LifeWise
Health Plan of Washington

MEDICAL POLICY – 13.01.500

Prescription Digital Therapeutics

BCBSA Ref. Policy: 3.03.02

Effective Date:	Oct. 1, 2024
Last Revised:	Sept. 10, 2024
Replaces:	N/A

RELATED MEDICAL POLICIES:

3.03.01	Prescription Digital Health Diagnostic Aid for Autism Spectrum Disorder
3.03.03	Prescription Digital Therapeutics for Attention Deficit/Hyperactivity Disorder
5.01.643	Prescription Digital Therapeutics for Substance Use Disorder
10.01.523	Preventive Care

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Prescription digital therapeutics (PDTs) are software applications that are prescribed by a licensed healthcare practitioner who is legally authorized to prescribe medications and devices in the states in which they practice. They are used on mobile devices such as a mobile phone, tablet, smartwatch, or laptop computer. The goal of prescription digital therapeutics is to evaluate, diagnose, manage symptoms, or treat an illness, injury, or disease. Other types of software applications are used for general wellness and do not require a prescription by a health care practitioner. These are not reviewed in this policy. This policy describes when prescription digital therapeutics may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Service	Medical Necessity
Prescription digital therapeutics	**Prescription digital therapeutics are considered medically necessary when ALL of the following criteria in A and B have been met:** **A. Criteria to evaluate the prescription digital therapeutic:** ○ The prescription digital therapeutic has been approved by the Food and Drug Administration (FDA); **and** ○ There is credible scientific evidence* which permits reasonable conclusions regarding the impact of the prescription digital therapeutic on health outcomes; **and** ○ The prescription digital therapeutic has been proven to improve the net health outcome or is considered as beneficial as another established alternative. (See **Related Policies**) **AND** **B. Criteria to evaluate the appropriateness of the prescription digital therapeutic for the individual:** ○ The prescription digital therapeutic requires a prescription by a licensed healthcare practitioner; **and** ○ There is documentation supporting that the prescription digital therapeutic was ordered for a covered purpose such as preventing, evaluating, diagnosing, or treating an illness, injury or disease or its symptoms and in accordance with generally accepted standards of medical practice**; **and** ○ The requested prescription digital therapeutic is not primarily for the convenience of the individual, physician, or health care provider ***Note:** Credible scientific evidence means well-designed, well conducted investigations published in peer-reviewed journals that demonstrate the technology can measure or alter physiological or psychological changes

Service	Medical Necessity
	related to a disease, injury, illness, or condition and that these changes positively affect health outcomes for an extended period of time. **Note: Generally accepted standards of medical practice mean standards that are based on reliable 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.

Service	Investigational
Prescription digital therapeutics	**Prescription digital therapeutics are considered investigational when ALL of the above criteria are not met.** **FDA approved prescription digital therapeutics that are considered investigational include, but are not limited to, the following: (this list may not be all inclusive)** • BlueStarRx System • Canvas Dx autism diagnosis aid (See **Related Policies**) • CureSight CS 100 System • d-Nav Insulin Management Program • EndeavorRx (See **Related Policies**) • EpiMonitor • HaloAF Detection System • Insulia Diabetes Management Companion • Ieva Pelvic Digital Health System • Luminopia One • Mahana for irritable bowel syndrome • MamaLift Plus • MindMotion GO • My Dose Coach • NightWare (See **Related Policies)** • Regulora for irritable bowel syndrome • Rejoyn • RelieVRx • ReSet (See **Related Policies)** • ReSet-O (See **Related Policies)** • RevitalVision

Coding

Note: Please see 10.01.523 Preventive Care for FDA approved or cleared mobile apps related to contraception and birth control that are prescribed by a health care provider.

Code	Description
CPT	
0687T	Treatment of amblyopia using an online digital program; device supply, educational set-up, and initial session (used to report RevitalVision)
0688T	Treatment of amblyopia using an online digital program; assessment of patient performance and program data by physician or other qualified health care professional, with report, per calendar month (used to report RevitalVision)
0704T	Remote treatment of amblyopia using an eye tracking device; device supply with initial set-up and patient education on use of equipment (used to report CureSight CS 100)
0705T	Remote treatment of amblyopia using an eye tracking device; surveillance center technical support including data transmission with analysis, with a minimum of 18 training hours, each 30 days (used to report CureSight CS 100)
0706T	Remote treatment of amblyopia using an eye tracking device; interpretation and report by physician or other qualified health care professional, per calendar month (used to report CureSight CS 100)
0740T	Remote autonomous algorithm-based recommendation system for insulin dose calculation and titration; initial set-up and patient education (used to report d-Nav Insulin Management Program)
0741T	Remote autonomous algorithm-based recommendation system for insulin dose calculation and titration; provision of software, data collection, transmission, and storage, each 30 days (used to report d-Nav Insulin Management Program)
99199	Unlisted special service, procedure or report
HCPCS	
A9291	Prescription digital cognitive and/or behavioral therapy, FDA-cleared, per course of treatment (used to report ReSet and ReSet-O)
A9292	Prescription digital visual therapy, software-only, FDA cleared, per course of treatment (used to report Luminopia)
A9999	Miscellaneous DME supply or accessory, not otherwise specified
E1399	Durable medical equipment, miscellaneous

Code	Description
E1905	Virtual reality cognitive behavioral therapy device (CBT), including pre-programmed therapy software (used to report RelieVRx)
S9002	Intravaginal motion sensor system, provides biofeedback for pelvic floor muscle rehabilitation device (used to report Leva Pelvic Health System) (new code effective 4/1/2024)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Definition of Terms

Digital therapeutics (DTx): Deliver therapeutic, evidenced-based interventions driven by software to treat, manage, and prevent a broad spectrum of behavioral, mental, and physical diseases and disorders.[12]

Direct to consumer: products that are sold directly to customers, commonly online via the internet, but may include products sold via a television, print advertisements, a brick-and-mortar store, or other marketing venues. These products typically do not require a prescription.

Mobile application (app): A software application designed to run on a mobile device (off the-shelf commercial computing platform that is handheld, with or without wireless connectivity), or an internet-based software application tailored to a mobile platform but run on a server.

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

Off-the shelf: As purchased or as commonly available without modification or customization; taken from existing stock or supplies.

Over-the counter: Therapeutic interventions that do not require a prescription.

Software: A set of instructions or programs that instruct a computing device on how to work and what to do.

Benefit Application

Digital therapeutics that are available "over the counter" or without a prescription are generally excluded from most Plans, even if they are ordered by a licensed healthcare practitioner. Please see the individual contract Plan language for specific benefit determination.

Some health plans or employer groups may choose to cover digital therapeutics that do not meet the criteria of this policy or are excluded from coverage under the health plan benefits. Such coverage is considered to be separate from benefits available under the health plan. If coverage is requested utilizing benefits under the health plan, the criteria of this policy will apply.

Evidence Review

Description

Prescription digital therapeutics are software applications that are prescribed by a licensed healthcare practitioner and used on a mobile device such as a mobile phone, tablet, smartwatch, or laptop computer with the intent of evaluating, diagnosing, or treating an illness, injury, disease or its symptoms.

Background

There has been an explosion of health and wellness apps in the last decade, but many of these apps do little more than track activities such as sleep or exercise, calculate calories eaten, or monitor heart rate or weight trends. Digital therapeutics, however, are different in that they are evidenced-based, software-driven interventions that are used to evaluate, diagnose, or treat a particular illness, injury, or disease or its symptoms. Currently, digital therapeutics are being used and evaluated for a plethora of medical and behavioral health conditions. Rather than just gathering data, these software applications are proposed to actually affect the treatment of individuals. Services available through digital therapeutics may complement and add value to the traditional healthcare delivery system but they also offer new challenges such as burdening physicians with having to learn new technology for many different applications and be overloaded with data that requires interpretation, increased cybersecurity risks for individuals' healthcare and personal data, and lack of acceptance among the elderly due to inexperience

with digital platforms. The field of prescription digital therapeutics is rapidly evolving and with it comes many opportunities to improve access to healthcare and perhaps lower healthcare costs, but at the same time, these software applications need to be held accountable to the same levels of scientific review and oversight that are expected of traditional medical treatments.

To provide some type of framework to evaluate and review the clinical evidence, safety and efficacy of these products, the International Medical Device Regulators Forum, a consortium of medical device regulators from around the world, which is led by the FDA, distinguishes between 1) software in a medical device and 2) software as a medical device (SaMD). The Forum defines SaMD as "software that is intended to be used for one or more medical purposes that perform those purposes without being part of a hardware medical device".[29]

FDA's Center for Devices and Radiological Health has taken a risk-based approach to regulating SaMD. Medical software that "supports administrative functions, encourages a healthy lifestyle, serves as electronic individual records, assists in displaying or storing data, or provides limited clinical decision support, is no longer considered to be and regulated as a medical device".[48]

Regulatory review is focusing on mobile medical apps that present a higher risk to individuals.

- The FDA is not enforcing compliance for lower risk mobile apps such as those that address general wellness.
- The FDA is not addressing technologies that receive, transmit, store, or display data from medical devices.

The agency has launched a software pre-cert pilot program for SaMD that entered its test phase in 2019. Key features of the regulatory model include the approval of manufacturers prior to evaluation of a product, which is based on a standardized "Excellence Appraisal" of an organization, and its commitment to monitor product performance after introduction to the US market. Criteria include excelling in software design, development, and validation. Companies that obtain pre-certification participate in a streamlined pre-market review of the SaMD. Pre-certified organizations might also be able to market lower-risk devices without additional review. In 2017, the FDA selected 9 companies to participate in the pilot program out of over 100 applications: Apple, Fitbit, Johnson & Johnson, Pear Therapeutics, Phosphorus, Roche, Samsung, Tidepool, and Verily.

Other organizations have initiated similar efforts to develop a framework for evaluation of the myriad digital therapeutics that are coming to market. The American Medical Association stated in their proposed guidelines for safe, effective mobile health apps, "mobile health technologies should have a high-quality clinical evidence base to support their use in order to ensure mobile health app safety and effectiveness." The proposed guidelines note some mobile apps are

subject to FDA regulation, while others are not and do not undergo rigorous evaluation before deployment for general use. This raises a concern for the safety and quality of the mobile apps that are available to the public.[4] The American Psychiatric Association developed The App Evaluation Model which poses questions for consideration when selecting and using a particular app.[5] Other regulatory authorities such as the United Kingdom's National Institute for Health and Care Excellence (NICE) have also proposed standards to evaluate SaMD.[46]

The types of prescription digital therapeutics addressed in this policy are ones that have received FDA de novo premarket pathway, 510(k) clearance, or pre-market approval, are prescribed by a licensed healthcare practitioner, and the intent of the digital therapeutic is to evaluate, diagnose, or treat an illness.

Prescription Digital Therapeutics

BlueStarRx System (WellDoc, Inc.) is a software app for use on mobile phones or personal computers for individuals 18 years of age or older who have type 1 or type 2 diabetes. It enables the user to input personal health information and captures, stores, and transmits blood glucose data. The system analyzes and reports blood glucose test results and provides coaching messages (motivational, behavioral, and educational) driven by clinical guidelines based on real-time blood glucose values including daily medication administration, physical activity, and smart food choices. It can connect to certain glucose meters via Bluetooth (e.g., One Touch, Accu-Chek, Contour, as well as the Dexacom CGM system). The BlueStarRx includes an insulin dose calculator that allows individuals to use their prescribed insulin regimen to calculate doses of mealtime insulin for a given amount of carbohydrates and/or blood glucose value taking into consideration factors such as the insulin: carbohydrate (I:C) ratio, insulin sensitivity factor, or programmed sliding scale. The BlueStarRx also includes an Insulin Adjustment Program (IAP) which calculates appropriate long-acting basal insulin doses for titrating insulin levels based on configuration by a healthcare provider (the healthcare provider must activate and configure the IAP for individual-specific parameters). This function will then recommend the next long-acting dose based on a target blood glucose, hypoglycemia events, or other factors. Healthcare providers can view individual-generated data and dialogue with individuals through a care management portal. It is available by prescription only. (Note the BlueStar System that does not include the insulin dose calculator is available without a prescription).

CureSight CS 100 System (NovaSight, Ltd.) is an eye-tracking-based system designed to improve visual acuity and stereoacuity using a binocular therapy to train the visual system to use

both eyes simultaneously. It is designed for pediatric patients aged 4 to ≤ 9 years diagnosed with amblyopia for in-home use. CureSight consists of red-blue treatment glasses that are worn over full-time refractive correction (i.e., glasses), a dedicated computer with video display, and a cloud platform with real-time remote compliance monitoring. During a treatment session, the child wears the red-blue glasses while watching personally selected streaming videos (e.g., Disney, Netflix, Prime Video, Hulu, History Channel, and National Geographic) from the computer touchscreen display. The streaming video is presented in different colors for each eye and altered by the software algorithm using embedded eye-tracking and image-processing sensors by blurring the images in the center of vision of the dominant eye, while the amblyopic eye receives normal, sharp images, thereby encouraging the visual system to integrate the visual information to have both eyes working together simultaneously. The cloud platform monitors in real-time patient compliance and progress and provides a treatment summary and progress report to the prescribing eye care provider. Treatment sessions are 90 minutes per day, 5 days a week for 16 weeks for an overall cumulative time of 120 hours. This treatment is seen as an alternative to conventional patching of the non-amblyopic eye. The CureSight Monitoring Center aids with initial installation and set-up along with providing training and technical support if needed. CureSight is available by prescription only.

d-Nav Insulin Management Program (Hygieia, Inc.) is an insulin management program for adult individuals with type 2 diabetes who are using insulin and have an A1C above their treatment goal by providing the next insulin dose recommendation. The program does this through two user-interactive software elements: 1) a mobile phone app is used by the individual to enter glucose event data which then prompts a recommended insulin dose. The blood glucose data is obtained from a cleared blood glucose device and entered manually into the software system or via a cloud-pushed mechanism from a linked blood glucose meter. 2) the d-Nav website is used by trained health care providers that set up the individual's software with starting insulin dose instructions that includes the treatment plan algorithm, insulin drug, and doses. The d-Nav program also provides the Get-Dose library that provides the next insulin dose based on comparing blood glucose data trends to a device specified target range. The program can be implemented either in the cloud (deployed on Amazon Web Services) or on a mobile phone. It is available by prescription only.

EndeavorRx (Akili Interactive Labs, Inc.) is a digital, non-drug treatment delivered through an action video game on a mobile device proposed to improve attention function in children with attention-deficit hyperactivity disorder (ADHD). The treatment is a proprietary and patented technology that is purported to activate specific neural systems in the brain which play a key

role in attention function. The platform algorithms automatically adjust the difficulty level in real time and between treatment sessions to challenge an individual to an optimal level of performance. The individual plays a video game on a tablet or smartphone for thirty minutes, five days per week for four weeks to improve attention and the ability to focus on multiple tasks. It is available by prescription only.

EpiMonitor (Empatica Inc.)-is a non-EEG physiological signal-based seizure monitoring system. It is composed of a wearable medical device worn on the wrist called EmbracePlus that is paired with a mobile software application which runs on a smartphone called EpiMonitor. The EmbracePlus collects via sensors Electrodermal Activity (EDA) and motion data to detect patterns that may be associated with primary or secondary generalized tonic clonic seizures in patients with epilepsy or at risk of having epilepsy. This data is then analyzed by an algorithm that determines if the user is undergoing a generalized tonic-clonic seizure. If a seizure is detected, the EmbracePlus sends a message to the EpiMonitor via Bluetooth through the Empatica Cloud with a voice call or text message to a designated caregiver. Besides initiating alerts, the EpiMonitor app receives all the raw sensor data collected by the EmbracePlus such as physiological parameters of EDA, activity during sleep, and peripheral skin temperature and transmits this data to the Empatica Cloud where it is stored and made available to the prescribing health care provider. It is available by prescription only for adults and children 6 and older.

Halo AF Detection System (LIVMOR Inc.) monitors pulse rhythms for the detection of atrial fibrillation via a compatible Samsung smartwatch worn at night while the user is resting or on demand during the day. The software for this device is based on an algorithm which filters and detects irregular pulse rhythms that may be suggestive of atrial fibrillation from photoplethysmography (PPG) data. The PPG signals recorded by the smartwatch are then analyzed by the LIVMOR Halo + Home Monitoring System tablet when connected to WIFI. When a signal is suggestive of AF, the rhythm is flagged for physician review through a cloud-based portal. It is available by prescription only.

Insulia Diabetes Management Companion (Voluntis) is available via a mobile app or web portal and recommends basal insulin doses for adults with type 2 diabetes based on the treatment plan created by an individual's healthcare provider. The program takes into account the individual's profile entered, blood glucose checks, and any entered hypoglycemic events and

recommends a tailored dose in real-time. Dose explanations for every recommended dose are available detailing how the calculation was made. Educational coaching messages may be given, and physicians can remotely monitor an individual's progress and adjust their treatment plan as needed. It is available by prescription only.

Ieva Pelvic Digital Health System (Renovia, Inc.) is a battery powered, intravaginally used wand device with motion sensors that facilitates pelvic floor exercise training to strengthen pelvic floor muscles for the treatment of stress, mixed, and mild to moderate urgency urinary incontinence in women, including overactive bladder. It may be used repeatedly by a single individual. The device interacts with the user via a smart phone app and Bluetooth technology enabling the user to visualize their exercise performance to help the individual target the muscles used to help maintain continence. The app provides programmed coaching sessions to optimize pelvic floor muscle training. The individuals perform the exercises while standing twice a day for 2.5-minute sessions for up to 12 weeks. These sessions can be tracked, reviewed, and shared with the prescribing healthcare professional. It is available by prescription only.

Luminopia One (Luminopia, Inc) is a software-only digital therapeutic used with a compatible, commercially available virtual reality headset (Head-Mounted Display) (Samsung Gear HMD). Luminopia One is indicated for improvement in visual acuity in amblyopia patients, aged 4 to 7 years, associated with anisometropia and/or mild strabismus. Luminopia One is to be used as an adjunct to full-time refractive correction, such as glasses, which should be worn under the virtual realilty headset during Luminopia One therapy. Treatment is provided through algorithmic modifications to over 700 hours of popular tv shows and movies that can be selected to encourage use of the amblyopic eye. The selected video exhibits a modified version of the original through each eye to rebalance the visual input to the eyes and encourage the weaker eye usage. Selected videos are to be watched 1 hour per day, 6 days per week for a total of 12 weeks. An online Patient Portal is also available for a caregiver to select/block videos and monitor a patient's compliance and progress with the prescribed treatment. It is prescribed by a trained eye-care professional and is to be used in the home.

Mahana for IBS (previously Parallel or Regul8) (Mahana Therapeutics, Inc.) is a mobile application designed to deliver a three-month program of Cognitive Behavioral Therapy (CBT) for individuals aged 22 years or older with irritable bowel syndrome (IBS). The skills taught are to help build a healthier brain-gut relationship by tracking symptoms, managing flare-ups,

changing behaviors, and personalizing helpful techniques for symptom relief such as relaxation, improving eating habits, reducing stress, managing emotions differently, and reducing unhelpful thoughts. The program is to be used as an adjunctive treatment with other treatments for IBS to reduce the severity of symptoms associated with IBS. The mobile application is to be used daily for 10 minutes. The program consists of 10 sessions with multiple lessons in each session. The skills taught are to be practiced outside of the app use. It is available by prescription only.

MamaLift Plus (Curio Digital Therapeutics Inc.)-is a digital therapeutic designed to treat symptoms of postpartum depression through software on a mobile application such as a smartphone or tablet that delivers therapeutic components of Cognitive Behavioral Therapy (CBT). The content is delivered via eight self-guided and interactive treatment modules that are to be used daily over an eight-to-nine-week period at the rate of one module per week. MamaLift Plus includes a daily tracker where self-reports of sleep, energy level, activity, and mood can be tracked. It also includes a clinician dashboard where a summary of the patient's usage and progress can be monitored by the prescribing healthcare provider. It is to be used as an adjunct to clinician-managed outpatient care to treat mild to moderate postpartum depression. It is not intended to be used as a stand-alone therapy or for patients with serious mental illness, psychosis, or thoughts of harming themselves or others. It is available by prescription only for individuals 22 years of age and older.

MindMotionGO (MindMaze) is a telerehabilitation program used in stroke recovery or brain injury that uses video games (software used in combination with the Microsoft Kinect v2 and Leap Motion controller) designed by neuroscientists to promote certain therapeutic movements to aid in the restoration of motor function to maximize an individual's recovery potential. Therapists create a customized training program that can be used both in clinic and at home. The therapist can continue to follow the individual via videoconferencing or in-person as well as monitor their progress remotely from their personalized dashboard. The MindMotion GO tracks an individual's movements using motion-tracking cameras. Wi-Fi is needed for home use. Currently, it is available through Johns Hopkins and Mount Sinai Abilities Research Centre in the US and abroad at centers in the U.K. It is available by prescription only.

My Dose Coach (Sanofi, Inc.) Basal Titration is an app designed for adult individuals with type 2 diabetes who have been prescribed and are taking a once-daily long-acting basal insulin by their healthcare provider. It is used as an aid to track fasting blood glucose levels and

adjust/calculate long-acting basal insulin doses based on a prescribing healthcare provider's creation of an individualized dose plan. It is available by prescription only. (Note: There is also a My Dose Coach Maintenance that is designed to enable individuals to log their insulin, non-insulin medication use, and blood glucose measurements to provide dosing and measurement reminders. When it is used with supported accessory wireless devices, it can receive values and be used as an aid to track blood glucose and diabetes medication manually in the app or with a connected Bluetooth device). It is available by prescription only.

NightWare (NightWare, Inc.) is a therapeutic platform using a proprietary AppleWatch application that helps people who suffer from traumatic nightmares sleep more restfully. The app learns the wearer's sleep patterns and customizes a treatment to the individual. The app monitors the wearer's heart rate and movement while sleeping and arouses the wearer with a vibration alert when a stress threshold is reached so as not to awaken the individual. Users wear the watch only while sleeping and not during the day. It is available by prescription only.

Regulora (metaMe Health, Inc.)-is a mobile device application of seven, self-directed gut-directed hypnotherapy sessions used as an adjunct treatment for the symptom of irritable bowel syndrome abdominal pain. Each session is thirty minutes, and the sessions are to be accessed every other week for twelve weeks. It is to be used by adults 22 years of age and older. The software digitizes scripted therapist-administered gut-directed behavior therapy designed to induce deep relaxation followed by direct and indirect suggestions targeted at somatic control mechanisms. The mobile application also provides IBS symptom tracking, which can be shared with a healthcare provider.

Rejoyn (Otsuka America Pharmaceutical Inc.)-is a digital therapeutic smartphone application that delivers a proprietary interactive cognitive-emotional and behavioral therapy to patients with Major Depressive Disorder (MDD) aged 22 years and older who are on anti-depressant medication. It is intended as an adjunct to clinician-managed outpatient care for adult patients to reduce MDD symptoms. The components include Emotional Faces Memory Task (EFMT) exercises, and cognitive behavioral therapy (CBT)-based lessons to help apply therapeutic skills and short message service (SMS) text messaging to reinforce CBT-based lesson content and to provide encouragement in using the app. The content is to be used over 6 weeks and may be followed by a 4-week extension where the content will be accessible, but no new content or exercises are provided. It is not intended to be a stand-alone therapy or as a substitution for the

patient's clinician prescribed medications. It is available by prescription only. There is no physician portal with this device and as such, there is no monitoring or alerts sent to the prescribing healthcare provider. It is available by prescription only.

RelieVRx (formerly EaseVRx) (AppliedVR, Inc.) is an immersive in home-use virtual reality system designed to provide adjunctive pain relief treatment for chronic low back pain based on cognitive behavioral therapy (CBT) skills for individuals aged 18 and older. It consists of an 8-week curriculum of pain management techniques such as body awareness, pain distraction, mindfulness-based relaxation, diaphragmatic breathing biofeedback training, pain neuroscience education, and behavior modification. The daily virtual reality sessions average 7 minutes in length. It is available by prescription only and the device is returned once the curriculum has been completed.

RevitalVision (Talshir Medical Technologies LTD)-is described as a perceptual learning, vision training software program used in the home setting for individuals 9 years of age or older for the treatment of amblyopia. Through a series of 20 to 40 interactive computerized training sessions, the device displays a series of linear images shown in both vertical and horizontal planes on a video imaging screen that is designed to identify and correct visual dysfunction from reduced visual acuity by re-training the eye to use its most optimal visual response. Training is done with the dominant eye blurred with a semi-transparent cover, but with the eye remaining open. Individualized algorithms analyze the user's performance and adjust training session tasks to become more difficult resulting in an improvement in visual acuity. The device pre-programs user-specific series of visual stimuli tasks (described as Gabor patches) whereby the user is asked to identify various objects on the video screen. Practicing these repetitive tasks leads to an improvement in the user's visual performance. At the completion of the training sessions, the user's visual acuity is measured. Each training session is about 30 minutes in length and the program is generally completed within 3 months. The program is available for the treatment of amblyopia by prescription only.

Summary of Evidence

BlueStarRx

Note: There is no published peer-reviewed evidence for BlueStarRx with the insulin dose calculator or Insulin Adjustment Program. The pilot trial for Blue Star included below did provide for medication dosing and for that reason, it is included in this summary.

For individuals who have type 2 diabetes who receive cell phone-based diabetes management software system with web-based data analytics and therapy optimization, the evidence includes one nonblinded, randomized controlled pilot trial (Quinn et al., 2008) of N=30 individuals with type 2 diabetes with an A1c ≥ 7.5% diagnosed for at least 6 months and on a stable therapeutic regimen for at least 3 months, recruited from three community physician practices and followed for 3 months. The intervention group N=15 received cell phone-based software (a Bluetooth enabled One Touch Ultra blood glucose meter and a cellphone with WellDoc's proprietary software) providing real-time feedback on the individuals' blood glucose levels, incorporated treatment algorithms, and additional data when requested and needed to evaluate diabetes management. Individual data was analyzed by proprietary algorithms and computer-generated logbooks were sent to the individuals' healthcare providers with suggested treatment plans. The control group N=15 received One Touch Ultra blood glucose meters, testing strips and lancets for the duration of the trial. They sent logbooks of their blood glucose levels to their provider every two weeks until their levels stabilized. The healthcare providers followed their usual standards of care for diabetes management. All individuals received A1c levels and completed the Summary of Diabetes Self-Care Activities (SDSCA) questionnaire at the beginning and end of the study. Two subjects from each study group were noted to have dropped out of the study. The demographic characteristics between the two groups were comparable. The intervention group had a decrease in the mean A1c from 9.51% to 7.48% vs. the control group of 9.05% to 8.37%. The authors note that the experimental variance was inflated by an unusual decrease of A1c in one individual in the intervention group and when that outlier is removed, the variance is equivalent in the two groups. ($P<0.04$ corrected to ~0.02). The intervention group had medications intensified (84.6% vs. 23.25%, $P= 0.002$), inaccurate use of medications identified (53.4% vs. 0, $P=0.002$), and providers received logbooks (100% vs. 7.7%, $P < 0.001$). Limitations include the following: Sample size was very small with no power analysis and some of the outcome data was not reported, lack of blinding could influence the results as the participants knew their actions and behaviors were being monitored as the intervention group received requests from the study interviewers to complete follow-up surveys, and there were some reported technical difficulties where the Bluetooth adapter did not always transmit data and had to be manually entered into the phone as it was acknowledged that actually only 5 of 15 individuals regularly used the Bluetooth mode of data entry. Longer-term follow-up is needed.

The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CureSight CS 100 System

For children with amblyopia who received digital therapeutic treatment with CureSight, the evidence includes one prospective, multicenter RCT (Wygnanski-Jaffe et al., 2022), n= 103 children aged 4 to ≤ 9 years with anisometropic, small-angle strabismic, or mixed-mechanism amblyopia randomized 1:1 to either CureSight, a digital binocular, eye-tracking-based home treatment delivered through watching passive video streaming content (n=51) or eye patching of the non-amblyopic eye (n=52). Examiners who performed primary outcome measurements were masked to the treatment group assignments at all follow-up visits. The CureSight treatment group received home treatment for 90 minutes per day, 5 days a week for 16 weeks for a total of 120 hours. The control group participants were instructed to wear an adhesive patch over their dominant eye for 2 hours per day, 7 days per week for 16 weeks for a total of 224 hours. Outcome assessments were performed in weeks 4, 8, 12, and 16. Outcome measures were comprised of the Amblyopia Treatment Study (ATS) Diplopia assessment, a Symptom Survey (5-question ocular symptom survey from the ATS Miscellaneous Testing Procedures Manual), and the masked examiners performed distance visual acuity and stereoacuity testing chosen based on the participants age at the time of enrollment. The primary effectiveness outcome was defined as the mean improvement from baseline in amblyopic eye visual acuity to week 16 in both study groups. The pre-specified non-inferiority margin was 1 logMAR line. Results were reported on 95 participants who had 16-week outcome data available. At baseline, the mean amblyopic eye visual acuity in the CureSight treatment group was 0.37±0.15 logMAR and 0.37±0.14 logMAR in the patching group. The mean improvement from baseline at 16 weeks was 0.28±0.13 logMAR in the CureSight treatment group ($p<0.0001$) and 0.23±0.14 logMAR in the patching group ($p<0.0001$). Thus, the study met its primary effectiveness endpoint of non-inferiority of improvement in amblyopic eye visual acuity in the CureSight treatment group compared to patching. Secondary outcome adherence to the assigned regimen of the CureSight treatment group was significantly greater than that of the patching group at 16 weeks, mean adherence of 91% vs 83% respectively, a difference of 8%, 95% CI (-4-21%); ($p=0.0114$). Secondary outcome stereoacuity improvement of 0.40 log-arcseconds ($p<0.0001$) and binocular visual acuity improvement (0.13 logMAR, $p<0.0001$) were similar in both groups and these improvements were not significantly different between the two groups. The percentage of participants with a 2-line or more improvement from baseline of amblyopic visual acuity in the treatment group was 79% (34/43) vs. 61% (30/49) in the patching group which was not statistically significant. There were no serious adverse effects reported. Limitations of the study

include the following: 90% of the participants were anisometropic amblyopes thus, generalizability to strabismic and mixed amblyopia populations is limited, the method of a self-reporting compliance diary of the patching group could have led to overestimating compliance, and a larger sample size with longer term follow-up is needed to see if the improvement in amblyopic eye visual acuity is sustained as the improvement for both groups was similar until week 12 and it was not until week 16 that the CureSight treatment group continued to demonstrate a more significant improvement than the patching group. Also, all the authors have some affiliation with NovaSight, Ltd, some have financial stock options and patent interests with the study sponsor or device, which may pose a bias.

d-Nav Insulin Management Program

For adults with Type 2 diabetes who receive insulin injections to manage their diabetes and use the d-Nav Insulin Management Program for calculating their next dose of insulin, the evidence reviewed here includes 1 open-label, multicenter RCT (Bergenstal et al., 2019), n=181 individuals randomized to either the d-Nav + health care professional (HCP) intervention group (n=93) or to the HCP control group (n=88). The difference in equipment used between the two groups was not blinded. Participants were between 20 and 70 years of age (mean 60.3) with an HbA1c ≥ 7.5% and ≤11% and a stable insulin dosage for the 3 months prior to enrollment. They were followed for 6 months and HbA1c was measured at 0, 3, and 6 months. Phone visits were conducted in weeks 1, 2, 4, and 20. 13 participants discontinued the study (6 in the d-Nav + HCP group, 7 in the HCP control group). Mean HbA1c was 8.6% at baseline (8.7 % in the d-Nav + HCP group, 8.5% in the HCP control group). The results demonstrated a mean decrease of HbA1c from baseline to 6 months was 1.0% in the d-Nav + HCP group and 0.3% in the HCP control group ($p < 0.0001$) which was statistically significant. Limitations: These preliminary findings need to be validated with a larger sample size and with longer-term follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

EndeavorRx

For children who have attention-deficit hyperactivity disorder (ADHD) who receive treatment with EndeavorRx, the evidence includes one double blind, randomized controlled trial of 348 individuals aged 8 to 12 years who received treatment with the AKL-TO1 (earlier non-prescription version) video game, N= 180, compared with an inactive control digital intervention, N= 168, in children with ADHD over 4-weeks (Kollins et al., 2020). Only the study

coordinator was aware of which video game each child received. The final sample was 329 individuals due to loss to follow-up, withdrawal, and invalid test scores. The study reported that scores of validated attention-measurement tools, (Test of Variables of Attention, Attention performance index [TOVA-API]) improved 47% vs 32% with the EndeavorRx than with the control inactive digital intervention. However, there were no between-group differences for secondary measures, which included the parent and clinician ratings of ADHD symptoms. The authors note that the trial is insufficient to suggest that AKL-T01 should be used as an alternative to established and recommended treatments for ADHD. Additional RCTs with more than one validated scale, and with longer-term follow-up are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

EpiMonitor

There is no published peer-reviewed evidence for EpiMonitor.

HaloAF Detection System

There is no published peer-reviewed evidence for Halo AF Detection System.

Insulia Diabetes Management Companion

Note: There are no published studies on Insulia Diabetes Management Companion. The following summary is on its predecessor, Diabeo system, which is a class IIb CE marked device in Europe; it does not have FDA approval. The Diabeo system was developed in partnership between Voluntis and Sanofi of France; their partnership ended in December of 2020.

For adults with Type 1 or Type 2 diabetes treated with long-acting insulin analog using the Diabeo system, the evidence reviewed here includes 3 RCTs. TeleDiab-1 (Charpentier et al, 2011) was a multicenter, open-label parallel-group, randomized control trial with 6 months follow-up, n= 180 adult participants >18 years of age with type 1 diabetes for > 1 year and on a basal-bolus insulin regimen for > 6 months, either with multiple daily injections or an insulin pump, and with HbA1c ≥ 8% (mean was 9.07%). The participants were randomized to three groups of equal size using a Web-based system: the control group with usual quarterly in person follow-up at 3 and 6 months, n-61 (G1), home use of a smartphone recommending insulin doses with

in person quarterly visits at 3 and 6 months, n=60 (G2), or use of the smartphone with brief teleconsultations every 2 weeks but without a face-to-face visit until the end of the study at 6 months, n=59 (G3). The authors note that 10 participants who did not meet the inclusion criteria of a HbA1c ≥ 8% were included and were equally distributed between the 3 groups with their data being retained for analysis. At the study completion, HbA1c measurements were available for 162 participants with 7 participants lost to follow-up. The results demonstrated that the end point HbA1c at 6 months was higher in G1 (9.10%) than in G2 (8.63%) or G3 (8.41%); however, the difference between G1 and G2 was not statistically significant (p=0.022). The difference between G1 and G3 was, however, statistically significant (p= 0.0019). The proportion of participants reaching the target of HbA1c ≤ 7.5% at the end point of 6 months was 17% in G3 (10/59), 6.7% in G2 (4/60), and 1.6% in G1 (1/61). The difference between G3 and G1 was statistically significant (p=0.007). The frequency of non-severe, symptomatic hypoglycemia episodes did not differ between groups at the end point of 6 months, nor did they increase from baseline reports. Limitations: There was unclear reporting on the use of intention to treat vs per protocol participants analysis. Larger sample sizes and longer-term follow-up are needed.

TeleDiab-2 (Franc et al., 2019) was a multicenter, randomized controlled, open-label study completed at 4 months, n=191 participants with type 2 diabetes mellitus who had inadequately controlled HbA1c between 7.5% and 10% on maximum dose oral medications and required initiation of basal insulin (BI). The mean age of the participants was 58.7 years and mean HbA1c was 8.9%. The participants were randomized into three groups: 1) standard care, n=63, 2) interactive voice response system (IVRS), n= 64, and 3) Diabeo-BI app software, n=64. A 13-month follow-up of an extension phase included n=158 participants 98.1% (52/53) from G3 continued using the Diabeo-BI app software and G2 IVRS software was discontinued, and those participants continued with standard follow-up, as in the initial control arm (G1), with face-to face visits every 3 months without telemedicine. Results demonstrated at 4 months follow-up HbA1c decreases from baseline group 2 (-1.44%) and group 3 (-1.48%) arms compared with the control arm, group 1 (-0.92%, p<0.002). Target fasting blood glucose was reached by twice as many individuals in the telemonitoring groups as in the control group, and insulin doses were also able to be titrated to higher levels. No severe hypoglycemia was observed in the telemonitoring groups and mild hypoglycemia frequency was similar in all groups. At the 13-month extension, the G2 and G1 had similar values of HbA1c and insulin doses. HbA1c levels were lower in G3 compared with the control arm (G1=G2), but the difference was not statistically significant (numerical values not reported). The glycemic control target (HbA1c < 7.0%) was greater in the G3 participants (30.2%) than the control arm (13.8%, p=0.023). Basal insulin was 0.65±0.49; 0.48±0.31; 0.47±0.28 U/kg/day for G3, G2, G1 respectively (p=0.05 G3 vs G1). Mild hypoglycemic episodes were rare with no differences between the three groups. These findings need to be validated with a larger sample size and with longer-term follow-up.

TELESAGE (Franc et al., 2020) was a multicenter, randomized, open study. N=665 with 3 arms: 1) standard care, n=221 (control group) 2) Diabeo alone, n=231 (25.1% of participants were users n=58), and 3) Diabeo+telemonitoring by trained nurses, n=213 (37.6% of participants were users n=80) (arms 2 and 3, the intention to treat population). The mean age was 38.5 years, and the majority had type 1 diabetes (91.6%). The mean HbA1c was 9.1% and insulin was delivered either by a pump (53.0%) or multiple daily injections (47.6%). In a post hoc analysis in those who used Diabeo at least once daily, there was a significant reduction in HbA1c after 12 months follow-up: mean difference -0.41% for arm 2-arm 1 (p= 0.001) and -0.51% for arm 3-arm 1 (p ≤ 0.001). There was even a greater reduction in HbA1c in those who used Diabeo at least twice a day (13.9% of participants, n= 32 from arm 2 and 24.4% participants, n= 52 of arm 3) -0.50% for arm 2-arm 1, p=0.002 and -0.66% for arm 3-arm 1, p≤ 0.001. There were no significant differences between the three groups for the percentage of participants who reported at least one symptomatic hypoglycemia. Limitations of the study: Statistical significance of the intention to treat analyses were not reported, thus the study conclusions were reliant on the post hoc analysis. There was a considerable attrition rate of persons in the intention to treat population, 40-50% of participants in arm 2 and 20-30% of participants in arm 3 never actually used Diabeo, thus the sample size fell short of the number defined in the power analysis. These preliminary findings need to be validated with a larger sample size of actual users of the device. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ieva Pelvic Digital Health System

For women with stress or mixed, urinary incontinence (UI) who receive treatment with the Ieva Pelvic Digital Health System, the evidence includes one pilot, single center, prospective, open label study (Rosenblatt et al., 2019). N=23 female premenopausal participants, > 18 years of age (mean 42 years old) with mild stress UI who performed pelvic floor muscle (PFM) exercises while standing with use of the accelerometer-based system twice daily for 6 weeks. Each training session entailed five repetitions of 15-second PFM contraction followed by 15-second relaxation over 2.5 minutes. These sessions took place in an outpatient clinic and were supervised by the same research assistant. Pelvic floor angle measurements at rest, with strain, and with PFM contraction were taken at baseline, and then weekly for 6 weeks. Each participant also answered the following validated questionnaires: Urogenital Distress Inventory (UDI-6) which measures the severity of urogenital complaints, Incontinence Impact Questionnaire (IIQ-7) which measures the impact of UI on daily activities, and Patient's Global Impression of Severity (PGI-S). At 3 and 6 weeks, the participants also completed the Patient's Global Impression of Improvement questionnaire, and at 6 weeks the participants indicated user-friendliness on a scale of 0 to 10

(easiest to impossible). Results demonstrated the pelvic floor angle at maximal effort contraction increased by 16° from 65.1° at baseline to 81.1° at 6 weeks ($p < 0.0001$). The pelvic floor angle upon bearing down reduced from 48.3° at baseline to 43.7° ($p=0.0043$). The mean maximum duration of continuous voluntary PFM contraction increased by 174.8 seconds from baseline to 6 weeks ($p < 0.0001$). The maximum number of contractions performed within 15 seconds increased by 3.7 repetitions from enrollment to the study endpoint ($p < 0.0001$). Participants also reported decreasing scores on the UDI-6, IIQ-7, and PGI-S from baseline to 6 weeks, indicating improvements in symptom severity and quality of life. Limitations: Study sample size was small, there was no comparison group, and regular interaction with a research assistant may have affected the subjective improvement reported by the participants and may not be generalizable to the same at home users. Longer follow-up is also needed to see if the reported improvements are sustainable. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Weinstein et al (2022) reported on a multicenter RCT that compared an intravaginal motion-based digital therapeutic device for pelvic floor muscle training (PFMT) (intervention group) with PFMT alone (control group) in female individuals with stress or mixed urinary incontinence (UI). N=77 with final analysis of 61 participants (29 in intervention group and 32 in control group) that showed no statistical difference in primary outcomes (scores on Urinary Distress Inventory or Patient Global Impression of Improvement). However, scores on the Pelvic Organ Prolapse and Colorectal-anal Distress Inventories and Pelvic-Floor-Impact Questionnaire did improve significantly more in the intervention group than the control group. The median number of stress UI episodes decreased more in the intervention group than the control group. The trial was prematurely terminated due to device technical considerations. A larger powered trial is underway.

Luminopia One

For children aged 4 to 7 years with a diagnosis of amblyopia who receive treatment with the Luminopia One digital therapeutic, the evidence includes one RCT of n=105 children 4 to 7 years of age with amblyopia. The treatment group, n=51 used the therapeutic head-mounted display one hour per day, 6 days per week with full time refractive correction for 12 weeks, Participants in the comparison group, n=54, wore refractive correction alone for 12 weeks. The primary efficacy outcome was change in amblyopic eye visual acuity (VA) from baseline at 12 weeks. In the treatment group, the software in the device modified the video content by contrasting the images presented to the fellow eye by 15% of that presented to the amblyopic eye and dichoptic masks were superimposed on the images so that both eyes were required to fully view

the video content. Participants were evaluated at 4, 8, and 12 weeks for VA. Outcome assessors were masked to treatment group; however, participants and study coordinators were not masked. Participants were asked not to discuss their treatment with the examiner. Results demonstrated that at 12 weeks, amblyopic eye VA improved by 1.8 lines (95% CI, 1.4-2.3 lines; n=45) in the treatment group and by 0.8 lines (95% CI, 0/4-1.3 lines; n=45) in the comparison group. At a planned interim analysis, the difference between groups was statistically significant (1.10 lines; P= 0.0011, 96.14% CI, 0.33-1.63 lines) and the study was stopped early due to successful outcomes per the protocol. No serious adverse events were reported. Headaches in the treatment group were the most common adverse event reported and worsening VA in the amblyopic eye was the most common in the comparison group. Adherence in the treatment group was 88.2% with the therapeutic and 100% adherence in both groups with refractive correction throughout the 12-week follow-up. Limitations of the study: the authors note a large proportion of participants had undergone prior active amblyopia treatment so it is difficult to know what impact this may have had on the study results. There was missing outcome data for 15 of the 105 participants which could have biased the results of the study. There was no comparator to the standard treatment of patching, atropine, or a sham comparator. Longer follow-up is needed to determine the durability of the treatment benefit and replication in a larger sample size would be beneficial.

Mahana for IBS

There is no published peer-reviewed evidence for Mahana for IBS.

One pilot RCT evaluated an earlier website-delivered version of Mahana for IBS called Regul8. Previous iterations of Mahana for IBS (previously Parallel) underwent technological changes from the website to the mobile version which include technical optimization of certain features along with content adjustments such as updating information to reflect best practices[37]. Therefore, this study is not included for this summary of evidence due to the difference in mode of application.

MamaLift Plus

There is no published peer-reviewed evidence for MamaLift Plus.

MindMotionGO

There is no published peer-reviewed evidence for MindMotionGO.

My Dose Coach

For adults with Type 2 diabetes treated with any long-acting basal insulin using the My Dose Coach smartphone app, the evidence includes one prospective single-arm, pilot study of N=158 individuals, aged 18-75 years (mean age 51) with an HbA1c > 7% (mean at baseline 9.6%) who used the My Dose Coach app programmed according to the individual profile suggesting optimal basal insulin titration dosing using fasting self-measured plasma glucose and hypoglycemia data with 16 weeks of follow-up. Results demonstrated in the 141 participants who completed the study a mean reduction in HbA1c of 1.97% from baseline (P<0.001) which was statistically significant. The predefined glycemic target of 90-130 mg/dl was achieved in 58.9% of the participants within 66 days with no severe hypoglycemia events. Limitations of the study: It was a single center study, there was no control or comparator, there was an attrition rate of 11%, and longer-term follow-up is needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

NightWare

For individuals with nightmare disorder or PTSD-associated nightmares who receive NightWare, the evidence includes a single trial. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The single pivotal trial did not meet the primary efficacy endpoint. This trial failed to achieve recruitment goals and was likely underpowered. A well-designed blinded randomized controlled study with a clear design for testing a pre-specified hypothesis is needed. Given these limitations, the benefit of NightWare in individuals with nightmare disorder and post-traumatic stress disorder-associated nightmares is uncertain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Regulora for IBS

For adults with irritable bowel syndrome treated with Regulora (digital gut-directed hypnotherapy), the evidence includes a randomized parallel-group study. After a four-week run-

in period, 362 participants were randomized to 12 weeks of Regulora or digital muscle relaxation via a mobile app on a smartphone or tablet. The primary endpoint was ≥30% reduction in abdominal pain from baseline in average daily abdominal pain intensity in the 4 weeks following treatment. The results demonstrated that 30.4% of the Regulora and 27.1% of the muscle relaxation group met the primary endpoint with no significant difference between the groups (p .5352). Based on these findings, further investigation is needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Rejoyn (also known as CT-152)

There is no published peer-reviewed evidence for Rejoyn.

RelieVRx (formerly known as EaseVRx)

For adults with chronic low back pain treated with EaseVRx virtual reality (VR) system, the evidence includes one double-blind RCT (Garcia, et al, 2021). N=179 individuals (76.5% female, 90.5% Caucasian, 91.1% have some college education, mean age 51.5 years, average pain intensity 5/10, 67% back pain duration > 5 years, 76.5% resided in highly urban or metropolitan area) chosen from a national online convenience sample (obtained through internet advertisements). The participants had self-reported low back pain with duration of six months or more with average pain intensity of 4 or >/10 and were randomized 1:1 to a 56-day EaseVRx program, or a Sham VR (2D nature content delivered in a VR headset). The primary outcome was the effects of EaseVRx versus the Sham VR representing change in average pain intensity and pain-related interference with activity, stress, mood, and sleep from baseline to end of treatment at 56 days. Change was measured using the Defense and Veterans Pain Rating Scale (DVPRS), where 0= no pain and 10= as bad as it can be, and the DVPRS interference scale (DVPRS-II), where 0= does not interfere and 10= completely interferes. Twice-weekly surveys were obtained with a final survey at treatment completion. Results demonstrated user satisfaction ratings were higher for EaseVRx versus Sham VR ($p<0.001$). EaseVRx was superior to Sham VR for all primary outcomes with greater reductions in average pain intensity and pain-related interferences with activity, mood, and stress (highest p value=0.009). Between group difference Cohen d effect sizes ranged from 0.40-0.49, indicating superiority was moderately clinically meaningful. From baseline to end of treatment Cohen d effect sizes ranged from 1.117 to 1.3, indicating moderate to substantial clinical importance for reduced pain intensity and pain-related interference with activity, mood, and stress. Between-group comparisons for physical function and sleep disturbance demonstrated superiority for the EaseVRx versus the Sham VR (p=0.022 and 0.012,

respectively). However, pain catastrophizing, pain self-efficacy, pain acceptance, and prescription opioid use (morphine milligram equivalent) did not reach statistical significance for either group. Use of over-the-counter analgesic use was reduced for EaseVRx ($p<0.01$) but not for Sham VR. A three-month follow-up study by the same authors (Garcia, et al, 2022) analyzed data for n=188 participants who were surveyed at 1, 2, and 3 months post the original 56- day end of treatment The n=188 included all participants with baseline data from the previous study, 168 of which completed the 56-day treatment and remained blinded during this follow-up. Of those 168 participants, at least 20 did not complete their surveys at month 1, 2, and 3 but were still included in the dataset analysis. The researchers were unblinded during this 3-month follow-up. The results demonstrated that the EaseVRx had lower pain intensity, lower pain-interference with activity, sleep, and stress than the Sham VR, which was maintained to month 3 (effect sizes, d_{rm} = 0.56-0.88), as well as higher physical function. Pain-interference with mood did not survive multiplicity correction at 3 months. There was also not a significant difference between EaseVRx and Sham VR for sleep disturbance in the post-treatment 3 months. (Of note, a 6-month follow-up is ongoing but is not published at this time). Limitations of the study: The findings need to be validated in a larger sample size with longer follow-up to determine the durability of any treatment effects. Because all data was self-reported, it would be beneficial to have diagnoses confirmed and specific analgesic prescription information provided to effectively measure a change in opioid use. The study sample was predominantly urban, white, females and so may not be generalizable to the general population. The study was performed during COVID-19 when most people were staying home and isolating. It would be helpful to know if the findings are reproducible in a more realistic environment. Lastly, there is a potential for bias as the study authors were all affiliated with AppliedVR, Inc.

RevitalVision

For individuals with amblyopia treated with RevitalVision, the evidence includes a prospective observational study, a prospective cohort study, and an RCT. A prospective study by Magdlene et al (2022) enrolled 45 subjects with unilateral or bilateral amblyopia between the ages of 8 to 48 years old with the mean age being 17.2 +/-10.2 years who had plateaued with six months of part-time occlusion therapy or refractive adaption for >16-18 weeks prior to the start of the study[51]. Training sessions were three per week and 9 per month for a total of 30 to 40 sessions. The dominant eye was blurred during the training sessions for unilateral amblyopia or both eyes open and uncovered for bilateral amblyopia. Baseline mean distance best corrected visual acuity was 0.54 logMAR. After treatment, the mean best corrected visual acuity improved to 0.32 logMAR, which was statistically significant ($p<.001$, paired t-test). Limitations of the study were the small sample size, lack of randomized treatment assignment, data for visual acuity improvement by age group was not reported, and the clinical significance of improvement in

visual acuity is not clear. A prospective study by Yalcin and Balci (2014) enrolled 99 subjects aged 9-50 years, 53 in the perceptual vision therapy group (RevitalVision) and 46 in the control group[107]. All subjects had occlusion treatment during childhood. The treatment group completed 45 training sessions lasting for 30 minutes each, three times a week, followed by an end of treatment examination. The control group underwent 30 minutes of eye patching three times a week. Instead of the perceptual vision therapy, they played placebo computer games at home. All subjects were followed for four months. The results demonstrated a mean improvement of 2.6 logMAR lines in visual acuity from baseline which was statistically significant ($p=0.001$). Contrast sensitivity function improved at 1.5, 3, 6, 12, and 18 cycles per degree spatial frequencies. The control group did not show any significant change in visual acuity or contrast sensitivity function. Limitations of the study were lack of randomization of the treatment assignment. The study was not blinded in evaluation of outcomes. An RCT by Zhong et al (2022) enrolled children with limbal dermoid (LD) (N=25) (LD group) and 25 children without LD (N group) were compared regarding contrast sensitivity function (CSF) and visual acuity (VA).[108] The average age in both groups was 10.20 years. Eight children quit the amblyopia treatment group so 17 children with limbal dermoid (LD) postsurgical lamellar keratoplasty (LKP) diagnosed with amblyopia were randomly assigned to two arms: 9 in the perceptual learning (PL) group, combined with patching and 8 in the control group that received patching only. The allocation details were kept sealed until all baseline assessments were completed. Follow-up was at week 1 and thereafter, monthly for 6 months. The children in the PL group underwent 30-minute daily sessions along with 2 hours of patching. The children in the patching group were prescribed 2 hours of daily patching alone. Examiners who were blinded to the treatment allocation measured VA and CSF at one, three, and six months. The primary outcome was the area under log CSF and the secondary outcome was the best corrected (VA). The results demonstrated a reduction in the LD group compared to controls. After six months of training, the difference in the changes in the AULCSF between the PL and patching groups was 0.59 (95% CI: 0.32, 0.86, $p < 0.001$), and the between-group difference in VA at six months was -0.30 (95% CI: -0.46, -0.14, $p < 0.001$) concluding that perceptual learning for those who have undergone lamellar keratoplasty with amblyopia could better improve CSF and visual acuity in the amblyopic eye than patching alone. Limitations of the study were the small sample size, the short-term follow-up, the interval since the keratoplasty was not reported, and the presence or absence of amblyopia prior to the keratoplasty surgery was not reported. Thus, the results may not be generalizable to individuals with typical amblyopia etiology or to those whose amblyopia has been corrected, when possible with conventional measures.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05365607[a]	NightWare Therapeutic Platform for Improving Cardiovascular Health in Adults With Nightmares Associated With PTSD	40	Dec 2024
NCT04040387[a]	Traumatic Nightmares Treated by NightWare (To Arouse Not Awaken) (TNT/NW)	270	Aug 2024
NCT05148052	Effect of Upper Extremity Rehabilitation Using Immersive Virtual Reality in Chronic Stroke Patients: A Prospective, Multicenter, Single-blind, Explorative, Randomized Crossover Trial	36	Oct 2025
NCT04379687	Immersive Virtual Reality in Post Stroke Physiotherapy	44	Dec 2023
NCT05263037	A Decentralized, Randomized, Controlled Trial to Study Health Outcomes of EaseVRx-8w+ for the Treatment of Chronic Lower Back Pain	1093	June 2026
NCT05185076	A Prospective, Multicenter, Randomized, Masked, Controlled Pivotal Trial to Assess the Safety and Effectiveness of an Eye-Tracking-Based Treatment for Amblyopia Under Binocular Conditions Versus the Standard of Care, Monocular Deprivation Treatment (Occlusive Patching)	114	May 2022
NCT03206502	Characterizing Sleep, Stress, and Seizures in Daily Life: An Internet-based Study With the Empatica Embrace Watch and Smartphone-based Diary-alert System	100000	May 2026
NCT05958095	Supporting Maternal Mental Health and Emotional Regulation (SuMMER): Assessment of the Clinical Effectiveness of a Mobile	142	August 2023(active, not recruiting)

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Application for Patients With Postpartum Depression		
Unpublished			
NCT03934658	A Remote Randomized Double-Blind Sham-Controlled Clinical Trial of NightWare in Adults with Post-Traumatic Stress Disorder and Co-Morbid Nightmare Disorder	81	Dec 2021 (completed)
NCT03649074	Software Treatment for Actively Reducing Severity of ADHD as Adjunctive Treatment to Stimulant (STARS-ADHD Adjunctive)	203	Sept 2019 (completed) (results submitted)
NCT04104191	The LIVMOR Data Collection Study for the Development and Validation of L-1000 AF System	271	Feb 2019 (completed)
NCT04897074[a]	A Single Arm Pivotal Trial to Assess the Efficacy of AKL-T01, a Novel Digital Intervention Designed to Improve Attention in Adolescents, Aged 13-17 Years Old, Diagnosed with Attention Deficit Hyperactive Disorder (ADHD).	165	Sept 2022 (completed)
NCT04678661	My Dose Coach Titration and Maintenance in Patients with Type 2 Diabetes Mellitus on Basal Insulin	60	Feb 2023 (completed)
NCT04139564	Safety and Effectiveness of Virtual Reality Utilizing EaseVRx for the Reduction of Chronic Pain and Opioid Use	108	Aug 2022 (completed)
NCT05333926	A Prospective, Open-Label Study of MahanaIBS, a Smartphone-Delivered Cognitive Behavioral Therapy (CBT) Treatment, in Young Adults Aged 18-21 Years Old with Irritable Bowel Syndrome	194	Dec 2022 (completed)
NCT04826939	Validity (and Reliability) of Two Forms of an Accelerometer-Based Intravaginal Device for Detecting Pelvic Floor Motion	30	Sept 2022
NCT04785690	A Prospective, Multicenter, Randomized, Masked, Controlled Pivotal Trial to Assess the Safety and Effectiveness of an Eye-Tracking-Based Treatment for Amblyopia Under Binocular Conditions Versus the Standard of	23	May 2023

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Care, Monocular Deprivation Treatment (Occlusive Patching)		

NCT: National Clinical Trial

a Denotes industry sponsored or cosponsored trial.

Practice Guidelines and Position Statements

American Academy of Ophthalmology (AAO)

In 2017, the AAO Amblyopia Preferred Practice Pattern acknowledged there was insufficient evidence to recommend vision therapy techniques or binocular therapy for treatment of amblyopia. This preferred practice pattern was updated in 2022 to state, "Suitable treatment options for amblyopia include optical correction, patching, pharmacological treatment, optical treatment, Bangerter (translucent) filters, and digital therapeutics, in addition to managing the underlying cause of amblyopia."

American College of Gastroenterology (ACG)

In 2021, the ACG Clinical Guideline: Management of Irritable Bowel Syndrome recommended that "the use of gut-directed psychotherapies in conjunction with other IBS therapies for patients who are emotionally stable but who exhibit cognitive-affective drivers of IBS symptoms because 1) gut-directed psychotherapies are low risk when used by qualified health professionals-no studies to date have reported serious adverse effects or negative outcomes; 2) there are long-term benefits of these therapies even after they are discontinued; and 3) gut-directed psychotherapies are IBS-subtype agnostic and can address the large group of patients with IBS-M or IBS-U for whom fewer pharmacological treatments are available". Regulora or Mahana are not specifically discussed.

National Institute for Health and Care Excellence (NICE)

In 2008, NICE Guidance on Irritable Bowel Syndrome in Adults: Diagnosis and Management recommend in the clinical guideline that "referral for psychological interventions (cognitive behavioral therapy, hypnotherapy, and/or psychological therapy) should be considered for

people with IBS who do not respond to pharmacological treatments after twelve months and who develop a continuing symptom profile (described as refractory IBS)." Regulora or Mahana are not specifically discussed.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

In April 2024, MamaLift Plus received FDA 510(k) marketing clearance (K223515) as substantially equivalent to a marketed predicate device (Somryst). "It is intended to provide neurobehavioral interventions to individuals 22 years of age and older as an adjunct to clinician-managed outpatient care. MamaLift Plus treats mild to moderate postpartum depression by improving a patient's symptoms of depression." FDA Product Code: SAP.

In March 2024, Rejoyn received FDA 510(k) marketing clearance (K231209) as substantially equivalent to a marketed predicate device (ReSET). It is also known as CT-152. "It is a prescription digital therapeutic for the treatment of Major Depressive Disorder (MDD) symptoms as an adjunct to clinician-managed outpatient care for adult patients aged 22 years and older who are on antidepressant medication. It is intended to reduce MDD symptoms." FDA Product Code: SAP.

In February 2024, EpiMonitor received FDA 510(k) marketing clearance (K232915) as substantially equivalent to a marketed predicate device. It is indicated as an adjunct to seizure monitoring in adults and children aged 6 and older in a home environment or healthcare facility. It is composed of a wearable device (EmbracePlus) that is paired with a mobile software application (EpiMonitor). The device worn on the wrist senses Electrodermal Activity (EDA) and motion data to detect patterns that may be associated with primary or secondary generalized tonic clonic seizures in patients with epilepsy or at risk of having epilepsy. When a seizure event is detected, the wearable device sends a command to a paired mobile device which initiates an alert to a designated caregiver. The EpiMonitor mobile app stores and transmits accelerometer, EDA, peripheral skin temperature and activity data for review by a trained healthcare professional via Cloud-based software. FDA Product Code: POS

In 2022, CureSight-CS100 (NovaSight, Ltd.) received FDA 510(K) marketing clearance (K221375) as substantially equivalent to a marketed predicate device (the Luminopia One). "It is indicated

for improvement in visual acuity and stereo acuity in amblyopia patients, age 4 to <9 years, associated with anisometropia and/or with mild strabismus, having received treatment instructions (frequency and duration) as prescribed by a trained eye care professional" It is intended to be used as an adjunct to full-time refractive correction (i.e., glasses). FDA Product Code: QQU.

In 2021, Luminopia One (Luminopia, Inc.) received FDA clearance through the De Novo pathway (DEN210005) under 21 CFR Part 886.5500. It is indicated for improvement in visual acuity in amblyopia patients, aged 4 to 7, associated with anisometropia and/or with mild strabismus, having received instructions (frequency and duration) as prescribed by a trained eye-care professional. Luminopia One is intended to be used as an adjunct to full-time refractive correction, such as glasses, which should also be worn under the virtual reality headset during Luminopia One therapy. It is for prescription use only, in an at-home environment. FDA Product Code: QQU.

In 2021, Regulora (metaMe Health, Inc) received FDA 510(k) marketing clearance (K211463) as substantially equivalent to a marketed predicate device (Mahana). It is indicated for the provision of behavioral therapy through gut-directed hypnotherapy for adults 22 years of age and older diagnosed with irritable bowel syndrome (IBS). Regulora is a three-month treatment for those with abdominal pain due to IBS as an adjunctive treatment to other treatments for IBS. FDA Product Code: QMY.

In 2021, Mahana Parallel Digital Cognitive Behavioral Therapy (CBT) Mobile Application for Irritable Bowel Syndrome (IBS) (Mahana Therapeutics, Inc.) received FDA 510(k) marketing clearance (K211372) as substantially equivalent to a marketed predicate device (Parallel, De Novo pathway clearance DEN200029 under 21 CFR 801.109 in 2020). It is indicated for use as a prescription only digital therapeutic intended to provide cognitive behavioral therapy for adults aged 22 years of age and older diagnosed with irritable bowel syndrome (IBS) as a 3-month treatment to reduce the severity of symptoms of IBS. It is intended to be used together with other treatments for IBS. FDA Product Code: QMY.

In 2021, RelieVRx (formerly EaseVRx) (AppliedVR, Inc.) received FDA clearance through the De Novo pathway (DEN210014) under 21 CFR Part 801.109. It is indicated as a prescription-use, in-home use immersive virtual reality system intended to provide adjunctive pain-relief treatment based on cognitive behavioral therapy skills for individuals aged 18 and older with a diagnosis of chronic low back-pain, defined as moderate to severe pain that has lasted longer than three months. FDA Product Code: QRA.

In 2020, EndeavorRx (Akili Interactive Labs, Inc.) received FDA clearance through the De Novo pathway (DEN200026) under 21 CFR Part 801.109. It is defined by FDA as “a software intended

to provide therapy for ADHD or any of its individual symptoms as an adjunct to clinical supervised treatment." It is indicated to improve attention function as measured by computer-based testing in children ages 8 to12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. FDA Product Code: QFT.

In 2020, Halo AF Detection System (LIVMOR, Inc.) received FDA 510(k) marketing clearance (K201208) as substantially equivalent to a marketed predicate device (FibriCheck). It is indicated for use by individuals who have been diagnosed with or are susceptible to developing atrial fibrillation and who would like to monitor and record their pulse rhythms on an intermittent basis and alert their physicians of any detected irregular heart rhythms. It is used in conjunction with the LIVMOR Halo + Home Monitoring System and is not validated for use with any other pulse monitoring system. FDA Product Code: DXH.

In 2020, NightWare (NightWare, Inc.) received FDA clearance through the De Novo pathway (DEN 200033) under 21 CFR Part 801.109. It is indicated to provide vibrotactile feedback on an Apple Watch, based on analysis of heart rate and motion during sleep for the temporary reduction of sleep disturbance related nightmares in adults 22 years or older who suffer from nightmare disorder or have nightmares from posttraumatic stress disorder (PTSD). It is intended for home use. FDA Product Code: QMZ.

In 2019, d-Nav Insulin Management Program (Hygieia, Inc.) received FDA 510(k) marketing clearance (K181916) as substantially equivalent to a marketed predicate device. It is indicated as a software device that calculates the next dose of insulin to aid in optimizing insulin management for adult individuals with type 2 diabetes. FDA Product Code: NDC.

In 2018, the leva Pelvic Floor Trainer received FDA 510(k) marketing clearance (K180637) as substantially equivalent to a marketed predicate device. The FDA states its indications for use are: "1) strengthening of the pelvic floor muscles and 2) rehabilitation and training of weak pelvic floor muscles for the treatment of stress, mixed, and mild to moderate urgency urinary incontinence in women." The device interacts with the user via smart phone technology. In 2019, the FDA expanded the indications for use of the leva Pelvic Digital Health System (K192270) to include women with overactive bladder. FDA Product Code: HIR.

In 2021, the leva Pelvic Health System (Renovia, Inc.) received 510(k) marketing clearance (K212495) as substantially equivalent to their previously marketed predicate device. This model is called leva-02 and was tested with a risk analysis performed for biocompatibility based on the changes made to the device in hardware and software. FDA Product Code: HIR.

In 2018, MindMotionGO (MindMaze) received FDA 510(k) marketing clearance (K173931) as substantially equivalent to previously marketed predicate devices. FDA states its indication for

use is, "as a medical device software used in combination with the Microsoft Kinect v2 and Leap Motion controller that supports the physical rehabilitation of adults in the clinic and at home. The software includes rehabilitation exercises for the upper extremity, trunk, and lower extremity." Approval by a medical professional is required prior to use. FDA Product Code: LXJ.

In 2017, BlueStar Rx (WellDoc, Inc.) received FDA 510(k) marketing clearance (K162532) as substantially equivalent to a marketed predicate device DiabetesManagerRx (the initial and subsequent clearances prior to this provided coaching messages based on real-time blood glucose levels but had no insulin dose calculator [K100066 2010, K112370 2011, K120314 2012, K141273, 2014 BlueStar name first used, K162225 2016]). The FDA states, "It is indicated for use in individuals 21 years of age or older who have type 2 diabetes. The software system captures, stores, and transmits blood glucose data and then analyzes and reports the data in support of diabetes self-management by providing coaching messages (motivational, behavioral, educational) based on real-time blood glucose values. The software is for use on mobile phones or personal computers. It also includes an insulin dose calculator which allows individuals to calculate a dose of their prescribed insulin regimen for a given amount of carbohydrates and/or blood glucose value". FDA Product Code: LNX, NDC.

In 2019, the FDA expanded the indications for use of BlueStarRx to individuals 18 years of age or older who have type 1 or type 2 diabetes. (K190013). FDA Product Code: MRZ, NDC.

In 2020, the FDA expanded the indications for use of BlueStarRx to basal insulin users with type 2 diabetes and now includes an Insulin Adjustment Program (IAP) (K193654) which calculates appropriate long-acting basal insulin doses for titrating insulin levels based on configuration by a healthcare provider (the healthcare provider must activate and configure the IAP for individual-specific parameters). FDA Product Code: MRZ, LNX, NDC.

In 2021, the FDA cleared a BlueStarRx modified device (K203434) to add a bolus titration feature and compatibility with pre-mixed insulin. FDA Product Code: NDC.

In 2017, My Dose Coach (Sanofi, Inc.) received FDA 510(k) marketing clearance (K163099) and as substantially equivalent to a marketed predicate device. The indications for use described by the FDA state "it is indicated for single individual use outside the clinic setting by a previously diagnosed Type 2 Diabetic who has been prescribed a once-daily long-acting basal insulin." The FDA notes it is to be used as an aid to the individual to provide dose suggestions based on individualized dose instructions configured and activated for the individual by the health care provider. These dose suggestions are based on the individual's fasting blood glucose and hypoglycemic occurrences. Later in 2017 it was updated (K171230) to state it provides dose suggestions of once-daily long-acting insulin (i.e., basal insulin titration) based on the individual's fasting blood glucose and hypoglycemic occurrences. FDA Product Code: NDC.

In 2016, Insulia Diabetes Management Companion (Voluntis) received FDA 510(k) marketing clearance (K161433) as substantially equivalent to a marketed predicate device. The FDA states, "it is indicated for use by healthcare professionals and their type 2 adult diabetes individuals treated with long-acting insulin analog." The FDA notes that the software provides "secure capture, storage, and transmission of diabetes-related healthcare information to enhance data management, to display reports and graphs, and to aid the healthcare professional and the individual in the review, analysis, and evaluation of individual data in order to support effective diabetes management." It includes a basal calculator to provide direction to the individual in response to blood glucose and health events based on the treatment plan provided by a healthcare professional for insulin adjustments. It is compatible for use with the following long-acting analogs: Lantus, Levemir, Toujeo, Basaglar, and Tresiba. Additional dosing modifications of these insulin analogs received FDA 510(k) marketing clearance in 2017 (K170669) and (K172177), and in 2020 (K202596) when it was modified to be compatible with Semglee long-acting insulin. FDA Product Code: NDC.

In 2001, RevitalVision (Talshir Medical Technologies LTD) (formerly AA-1 System by NeuroVision, Inc.) received FDA 510 (k) marketing clearance (K012530) as substantially equivalent to a marketed predicate device (Haploscope, Humphrey Visual Field Analyzer, and Eye Shield). The FDA states it is indicated "for the treatment of amblyopia using an interactive computerized program in patients 9 years of age or older suffering from amblyopia." FDA Product Code: HJT.

References

1. Alkili Interactive Labs Inc. EndeavorRx. Available at URL: **https://www.endeavorrx.com/**. Accessed May 7, 2024.
2. American Academy of Ophthalmology. Amblyopia Preferred Practice Pattern. September 9, 2022. Available at URL: **https://www.aao.org/education/preferred-practice-pattern/amblyopia-ppp-2022**. Accessed May 7, 2024.
3. American Medical Association. Proposed guidelines aim for safe, effective mobile health apps. January 22, 2018. Available at: URL: **https://www.ama-assn.org/practice-management/digital/proposed-guidelines-aim-safe-effective-mobile-health-apps.** Accessed May 7, 2024.
4. American Psychiatric Association (APA). The App Evaluation Model. Available at URL: **https://www.psychiatry.org/psychiatrists/practice/mental-health-apps/the-app-evaluation-model**. Accessed May 7, 2024.
5. AppliedVR, Inc., RelieVRx. Available at URL: **https://www.relievrx.com/**. Accessed May 7, 2024.
6. Bergenstal RM, Johnson M, Passi R, et al. Automated insulin dosing guidance to optimize insulin management in patients with type 2 diabetes: a multicentre, randomized controlled trial. Lancet 2019; 393(10176): 1138-1148. PMID: 30808512.
7. Charpentier G, Benhamou PY, Dardari D, et al. The Diabeo software enabling individualized insulin dose adjustments combined with telemedicine support improves HbA1c in poorly controlled type 1 diabetic patients: a 6-month, randomized, open-label,

parallel-group, multicenter trial (TeleDiab 1 study). Diabetes Care. 2011;34(3):533-539. PMID: 21266648.Cruz OA, Repka MX, Hercinovic A, et al. Amblyopia preferred practice pattern. Ophthalmology. 2023;130(3):P136-P178

8. Dang A, Arora D, Rane P. Role of digital therapeutics and the changing future of healthcare. J Family Med Prim Care. 2020; 9(5): 2207-2213. PMID: 32754475.
9. Darnall BD, Krishnamurthy P, Tsuei J, Minor JD. Self-administered skills-based virtual reality intervention for chronic pain: Randomized controlled pilot study. JMIR Form Res. 2020; 4(7): e17293. PMID: 32374272.
10. Davenport ND, Werner JK. A randomized sham-controlled clinical trial of a novel wearable intervention for trauma-related nightmares in military veterans. J Clin Sleep Med. Feb 01 2023; 19(2): 361-369. PMID 36305584.
11. Davis,NO, Bower J, Kollins SH. Proof-of-concept study of an at-home, engaging, digital intervention for pediatric ADHD. PLoS One. 2018; 13(1): e0189749. PMID: 29324745.
12. Digital Therapeutics Alliance. Available at URL: **https://dtxalliance.org/understanding-dtx/**. Accessed May 7, 2024.
13. Duda M, Daniels J, Wall D. Clinical evaluation of a novel and mobile autism risk assessment. J Autism Dev Disord. 2016; 46(6):1953-1961. PMID: 26873142.
14. Duda M, Kosmicki JA, Wall, DP. Testing the accuracy of an observation-based classifier for rapid detection of autism risk. Transl Psychiatry. 2014; 4(8): e424. PMID: 25116834.
15. ECRI Institute. Clinical Evidence Assessment. EndeavorRx (Akili Interactive Labs, Inc.) interactive cognitive training software for treating attention-deficit/hyperactivity disorder in children. Plymouth Meeting, PA. ECRI Institute Published July 2020.
16. Empatica. EpiMonitor. Available at URL: **https://www.empatica.com/store/epimonitor/**. Accessed May 7, 2024.
17. Everitt H, Landau S, Little P, et al. Therapist-telephone delivered CBT and web-based CBT compared with treatment as usual in refractory irritable bowel syndrome: the ACTIB three-arm RCT. Health Technol Assess. 2019; 23(17): 1-154. PMID: 31042143.
18. Everitt HA, Landau S, O'Reilly G, et al. Assessing telephone-delivered cognitive-behavioural therapy (CBT) and web-delivered CBT versus treatment as usual in irritable bowel syndrome (ACTIB): a multicentre randomized trial. Gut. 2019;68(9):1613-1623. PMID: 30971419.
19. Everitt HA, Landau S, O'Reilly G, et al. Cognitive behavioural therapy for irritable bowel syndrome: 24-month follow-up of participants in the ACTIB randomized trial. Lance Gastroenterol Hepatol. 2019; 4(11):863-872. PMID: 31492643.
20. Fleming GA, Petrie JR, Bergenstal RM, et al. Diabetes digital app technology: Benefits, challenges, and recommendations. A consensus report by the European association for the study of diabetes (EASD) and the American diabetes association (ADA) diabetes technology working group. Diabetes Care. 2020; 43(1): 250-260. PMID: 31806649.
21. Flynn RM, Colón-Acosta N, Zhou J, et al. A game-based repeated assessment for cognitive monitoring: Initial usability and adherence study in a summer camp setting. J Autism Dev Disord 2019; 49 (5): 2003-2014. PMID: 30656527.
22. Franc S, Jobert M, Daoudi A, et al. Efficacy of two telemonitoring systems to improve glycaemic control during basal insulin initiation in patients with type 2 diabetes: The TeleDiab-2 randomized controlled trial. Diabetes Obes Metab. 2019: 21(10):2327-2332. PMID: 31173451.
23. Franc S, Hanaire H, Benhamou PY et al, Diabeo system combing a mobile app software with and without telemonitoring versus standard care: a randomized controlled trial in diabetes patients poorly controlled with a basal-bolus insulin regimen. Diabetes Technol Ther. 2020; 22(12): 904-911. PMID: 32407148.
24. Garcia LM, Birckhead BJ, Krishnamurthy P. et al. An 8-week self-administered at-home behavioral skills-based virtual reality program for chronic low back pain: Double-blind, randomized, placebo-controlled trial conducted during COVID-19. J Med Internet Res. 2021; 23(2): e26292. PMID: 33484240.
25. Garcia LM, Birckhead BJ, Krishnamurthy et al. Three-month follow-up results of a double-blind, randomized placebo-controlled trial of 8-week self-administered at-home behavioral skills-based virtual reality (VR) for chronic low back pain. J Pain. 2022; 23(5): 822-840. PMID: 34902548.

26. Gauthier LV, Nichols-Larsen DS, Uswatte G, et al. Video game rehabilitation for outpatient stroke (VIGoROUS): a multi-site randomized controlled trial of in-home, self-managed, upper-extremity therapy. EClinicalMedicine. 2021; 43:101239. PMID: 34977516.

27. Hanlon I, Hewitt C, Bell K, et al, Systematic review with meta-analysis: Online psychological interventions for mental and physical health outcomes in gastrointestinal disorders including irritable bowel syndrome and inflammatory bowel disease. Aliment Pharmacol Ther. 2018; 48(3): 244-259. PMID: 29901820.

28. Hayes, Inc. Evidence Analysis Research Brief. EndeavorRx (Akili Interactive Labs Inc.) interactive digital therapy for treatment of ADD/ADHD. Lansdale, PA: Hayes, Inc.; July 2020.

29. Hayes, Inc. Health Technology Assessment. Prescription digital therapeutics for management of type 1 diabetes mellitus. Lansdale, PA. Hayes, Inc. March 1, 2022.

30. Hayes, Inc. Health Technology Assessment. Prescription digital therapeutics for management of type 2 diabetes mellitus. Lansdale, PA. Hayes, Inc. March 14, 2022.

31. Hayes, Inc. Evolving Evidence Review. MindMotion GO (MindMaze) for Stroke Telerehabilitation. Lansdale, PA. Hayes, Inc. April 1, 2022.

32. Hayes, Inc. Evidence Analysis Research Brief. RelieVRx (AppliedVR, Inc.) for management of low back pain. Lansdale, PA. Hayes, Inc. April 11, 2022.

33. Hayes, Inc., Evidence Analysis Research Brief. Mahana IBS Prescription Digital Therapeutic (Mahana Therapeutics) for Treatment of Irritable Bowel Syndrome. Lansdale, PA. Hayes, Inc., May 5, 2022.

34. Hayes, Inc., Evolving Evidence Review. Mahana IBS (Mahana Therapeutics Inc.) for Treatment of Irritable Bowel Syndrome. Lansdale, PA. Hayes, Inc., June 23, 2022.

35. Hayes, Inc. Evidence Analysis Research Brief. CureSight for Treatment of Amblyopia in Children. Lansdale, PA. Hayes, Inc. November 8, 2022.

36. Hayes, Inc. Evidence Analysis Research Brief. Regulora (metaMe Health, Inc.) for Treatmetn of Irritable Bowel Syndrome. Lansdale, PA. Hayes, Inc., January 23, 2023

37. Hayes, Inc., Evolving Evidence Review. Luminopia One (Luminopia Inc.) for Treatment of Amblyopia in Children. Lansdale, PA., Hayes, Inc. April 14, 2023.

38. Hayes, Inc. Evidence Analysis Research Brief. EpiMonitor (Empatica) for Detection of Seizures. Lansdale, PA. Hayes, Inc., April 5, 2024.

39. Hayes, Inc. Evidence Analysis Research Brief. MamaLift (Curio Digital Therapeutics Inc.) for Adjunctive Treatment of Postpartum Depression. Lansdale, PA. Hayes, Inc., May 6, 2024.

40. Hayes, Inc. Evidence Analysis Research Brief. Rejoyn (Otsuka American Pharmaceutical Inc.) for Adjunctive Treatment of Major Depressive Disorder. Lansdale, PA. Hayes, Inc., April 18, 2024.

41. Hayes, Inc. Evolving Evidence Review. RevitalVision perceptual learning vision training program (Talshir Medical Technologies LTD) for treatment of amblyopia.

42. Hygieia Inc, D-Nav Insulin Management Program. Available at URL: **https://d-nav.com/provider/**. Accessed May 7, 2024.

43. International Medical Device Regulators Forum. Software as a Medical Device (SaMD): Key Definitions. December 9, 2013. **http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf**. Accessed May 7, 2024.

44. Khirasaria R, Singh V, and Batta A. Exploring digital therapeutics: The next paradigm of modern healthcare industry. Perspect Clin Res. 2020; 11(2): 54-58. PMID: 32670828.

45. Kollins SH, DeLoss DJ, Cañada E, et al. A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD: a randomized controlled trial. The Lancet Digit Health. 2020 2(4): e168-e178. PMID: 33334505.

46. Kosmicki JA, Sochat V, Duda M, Wall, DP. Searching for a minimal set of behaviors for autism detection through feature selection-based machine learning. Transl Psychiatry. 2015; 5(2): e514. PMID: 25710120.

47. Lacy BE, Pimentel M, Brenner DM, Chey WD, et al. American College of Gastroenterology Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021; 116(1): 17-44. PMID: 33315591. Available at URL: **https://journals.lww.com/ajg/Fulltext/2021/01000/ACG_Clinical_Guideline__Management_of_Irritable.11.aspx** . Accessed May 7, 2024.

48. Laver KE, Lange B, George S, et al. Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev. 2017; 11(11):CD008349. PMID: 29156493.

49. LIVMOR, Inc. Halo AF Detection System. Available at URL: **https://www.livmor.com/#solutions1**. Accessed May 7, 2024.

50. Luminopia, Inc., Luminopia One. Available at URL: **https://luminopia.com/**. Accessed May 7, 2024.

51. Magdalene D, Dutta P, Deshmukh S, Jyoti Boran C, Prabha Nath R. Neural vision perceptual learning as an effective treatment of amblyopia. Vision Development & Rehabilitation. 2022;8(4). **http://dx.doi.org/10.31707/VDR2022.8.4.p260.** Accessed May 7, 2024.

52. Mahana Therapeutics, Inc., Mahana IBS. Available at URL: **https://www.mahana.com/treatments/ibs**. Accessed May 7, 2024.

53. metaMe Health Inc., Regulora. Available at URL: **https://www.regulorahcp.com/**. Accessed May 7, 2024.

54. MindMaze, MindMotionGO. Available at URL:. **https://mindmaze.com/**. Accessed May 7, 2024.

55. National Institute for Health and Care Excellence (NICE). Evidence standards framework for digital health technologies. Corporate document (ECD7). Published 10 December 2018. Last Updated August 9, 2022. Available at URL: **https://www.nice.org.uk/corporate/ecd7/**. Accessed May 7, 2024.

56. National Institute of Health and Care Excellence (NICE) CG61: Clinical guideline: irritable bowel syndrome in Adults: Diagnosis and Management. February 23, 2008. Available at URL: **https://www.nice.org.uk/guidance/cg61/resources/irritable-bowel-syndrome-in-adults-diagnosis-and-management-pdf-975562917829** . Accessed May 7, 2024.

57. Nightware, Inc. NightWare Available at URL: **https://nightware.com/**. Accessed May 7, 2024.

58. NovaSight, Ltd. CureSight. Available at URL: **https://nova-sight.com/curesight-amblyopia-treatment/**. Accessed May 7, 2024.

59. Owusu JT, Sibelli A, Moss-Morris R, et al. A pilot feasibility study of an unguided, internet-delivered cognitive behavioral therapy program for irritable bowel syndrome. Neurogastroenterol Motil. 2021; 33(11): e14108. PMID: 33745228.

60. Patel NA, Butte AJ. Characteristics and challenges of the clinical pipeline of digital therapeutics. NPJ Digit Med. 2020; 3(1): 159. PMID: 33311567.

61. Quinn CC, Clough SS, Minor JM, et al. WellDoc mobile diabetes management randomized controlled trial: change in clinical and behavioral outcomes and patient and physician satisfaction. Diabetes Technol Ther. 2008; 10(3):160-168. PMID: 18473689.

62. Renovia, Inc. leva Pelvic Health System. Available at URL: **https://renoviainc.com/leva-digital-therapeutic/**. Accessed May 7, 2024.

63. Rejoyn. Rejoyn for US healthcare professionals only. Available at URL: **https://rejoynhcp.com/**. Accessed May 7, 2024.

64. RevitalVision. Lazy Eye / Amblyopia. 2020.Available at URL: **https://doctors.revitalvision.com/treatments/amblyopia-in-adults/** Accessed June 12, 2024

65. Ritterband, LM, Thorndike, FP, Gonder-Frederick, LA, et al. Efficacy of an internet-based behavioral intervention for adults with insomnia. Arch Gen Psychiatry. 2009;66(7):692-698.PMiD: 19581560.

66. Ritterband LM, Thorndike FP, and Ingersoll Karen S. Effect of a web-based cognitive behavior therapy for insomnia intervention with 1-year follow-up. JAMA Psychiatry. 2017; 74(1):68-75.

67. Rosenblatt P, McKinney J, Rosenberg RA, et al. Evaluation of an accelerometer-based digital health system for the treatment of female urinary incontinence: a pilot study. Neurourol Urodyn. 2019: 38 (7): 1944-1952. PMID: 31310369.

68. Tamez-Pérez HE, Cantú-Santos OM, Gutierrez-González D, et al. Effect of digital-tool-supported basal insulin titration algorithm in reaching glycemic control in patients with type 2 diabetes in Mexico. J Diabetes Sci Technol. 2021; Jul 29: 19322968211034533. Online ahead of print. PMID: 34323110.

69. U. S. Food and Drug Administration (FDA). Developing the software precertification program: Summary of learnings and ongoing activities: September 2020 Update. Silver Spring, MD. Available at URL: **https://www.fda.gov/media/142107/download**. Accessed May 7, 2024.

70. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for LIVMOR Halo AF Detection System. (LIVMOR Inc; Irvine, CA). No. K201208 .2020. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf20/K201208.pdf**. Accessed May 7, 2024.

71. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) De Novo Classification Order for NightWare Kit (Apple iPhone, Apple Watch, Apple iPhone Charging Cable, Apple Watch Charging Cable). (NightWare, Inc.; Minneapolis, MI). No. DEN200033. 2020. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200033.pdf**. Accessed May 7, 2024.

72. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). De Novo Classification Decision Summary for EndeavorRx, (Akili Interactive Labs, Inc.; Boston, MA) No. DEN200026. 2020. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN200026.pdf**. Accessed May 7, 2024.

73. US Food and Drug Administration (FDA). Developing a software precertification program: a working model (v1.0). January 2019. Silver Spring, MD. Available at URL: **https://www.fda.gov/media/119722/download**. Accessed May 7, 2024.

74. US Food and Drug Administration (FDA). Policy for device software functions and mobile medical applications. September 2019. Updated September 28, 2022. Silver Spring, MD. Available at URL: **https://www.fda.gov/media/80958/download**. Accessed May 7, 2024.

75. US Food and Drug Administration. (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for BlueStarRx, (WellDoc, Inc.; Columbia, MD). No. K162532. 2017. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf16/K162532.pdf**. Accessed May 7, 2024.

76. US Food and Drug Administration. (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for BlueStarRx, (WellDoc, Inc.; Columbia, MD). No. K190013. 2019. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf19/K190013.pdf**. Accessed May 7, 2024.

77. US Food and Drug Administration. (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for BlueStarRx, (WellDoc, Inc.; Columbia, MD). No. K193654. 2020. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf19/K193654.pdf**. Accessed May 7, 2024.

78. US Food and Drug Administration. (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for BlueStarRx, (WellDoc, Inc.; Columbia, MD). No. K203434. 2021. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/reviews/K203434.pdf**. Accessed May 7, 2024.

79. US Food and Drug Administration. (FDA). Digital health innovation action plan. Silver Spring, MD. Available at URL: **https://www.fda.gov/media/106331/download**. Accessed May 7, 2024.

80. US Food and Drug Administration (FDA). Guidance document. Enforcement policy for digital health devices for treating psychiatric disorders during the Coronavirus disease 2019 (COVID-19) public health emergency. April 14, 2020. Silver Spring, MD. Available at URL: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-digital-health-devices-treating-psychiatric-disorders-during-coronavirus-disease**. Accessed May 7, 2024.

81. US Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for d-Nav Insulin Management Program. (Hygieia, Inc. Livonia, MI) No. K181916. 2019. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf18/K181916.pdf**. Accessed May 7, 2024.

82. US Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for Insulia Diabetes Management Companion, (Voluntis, S.A., Cambridge, MA) No. K161433. 2016. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf16/K161433.pdf**. Accessed May 7, 2024.

83. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for Insulia Diabetes Management Companion, (Voluntis, S.A., Cambridge, MA) No. K170669. 06/19/2017. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf17/K170669.pdf**. Accessed May 7, 2024.

84. US Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for Insulia Diabetes Management Companion, (Voluntis, S.A., Cambridge, MA) No. K172177. 11/07/2017. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf17/K172177.pdf**. Accessed May 7, 2024.

85. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for Insulia Diabetes Management Companion, (Voluntis, S.A., Cambridge, MA) No. K202596. 2020. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf20/K202596.pdf**. Accessed May 7, 2024.

86. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Statement for My Dose Coach (Sanofi, Inc., Cambridge, MA) No. K171230. 2017. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf17/K171230.pdf**. Accessed May 7, 2024.

87. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for leva Pelvic Digital Health System (Renovia, Inc.). No. K180637. 2018. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf18/K180637.pdf**. Accessed May 7, 2024.

88. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for leva Pelvic Digital Health System (Renovia, Inc. Boston, MA). No. K192270. 2019. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf19/K192270.pdf**. Accessed May 7, 2024.

89. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for leva Pelvic Digital Health System (Renovia, Inc., Boston, MA). No. K212495. 2022. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf21/K212495.pdf**. Accessed May 7, 2024.

90. U. S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Statement for MindMotionGO, (MindMaze S.A., Lausanne, Switzerland) No. (K173931). 2018. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf17/K173931.pdf**. Accessed May 7, 2024.

91. US Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). De Novo Classification Decision Summary for RelieVRx (formerly EaseVRx) (AppliedVR, Inc., Van Nuys, CA). No. DEN 210014. 2021. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN210014.pdf**. Accessed May 7, 2024.

92. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). De Novo Classification Decision Summary for Parallel (Mahana Therapeutics, Inc., San Francisco, CA). No. DEN 200029. 2020. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200029.pdf**. Accessed May 7, 2024.

93. US Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH) 510(k) Premarket Notification Summary for Mahana Parallel Digital Cognitive Behavioral Therapy (CBT) Mobile Application for Irritable Bowel Syndrome (IBS) (Mahana Therapeutics, Inc., San Francisco, CA). No. K211372. 2021. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf21/K211372.pdf**. Accessed May 7, 2024.

94. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for CureSightCS 100 System. (NovaSight, Ltd., Airport City, Israel) No. K221375. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf22/K221375.pdf**. Accessed May 7, 2024.

95. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for Regulora. (metaMe Health, Inc. Chicago, IL) No. K211463. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf21/K211463.pdf**. Accessed May 7, 2024.

96. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). De Novo Classification Decision Summary for Luminopia One (Luminopia, Inc., Cambridge, MA). No. DEN 210005. 2021. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN210005.pdf** . Accessed May 7, 2024.

97. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for EpiMonitor. (Empatica,. Milan, Italy) No. K232915. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf23/K232915.pdf**. Accessed May 7, 2024.

98. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for Rejoyn. (Otsuka America Pharmaceutical, Inc., Rockville, MD) No. K231209. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf23/K231209.pdf**. Accessed May 7, 2024.

99. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for MamaLift Plus. (Curio Digital Therapeutics, Inc., Princeton, NJ) No. K223515. Silver Spring, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf22/K223515.pdf**. Accessed May 7, 2024.

100. US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). 510(k) Premarket Notification Summary for AA-1 System for the Treatment of Amblyopia (NeuroVision, Inc.) Burlington, MA). No. K012530. Silver Sprimg, MD. Available at URL: **https://www.accessdata.fda.gov/cdrh_docs/pdf/K012530.pdf**. Accessed June 12, 2024.

101. Voluntis. Insulia Diabetes Management Companion. Available at URL: **https://insulia.com** /. Accessed May 7, 2024.

102. Wall DP, Kosmicki J, DeLuca TF, et al. Use of machine learning to shorten observation-based screening and diagnosis of autism. Transl Psychiatry. 2012; 2(4): e100. PMID: 22832900.

103. Weinstein MM, Collins S Quiroz L, et al. Multicenter randomized controlled trial of pelvic floor muscle training with a motion-based digital therapeutic device versus pelvic floor muscle training alone for treatment of stress-predominant urinary incontinence. Female Pelvic Med Reconstr Surg. 2022; 28(1): 1-6. PMID: 33787561.

104. WellDoc, Inc. BlueStarRx Indications for use. Available at URL: **https://www.welldoc.com/indications-for-use/**. Accessed May 7, 2024.

105. Wygnanski-Jaffe T, Kushner BJ, Moshkovitz A., et al. An eye-tracking based dichoptic home treatment for amblyopia: a multicenter randomized clinical trial. Ophthalmology. 2022; Oct 25: S0161-6420(22)00835-1. Online ahead of print. PMID: 36306974.

106. Xiao S, Angjeli E, Wu HC, et al. Randomized controlled trial of a dichoptic digital therapeutic for amblyopia. Ophthalmology. 2022;129(1):77-85. PMID: 34534556.

107. Yalcin E, Balci O. Efficacy of perceptual vision therapy in enhancing visual acuity and contrast sensitivity function in adult hypermetropic anisometropic amblyopia. Clin Ophthalmol. 2014; 8:49-53. PMID: 24376340.

108. Zhong J, Wang W, Li J, et al. Effects of perceptual learning on deprivation amblyopia in children with limbal dermoid: a randomized controlled trial. J Clin Med. 2022;11(7).1879. PMID: 35407483.

Berry S, Berry R., Recker D, et. al, A randomized parallel-group study of digital gut-directed hypnotherapy vs muscle relaxation for irritable bowel syndrome. Clin Gastroenterol Hepatol. 2023; 21(12):3152-3159. PMID: 37391055.

History

Date	Comments
08/01/21	New policy, approved July 13, 2021. Add to Miscellaneous section. Medically necessary when criteria are met. Investigational when all criteria are not met.
10/01/21	Updated Related Policies, added policy 3.03.03 Prescription Digital Therapeutics for Attention Deficit/Hyperactivity Disorder.

Date	Comments
04/01/2022	Coding update. Added new HCPC code A9291.
05/01/22	Interim Review, approved April 12, 2022. Added d-NavInsulin Management Program, Insulia Diabetes Management Companion, My Dose Coach basal titration, Ieva Pelvic Health System, and MindMotion GO to the list of FDA approved prescription digital therapeutics that are considered investigational.
07/01/22	Interim Review, approved June 14, 2022. Added RelievRx for the treatment of chronic low back pain to the list of FDA approved prescription digital therapeutics that are considered investigational.
09/01/22	Interim Review, approved August 9, 2022. Added Mahana for IBS to the list of FDA approved prescription digital therapeutics that are considered investigational.
10/01/22	Interim Review, approved September 12, 2022. Removed content on Canvas DX as it is now addressed in 3.03.01 Prescription Digital Health Diagnostic Aid for Autism Spectrum Disorder. Updated description of A9291. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/23	Annual Review, approved December 13, 2022. Policy reviewed. References added. Added CureSight to the list of FDA approved prescription digital therapeutics that are considered investigational. Added CPT codes 0704T, 0705T, 0706T. Added new CPT codes 0740T and 0741T effective 1/1/2023.
04/01/23	Coding update. Added new HCPC code E1905.
07/01/23	Annual Review, approved June 13, 2023. Policy reviewed. References added. Added Regulora and Luminopia One to the list of FDA approved prescription digital therapeutics that are considered investigational.
10/01/23	Coding update. Added new HCPCS code A9292.
11/01/23	Interim Review, approved October 10, 2023. Removed policy 5.01.35 Prescription Digital Therapeutics for Substance Use Disorder from Related Policies. Removed Pear Therapeutics products ReSet,, ReSet-O, and Somryst from this policy as they are longer in business. Removed HCPCS code A9281 from policy.
02/01/24	Interim Review, approved January 9, 2024. Added ReSet and ReSet-O back to the list of PDTs that are considered investigational as they were bought by PursueCare from Pear Therapeutics, Inc. Added 5.01.643 Prescription Digital Therapeutics for Substance Use Disorder to Related Policies. Added HCPCS code A9291. Correction to the above 11/01/23 History entry: the code removed was A9291, not A9281.
04/01/24	Interim Review, approved March 25, 2024. Added note to see 10.01 523 Preventive Care for FDA approved or cleared mobile apps related to contraception and birth control that are prescribed by a health care provider.
06/01/24	Interim Review, approved May 14, 2024. Policy reviewed. References added. Added EpiMonitor, Rejoyn, and MamaLift Plus to the list of FDA approved prescription digital therapeutics that are considered investigational. Added CPT codes 0687T and 0688T (moved from E&I policy.) Added HCPCS code S9002.

Date	Comments
10/01/24	Annual Review, approved September 10, 2024. Policy reviewed. References added. Added RevitalVision to the list of FDA approved prescription digital therapeutics that are considered investigational. Removed HCPCS code T1505.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.