a prescription digital therapeutic indicated for improving attention function in adults aged 22 to 55 years with primarily inattentive or combined-type ADHD; it received FDA 510(k) clearance in 2025 (approved as Prismira). Clearance was supported by the GAMES Study, a randomized, double-blind, sham-controlled trial enrolling approximately 560 adults, which demonstrated statistically significant improvements ($p=0.009$) in sustained and selective attention (TOVA Attention Comparison Score) and clinician-rated improvement on CGI-I, as well as quality of life gains and high adherence over a 9-week period. No serious adverse events were reported. Outcomes from this trial have not been published in the peer-reviewed literature.

MamaLift Plus^{TM,†}

MamaLift Plus is a prescription-only digital therapeutic designed to provide components of CBT for use in the treatment of mild to moderate postpartum depression. In 2024, MamaLift Plus received clearance for marketing by the FDA for individuals 22 years of age and older diagnosed with mild to moderate postpartum depression, as an adjunct to clinician-managed outpatient care. The mobile or tablet-based application's self-guided, interactive treatment modules are designed for daily use over a period of 8 to 9 consecutive weeks (FDA, 2024).

MamaLift Plus FDA clearance was based on unpublished results from the SuMMER (Supporting Maternal Mental health & Emotional Regulation) clinical trial (NCT05958095). SuMMER was a randomized, sham-controlled trial which enrolled 141 participants across 33 states. Study participants were randomized 2:1 to MamaLift Plus and treatment as usual (TAU) or the sham control arm (a digital placebo arm plus TAU). The study was powered to enroll 210 study participants with a planned interim analysis to meet a deadline for FDA input; as a result, the study was stopped at the enrollment of 141 participants. The primary outcome was a 4-point change on the Edinburgh Postnatal Depression Scale (EPDS) scale, which is considered a clinically significant change. In 2025, Dixit and colleagues published the results of the SuMMER trial. Participants were followed for 8 weeks. A significantly higher proportion of MamaLift Plus users met this threshold compared to sham (86.3% vs. 23.9%; $p<0.0001$), with similar differences observed for secondary outcomes including remission to EPDS < 13 and mean change in EPDS score. A total of 4 adverse events were reported across both groups, none of which were serious. Study limitations include short-term follow-up and reliance on self-reported outcomes. Long-term efficacy and prevention of depressive relapse following discontinuation have not been established. Several methodological concerns are worth noting, including that the study was unblinded, treatment as usual was not tracked, and missing data handled was not mentioned in the protocol (missing rates are higher in the sham arm). The long-term benefit of treatment with MamaLift Plus plus TAU on recurrent depression has not been evaluated in studies lasting beyond 8 weeks. The ability of MamaLift Plus to prevent potential depression relapse or recurrent depressive episodes after treatment discontinuation has not been studied.

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Mobile Insulin Dosing System (MIDS), Glooko, Inc.

MIDS is indicated for the management of type 2 diabetes by calculating appropriate long-acting basal insulin doses for titrating insulin levels based on a clinician-prescribed, individualized titration plan. Currently, there is no published peer-reviewed evidence evaluating MIDS which permits reasonable conclusions regarding impact on health outcomes.

My Dose CoachTM, Sanofi, Inc.

My Dose Coach is a smartphone application designed to help users diagnosed with type 2 diabetes titrate their basal insulin according to a clinician-prescribed individualized titration plan. Unnikrishnan (2022) and colleagues conducted a retrospective analysis included 2517 active users; 85% of users were from India, none resided in the US. Two weeks of data was analyzed. Just under 50% of users had high MDC usage and 44% (irrespective of usage frequency) achieved their individual fasting blood glucose target. High use was associated with significantly better fasting blood glucose target achievement and less time to achieve that target compared to the moderate- and low-usage groups ($p < 0.01$ for all). There was no significant difference in hypoglycemia incidence among usage groups. This relatively brief (2 weeks) retrospective trial did not include participants from the US, had limited usage amongst participants and lacked a comparison group.

In 2023, Hermanns and colleagues published results from an open-label, RCT which enrolled 236 individuals diagnosed with type 2 diabetes with a BMI ≥ 25.0 kg/m² who were on basal insulin therapy or were initiating basal insulin therapy, and had suboptimal glycemic control (HbA1c $> 7.5\%$; 58.5 mmol/mol). Completing participants in the intervention group ($n=117$) titrated their basal insulin dose using My Dose Coach for 12 weeks. Control group participants ($n=119$) titrated their basal insulin dose according to a written titration chart. The primary outcome was the baseline-adjusted change in HbA1c at 12 weeks. Investigators reported a between-group difference of -0.31% (95% CI: 0.01%-0.69%; $p=0.04$) in favor of the My Dose Coach group. Study outcomes demonstrated a low-magnitude statistically significant difference but not a clinically significant difference in HbA1c after 12 weeks of My Dose Coach use. Further study is warranted to permit reasonable conclusions regarding My Dose Coach's impact on health outcomes.

NightWareTM, Apple Watch[®]

NightWare is a mobile application that exclusively uses Apple's smartwatch motion and heart rate data to detect the occurrence of nightmares and arouses the wearer by vibrating with the intention of interrupting the nightmare without waking the sleeper. Davenport and colleagues (2022) conducted a 30-day, RCT to determine the efficacy of NightWare in 65 Veterans ($n=30$ in active arm; $n=35$ in control arm) with impaired sleep secondary to trauma-related nightmares. The primary outcome was the Pittsburgh Sleep Quality Index (PSQI). Other measures included self-reported sleep quality, PTSD/depression symptoms, and quality of life. Individuals in both the active and control arms demonstrated statistically significant improvement on all measures relative to their own baseline measures. However, none of the comparisons between arms reached a statistically significant difference. A post hoc analysis that excluded participants with low frequency usage ($<50\%$ of nights) demonstrated a statistically significant ($p=0.016$) improvement in perceived sleep quality (based on the Pittsburgh Sleep Quality Index) amongst the remaining 21 participants in the active arm, relative to 27 control participants. However, in this exploratory analysis of high utilizers, the relevant

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difference (2.2 points on the PSQI) did not reach the relevant MCID (2.5 points). This trial was of short duration, users exhibited low app usage and results did not demonstrate a clinically meaningful difference in the intent-to-treat population.

Oleena[®], Voluntas, Inc.

Oleena received FDA 510K clearance in 2019 as a prescription mobile app designed to help individuals diagnosed with cancer better manage their symptoms as well as enable remote monitoring by care teams. Currently, there is no published peer-reviewed evidence evaluating Oleena which permits reasonable conclusions regarding impact on health outcomes.

ParallelTM, Mahana Therapeutics, Inc.

Parallel (formerly known as Regul8) is a Digital program that uses CBT to reduce the severity of symptoms for irritable bowel syndrome (IBS). It is intended to be used together with other IBS treatments to treat adults, 22 years or older, for up to 3 months.

The premise behind Parallel (web-based CBT) was evaluated in the Assessing Cognitive behavioural Therapy for IBS (ACTIB) trial, a three-arm, RCT in which 558 participants were enrolled into either a telephone-delivered CBT (TCBT; n=186) group, web-based CBT (WCBT; n=185) group with minimal therapist support, or treatment as usual (TAU, n=187) (Everitt 2019a). Both intervention groups continued to also receive treatment as usual. The primary outcomes of interest were IBS Symptom Severity Score (IBS-SSS) and Work and Social Adjustment Scale (WSAS) at 12 months. At study end, 27% of the TCBT arm, 73% of the WCBT arm, and 30% of the TAU group were lost to follow-up. Of the remaining study participants, compared with TAU, IBS-SSS and WSAS scores were significantly lower in the TCBT group (both scores $p<0.001$) and the WCBT group ($p=0.002$ and $p=0.001$, respectively) at 12 months. There were no serious adverse reactions to any interventions. The study was limited by a substantial loss to follow-up and the dissimilarities between the interventions in the study and the Parallel application. Also, comparison to in-person CBT is lacking.

Everitt and colleagues (2019b) conducted a 24-month follow-up to the ACTIB trial, at which time, 58% (n=323 of the original 558 participants remained). At 24 months the IBS-SSS score was significantly lower in the TCBT group ($p=0.002$) relative to TAU but the differences in the WCBT group were not sustained ($p=0.33$). Similarly, the mean WSAS score was lower in the TCBT group ($p<0.001$) but differences in the WCBT group fell to marginal significance ($p=0.036$) relative to the TAU group. Given the continued substantial loss to follow-up and loss in significance in the WCBT group (more comparable to the Parallel application software design than TCBT), the efficacy of the application as an intervention for refractory IBS, remains to be established.

Regulora[®], metaMe Health Inc.

Regulora provides gut-directed hypnotherapy for adults 22 years of age and older who have been diagnosed with IBS. Regulora is indicated as a 3-month treatment for individuals with abdominal pain due to IBS and is intended to be used together with other IBS treatments.

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In 2023, Berry and colleagues published results of an open-label RCT in which 362 adults with IBS were enrolled to compare the safety and efficacy of Regulora with that of digital muscle relaxation accessed via a mobile app on a smartphone or tablet. The primary endpoint was reduction in self-reported abdominal pain (defined as $\geq 30\%$ reduction from baseline in average daily abdominal pain intensity) during the 4-week follow-up period. Study authors report an improvement in the Regulora group, however no significant difference between the two study groups was found ($p=0.54$). Further investigation is warranted.

Rejoyn™, Otsuka America Pharmaceutical, Inc.

Rejoyn is a smartphone-based digital therapeutic designed to be used by individuals diagnosed with major depressive disorder (MDD) to administer 6 weeks of CBT and emotion-focused mindfulness therapy (EFMT). Following the initial 6-week treatment period the CBT modules were available for repeat viewing for up to 4 additional weeks. In 2024, Rejoyn received 510K clearance from the FDA for the treatment of MDD as an adjunct to clinician-managed outpatient care for adults ages 22 years and older who are being treated with antidepressant medication (FDA, 2024).

The FDA clearance of Rejoyn was based on unpublished results from the remotely conducted Mirai trial, a multicenter, double-blinded RCT (NCT04770285). The primary objective of Mirai was to evaluate the effectiveness of Rejoyn in reducing depressive symptoms. The study's primary efficacy endpoint was the change in the Montgomery-Asberg Depression Rating Scale (MADRS) total score at week-6. Report of study outcomes are pending peer-reviewed publication.

reSET® and reSET-O®, PursueCare

reSET® and reSET-O are mobile device software applications intended to increase retention of individuals with opioid use disorder (OUD) and substance use disorder in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment, for individuals 18 years or older who are currently under the supervision of a clinician.

ReSET-O was evaluated in a randomized, unblinded, parallel trial conducted in 170 opioid-dependent adults who received supervised buprenorphine treatment paired with a behavior therapy program, with or without the addition of a desktop-based version of reSET-O, which was accessed at the clinic 3 times a week for 30 minutes per visit. At study-end (12 weeks), participants who used the desktop computer version of reSET-O had an overall retention rate of 80 percent compared with 64 percent overall retention rate for those who did not. Use of reSET-O was not shown to decrease illicit drug use or improve abstinence compared to the control group (Christensen, 2014). A secondary analysis of the pivotal study data reported outcomes of treatment retention and abstinence relative to 'treatment as usual' but was hampered by the same study limitations (Maricich, 2020a).

In 2020, Velez and colleagues reviewed retrospective pharmacy and medical claims data from commercial, Medicare and Medicaid databases (2018-2019). Ultimately, 334 study participants were included who activated reSET-O, and were continuously enrolled in their medical plan for at least 4 weeks of the 6-month pre-activation and post-activation periods. Despite the abundance of clinically significant pre- and post-activation measures reported (including but not limited to, inpatient encounters [45 less; $p=0.03$], emergency department visits [27 less; $p=0.25$] psychiatry encounters

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[349 less; $p < 0.04$], case management encounters [176 additional; $p = 0.59$], behavioral health services [111 additional; $p = 0.12$], alcohol and substance abuse services [96 less; $p = 0.35$], and mental health services [61 additional; $p = 0.10$]), some were only marginally statistically significant while most were not significant (i.e., $p\text{-value} > 0.05$), with the exception of 638 less drug test events recorded post reSET-O activation ($p < 0.001$) an outcome that may not be desirable in this clinical scenario. Claims data also revealed of the 240 participants who had pharmacy claims data, pre-/post-activation medication possession ratios increased from 0.73 to 0.82, respectively ($p = 0.004$); however, possession of buprenorphine is unlikely to be a valid surrogate measure for medication adherence. In this real-world clinical scenario, generalizability is lacking ($> 80\%$ Medicaid enrollees), mortality data (a crucial outcome in this setting) is not reported and reSET-O's ability to impact health behaviors or clinically relevant outcomes was not demonstrated.

In another pragmatic, retrospective evaluation, Maricich and colleagues (2020b) enrolled 3144 individuals upon their downloading the reSET-O application to their personal device. Engagement and therapeutic use data were collected and analyzed on a population, versus individual, level. Substance use was evaluated using a composite measure of self-reported data collected by reSET-O and urine drug screens which were nonuniformly administered by different clinic sites. When excluding participants with missing data from analysis, the abstinent rate (defined as abstinent in the last 4 weeks of treatment) was observed to be 91%, when missing data was considered 'positive' the abstinence rate was 66%. Just 29% of the study population used reSET-O appropriately and consistently for the first 4 weeks (completed 4 or more modules per week), thus adherence to reSET-O's proper use was low in this very large, real-world cohort. The study outcomes relied on self-report, lacking clinically meaningful measures beyond urine drug screens which were not routinely measured across study sites.

In 2020, the Institute for Clinical and Economic Review (ICER) published an evidence report which included published data, to date, evaluating the reSET-O. ICER concluded, "We found no randomized trials, cohort studies or case series that evaluated the DHTs [digital health technologies] reviewed in this report until after the draft report was released. Recently, two uncontrolled studies suggested potential benefits with reSET-O, but there was a high risk of bias for both studies."

Current data is limited to short-term follow-up, and impact on net health outcomes has not been demonstrated. Few of the published studies assess the use of the reSET-O when used outside of a clinic (for example, when downloaded directly to a personal device such as a mobile phone or tablet).

SleepCheckRx, Resapp Health Ltd

SleepCheckRx is a mobile software system that screens adults for the risk of moderate to severe OSA by analyzing breathing and snoring sounds recorded on an Apple iPhone. Currently there is no peer-reviewed published data on SleepCheckRx which permits reasonable conclusions regarding impact on health outcomes.

SleepioRx, Big Health

SleepioRx is a digital therapeutic intended for the improvement of poor sleep and the management of insomnia disorder in adults aged 18 years and older, as an adjunct to their usual medical care.

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SleepioRx received 510(k) FDA clearance in 2024 after evaluation in a pivotal 24-week, single-blind RCT to examine the effect of the website or app version on daytime functioning, mental health, and sleep compared to sleep hygiene education (SHE). The trial enrolled 1711 adults who screened positive on *DSM-5* criteria for chronic insomnia disorder, and randomized participants to either SleepioRx (n=853) or SHE (n=858) for up to 12 weeks of treatment. The self-reported demographics reflected a population sample that was 78% female, 91% White and a mean age of 48 years. The SleepioRx arm received 6 sessions of the program, lasting around 20 minutes each. The control group received a web page and materials that could be downloaded by users at their own pace. At 24 weeks, sleep-related quality of life scores measured by the Glasgow Sleep Impact Index favored SleepioRx ($p<0.01$). Non-response rates at 24 weeks for control and SleepioRx arms were 42% and 52%, respectively, a significant difference ($p<0.01$) that threatens the study's internal validity. Investigators state that non-respondent sensitivity analyses were performed but little detail of these analyses were described. Study limitations include limited external validity of the sample, high non-respondent rates, differential participation by study arm and limited reporting on statistical methods used to account for missing data (Espie, 2018).

In 2025, Prather and colleagues published results from a randomized, double-blind trial comparing SleepioRx to online sleep hygiene education (SHE) in 336 U.S. adults (22 and older) meeting *DSM-5* criteria for insomnia disorder. Participants were followed for 24 weeks. At study end, scores on the Insomnia Severity Index (ISI) significantly favored SleepioRx, with a 23% absolute increase in ISI-defined remission ($ISI < 8$) compared to control (OR, 5.0; 95% CI, 1.9-13.0; $p<0.001$). Wake after sleep onset (WASO) also improved significantly, while differences in sleep onset latency (SOL) were not sustained over time. No serious adverse events were reported. Strengths of the study include sham control, masked hypothesis design, and appropriate handling of missing data. However, results are limited by reliance on self-reported outcomes, absence of objective sleep measures, and short-term follow-up (24 weeks). Importantly, 84% of individuals initially deemed eligible were excluded prior to randomization for failing to complete both a 7-day sleep diary and video call, a demanding protocol step that may disproportionately exclude individuals with lower health literacy, digital access barriers, or competing life demands. This raises serious concerns about generalizability, particularly for a digital therapeutic intended for broad use. Additionally, the mean baseline sleep duration in the study population was 7.1 hours per night, which does not reflect clinically meaningful sleep restriction and suggests that participants may not represent the population most in need of intensive insomnia treatment. The trial used sleep hygiene education (SHE) as the control, despite its weak evidence base. Notably, the 2021 American Academy of Sleep Medicine (AASM) guideline provides a conditional recommendation against SHE as a single-component therapy, citing its minimal efficacy and potential to delay access to effective treatment. The guideline also makes a strong recommendation for multicomponent, clinician-delivered CBT-I as the first-line treatment for chronic insomnia disorder in adults, it states, "In-person one-on-one delivery of CBT-I by a trained CBT-I provider is the most widely evaluated delivery method and is generally considered the best available treatment." Use of this established standard of care as the comparator would have allowed for a more meaningful assessment of SleepioRx's clinical value. Although the guideline did review studies using various delivery formats, it concluded: "There was insufficient evidence to make recommendations for specific delivery methods (eg, individual, group, internet, self-help, video) for any of the treatments" (Edinger, 2021). Meaningful uncertainties

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remain regarding SleepioRx's effectiveness in real-world settings and its equivalence to established therapeutic alternatives.

In addition to the randomized trials summarized above, a number of additional peer-reviewed studies have evaluated SleepioRx across a range of populations and clinical settings, consistently reporting improvements in subjective sleep outcomes. Across this body of literature, results consistently show statistically significant improvements in subjective sleep outcomes favoring SleepioRx. However, outcomes are uniformly self-reported and comparators are low-intensity or waitlist. The evidence base lacks robust objective sleep data, and generalizability is limited in several trials due to population homogeneity (e.g., primarily White, female, highly educated). Attrition rates, particularly among underserved subgroups, were not uniformly reported and may affect the reliability of observed treatment effects. Few studies followed participants beyond 6 months, and most were not powered to detect adverse events (Barnes, 2017; Bostock, 2016; Cheng, 2019; Denis, 2020; Felder, 2020; Fleming, 2024; Freeman, 2017; Ho, 2022; Kalmbach, 2020; Kyle, 2020; Manber, 2024; McGrath, 2017; Pillai, 2015).

Stanza, Swing Therapeutics, Inc.

Stanza is a self-guided, smartphone-based digital therapeutic developed by Swing Therapeutics, Inc. that delivers Acceptance and Commitment Therapy (ACT) for individuals diagnosed with fibromyalgia. In May 2023, the FDA granted De Novo marketing authorization for Stanza as the first prescription digital therapeutic indicated for the treatment of fibromyalgia symptoms (FDA, 2023). The authorization was supported by data from an RCT (PROSPER-FM), a single-arm decentralized study (REACT-FM), and a 12-month extension study (REACT-FM-X).

In 2024, Gendreau and colleagues published results from the pivotal trial supporting this authorization, which was the PROSPER-FM study, an RCT conducted across 25 U.S. sites. A total of 275 adults aged 22-75 years with fibromyalgia were randomized to either the digital ACT program (n=140) or an active control consisting of symptom tracking and access to educational materials (n=135). Of the 275 participants randomized, 120 of 140 (86%) in the digital ACT group and 130 of 135 (96%) in the active control group completed the 12-week intervention, resulting in an overall attrition rate of 9.1%, with higher discontinuation observed in the digital ACT arm. The primary endpoint was improvement on the Patient Global Impression of Change (PGIC) scale at 12 weeks. At study end, 71% of remaining participants in the ACT group reported improvement on PGIC compared with 22% in the control group, a statistically significant between-group difference of 48.4% (95% CI, 37.9%-58.9%; $p<0.0001$). No device-related adverse events were reported. Limitations include the use of a subjective outcome measure (PGIC) as the primary endpoint and a potential imbalance in therapeutic intensity between the intervention and control arms, which may have contributed to observed differences.

Prior to PROSPER-FM, the digital ACT program was evaluated in a single-arm study (REACT-FM), the results of which were reported in abstract form at the 2022 American College of Rheumatology (ACR) Annual Meeting. In an interim analysis of 32 participants, 84% reported improvement on PGIC, with 47% reporting they were "much" or "very much" improved. Statistically significant improvements were observed across all measured domains, including FIQ-

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R, pain interference, sleep disturbance, depression, and quality of life. No device- or study-related adverse events were reported (Dai, 2022).

Long-term durability of effect was evaluated in a 12-month extension study (REACT-FM-X), which enrolled 41 of 60 eligible participants who had completed the original 12-week PROSPER-FM trial. At the 12-month follow-up, the PGIC response rate remained stable at 80.0%, and gains in pain interference, depression, sleep disturbance, and quality of life observed at 12 weeks were sustained. These findings were presented in abstract form at the 2025 Society of Behavioral Medicine (SBM) Annual Meeting but have not been published in the peer-reviewed literature (Shumay, 2025)

Supplemental Information

Definitions

Acceptance and Commitment Therapy (ACT): A form of cognitive behavioral therapy (CBT) that aims to improve psychological flexibility- the ability to engage in meaningful behavior while experiencing difficult thoughts, emotions, or sensations.

Cognitive behavioral therapy (CBT): A form of talk therapy that has proven effective for a variety of behavioral health issues. CBT focuses on helping individuals identify and modify unhelpful thinking and behavior patterns, fostering resilience and promoting healthier mental processes.

Mobile application (mobile app): Software application that can be executed (run) on a mobile platform (i.e., a handheld commercial off the-shelf computing platform, with or without wireless connectivity), or a web-based software application that is tailored to a mobile platform but is executed on a server.

Mobile platform: Commercial off-the-shelf (COTS) computing platforms, with or without wireless connectivity, that are handheld in nature (e.g., mobile computers such as smart phones, tablet computers, or other portable computers).

Off-the-self: As purchased or as commonly available, without modification or customization.

Over-the-counter: Non-prescription therapeutic device, test, software, or other product.

Software: A set of instructions, data or programs used to operate a computing device and execute specific tasks; a generic term used to refer to applications, scripts and programs.

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11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. New policy.
03/21/2022	Coding update
11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. Title changed to Digital Health Therapies for Substance Use Disorders. No change to coverage.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Title changed to Mobile Device-Based Health Management Applications. Entire policy rewritten.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Added AspyreRx and FibriCheck applications to body of policy.
07/03/2025	Medical Policy Committee review
07/09/2025	Medical Policy Implementation Committee approval. No change to coverage. DaylightRx, Big Health, Inc., MamaLift Plus™ Curio Digital Therapeutics, Inc., Rejoyn, Otsuka America Pharmaceutical, Inc., reSET® and reSET-O®, PursueCare, LLC., Sleepio® Rx, Big Health, Inc., added to table and background for support.
04/01/2026	Coding update
07/02/2026	Medical Policy Committee review
07/08/2026	Medical Policy Implementation Committee review
07/16/2026	Medical Quality Management Committee approval. Added the following:

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“The use of mobile-based health management applications when the coverage eligibility criteria have not been met is considered to be not medically necessary, including when the requested application constitutes duplication of services (e.g., the requested service duplicates another service or intervention that provides the same clinical function or therapeutic intent, or provides substantially similar clinical function or therapeutic effect as another covered or available intervention without evidence of incremental clinical benefit).”

Next Scheduled Review Date: 07/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	99199
HCPCS	A9291, A9294, T1505
ICD-10 Diagnosis	All Related Diagnoses

****Medically Necessary** (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

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- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.