Exploring Digital Therapeutics in Psychiatry

To read more, please visit https://www.psychiatrictimes.com/topics/digital-therapeutics or scan the QR code
I go to therapy for one hour, once a week, but with Woebot, I can check in as many times as I want during the day and it’s just comforting for me. It fills the gap.

— Lee, Woebot user

Visit www.WoebotHealth.com to learn more
I am delighted to introduce this important supplement of Psychiatric Times™. In the context of the COVID-19 pandemic, telepsychiatry has passed its tipping point and now become a mainstream method of providing mental health services. In contrast, more complex solutions such as artificial intelligence, technology-enabled care, and smartphone applications are not yet mainstream. However, the integration of digital technologies into psychiatric care has only just begun. Looking ahead, I believe that technology-enabled care will be the defining advancement of mental health services in this generation. I believe there are 3 key trends that have shaped how we got here and give us clues to what the future holds.

Rapid Erosion of Stigma and Surging Demand

The COVID-19 pandemic created a series of conditions that both increased the overall risk for mental illness and triggered specific episodes: uncertainty about life or death, bereavement of loved ones, chronic isolation, job loss, financial uncertainty, and loss of numerous life events (prom, graduation, weddings, etc). The result has been a rapid increase in anxiety, depression, and alcohol use, with a whopping 40% of Americans reporting at least 1 mental health condition, and more than 10% seriously considering suicide.¹

At the same time, the pandemic circumstances have made it easier to talk about these experiences of depression and anxiety, in part, because they were understandable reactions to the various facets of a global crisis. On top of that, celebrities and other influencers have been speaking about their own mental health challenges, thereby normalizing the experience and providing hope for treatment.

For example, 23-time Olympic gold medalist swimmer Michael Phelps, and singer-songwriter Demi Lovato have both shared their experiences as part of serving as marketing ambassadors for Talkspace. Similarly, tennis player Naomi Osaka, the highest-paid female athlete in the world, recently shared her experience with depression and anxiety in an Instagram post, explaining why she did not want to participate in postmatch conferences.

These are not isolated events, and they make a huge impression on individuals everywhere who have their own struggles with mental health. As a result, an increasing number of people are seeking treatment than ever before.

Great Influx of Private Investment in Mental Health

Observing the decline in stigma and rise in demand, investors have been pouring money into mental health. For instance, earlier this year I published a discussion on this topic after finding that venture capital investors dedicated a record breaking $637 million to mental health startups in 2019, which was a 23-fold increase from 2013.² Estimates now suggest that venture capital investment topped $1 billion in 2020 and is poised to surpass $2 billion in 2021.³

In addition to venture capital, private equity companies are also investing in mental health; they are focusing on consolidating addiction facilities, residential treatment centers, and outpatient mental health clinics. In June 2021, LifeStance Health, one of the nation’s largest providers of outpatient psychiatric services, joined the Nasdaq stock exchange in an initial public offering just 4 years after being launched.⁴ This trend will likely continue.

You may be wondering why private investment is relevant to technology. We know technologies provide opportunities for mental health treatments to be scaled up. For investors, technology is attractive, as it is the key to driving larger returns. As we see more and more investment in mental health from private investors, I expect to see a greater focus on digital technologies, ranging from the basics like appointment scheduling and messaging between patients and clinicians, to more advanced features like chatbots and do-it-yourself smartphone appli-
cations as initial or complementary treatments. For psychiatrists, these technologies will enable us to treat more patients and disseminate care more widely than ever before.

**Toward a Post–COVID-19 Future: Hybrid Care**

The big question is: How will we get from where we are now, which is a loose combination of telepsychiatry and traditional care, to this futuristic digitally enabled care model?

Like all sustainable innovation, I predict that technologies will advance incrementally, steadily marching toward the day when digitally enabled care will be the norm (Figure). Just as telepsychiatry is now a patient expectation, patients will also expect appointment rescheduling, billing, and documents (including signature) to be fully digital in the next 10 years. In addition, the ability to send asynchronous messages to the provider in a secure format will be common. Finally, as insurance companies play a role in how care is reimbursed and delivered, there will be a growing expectation that digital tools (e.g., smartphone application modules for cognitive behavioral therapy) will help to reduce either the length or number of sessions needed for milder conditions and treatments.

**Concluding Thoughts**

The world is digitally powered, and our treatments will have to be digitally enabled if we are going to meet patients where they are: on their smartphones. Demand is surging, stigma is declining, and private investors will continue to push technologies that scale up our treatments. The field of psychiatry is poised to take advantage of this brave new world to better care for patients. I have never been as excited to be a psychiatrist as I am today. Happy reading—our future awaits!

**REFERENCES**


---

**FIGURE.**

**Imagining Technology-Enabled Care in 2030**

“Aaliyah,” a 27-year-old woman presents to Dr. Sanchez for outpatient treatment of generalized anxiety disorder. This is what her care looks like.

1. **TELEPSYCHIATRY**

Aaliyah meets the psychiatrist in person for the first visit, as well as quarterly visits, but most follow-ups are conducted via video. This way, she can make the appointments during the workday without requesting time off.

2. **ASYNCHRONOUS MESSAGING**

Aaliyah requests her selective serotonin reuptake inhibitor refill through a portal and asks questions via messaging, such as: “I’m much sweeter since starting sertraline. Is that normal?” She expects a response within 1 business day, but understands this messaging is not for complicated questions or emergencies.

3. **RESCHEDULING**

An unexpected work meeting came up that Aaliyah cannot miss. She logs into the practice portal and reschedules the appointment from Tuesday at 2:00 PM to Thursday at 3:30 PM, which is an open slot that works for her schedule.

4. **MEASUREMENT-BASED CARE**

Aaliyah fills out the Generalized Anxiety Disorder-7 questionnaire monthly, to track her progress and ensure she is regularly monitoring her symptoms. The results are sent to Dr. Sanchez for review and are automatically populated into Dr. Sanchez’s next clinical note. Dr. Sanchez also receives a copy in her inbox.

5. **DIGITAL APPLICATIONS**

At some point, Aaliyah develops insomnia and uses the patient portal to ask whether she needs to meet the psychiatrist. Dr. Sanchez replies, and suggests she try a free insomnia coach app for 8 weeks. He provides a link to the app and asks her to keep him posted.
Annual
Psychiatric Times™
WORLD CME CONFERENCE™

LIVE IN-PERSON AND VIRTUALLY ON SEPT. 30 – OCT. 2, 2021

Marriott Marquis San Diego Marina | San Diego, CA

BENEFITS OF ATTENDING

• Learn about state-of-the-art treatment in major depressive disorder
• Hear a debate-style presentation featuring 2 experts, each offering opposing viewpoints regarding the use of antidepressants to treat bipolar disorder, and weigh in on who you think has the most persuasive arguments
• Expand your skill set regarding strategies for self-care and creating resilience
• Learn about the psychiatric complications of COVID-19 and psychiatry in a postpandemic world
• Discover emerging research on the use of cannabis for psychiatric indications
• Explore cultural challenges in psychiatry

PROGRAM CO-CHAIRS

Anita Clayton, MD
David C. Wilson Professor and Chair
Department of Psychiatry and Neurobehavioral Sciences
University of Virginia
Charlottesville, VA

John J. Miller, MD
Medical Director, Brain Health
Editor-in-Chief, Psychiatric Times™
Staff Psychiatrist, Seacoast Mental Health Center
Consulting Psychiatrist, Insight Meditation Society
Barre, MA
Consulting Psychiatrist, Exeter Hospital
Exeter, NH

Sanjai Rao, MD
Associate Clinical Professor of Psychiatry
University of California, San Diego
Psychiatrist
VA San Diego Healthcare System
San Diego, CA

25% OFF REGISTRATION

Register with code PSYCH21AD.

To learn more and to register, visit event.gotoper.com/psych2021

Scan on smartphone to view full agenda
A

access to evidence-based psychotherapies remains limited by time constraints, affordability, stigma, and other factors.¹ Digital therapeutics (DTx) represent a valuable addition to psychiatrists’ toolkits. But before they recommend DTx, psychiatrists should consider how these programs are being evaluated by regulators and delivered to patients.²

Although existing DTx target a range of physical illnesses, those targeting mental health issues have received more funding in 2020 and 2021 than all other types.³ This development will have a direct impact on the practice of psychiatry: The scope of this impact depends in large part on how regulatory oversight evolves, since regulation determines which types of DTx are subject to oversight; whether a particular DTx is available via prescription or over the counter (OTC); and the required level of adjunctive care associated with it; and the evidence required for commercialization and reimbursement.

Given the unique set of applied psychotherapies associated with DTx, oversight will require an updated regulatory model. The US Food and Drug Administration (FDA) has recognized this need as well, given the recent launch of their new Digital Health Center of Excellence (DHCoE). One of the 3 primary goals of the DHCoE is to “innovate regulatory approaches to provide efficient and least burdensome oversight while meeting the FDA standards for safe and effective products.”³ As progress on this front unfolds, 3 aspects of DTx are particularly important for psychiatrists and other mental health providers to consider: evaluation, delivery, and reimbursement.

Evaluation of DTx
The necessary amounts and types of evidence required by the FDA for DTx are controversial. Most commercially available DTx for behavioral health conditions qualify as wellness interventions (ie, they do not make treatment claims), and the FDA has stated that these DTx do not need regulatory clearance to be on market because they are low risk. In contrast, DTx that make treatment claims for specific psychiatric disorders do require traditional FDA clearance.

DTx cleared by the FDA have gone through both de novo classification and premarket notification (510k) regulatory pathways. The de novo classification permits device clearance when no marketed predicate device in the space exists and empirical evidence provides reasonable assurance of safety and efficacy for the intended use. Despite these standards, the clinical significance of FDA-cleared devices for mental health has been called into question.⁴ Moreover, DTx pursuing the 510k pathway are required only to show equivalence to previously cleared devices. This has raised concerns that DTx will not have clinically significant effects, or that the results will not generalize to real-world psychiatric patients.⁵

In a March 2021 perspective on the FDA, Rathi and colleagues wrote: “The FDA, Rathi et al noted that “breakthrough devices were approved primarily on the basis of studies that used short-term, surrogate end points for effectiveness, which may not translate into clinical benefits.”⁶” For example, a DTX product that uses the Apple Watch to send vibrations to interrupt nightmares in those with posttraumatic stress disorder was given breakthrough designation and permission to market based on a 30-day study of 70 patients.⁷ Rathi and colleagues continued: “The FDA authorized some breakthrough devices without supporting effectiveness data (ie, they were approved on the basis of safety data alone) and authorized other devices that carried important known safety risks.”⁸ As a result of these concerns, the Medicare Coverage of Innovative Technology (MCIT) rule, designed to grant an immediate Medicare coverage pathway for DTx once they are designated as a breakthrough by the FDA, has been delayed multiple times.⁹

To improve the utility of DTx for psychiatric practice, regulatory agencies need to reach greater consensus and clarity on what constitutes sufficient evidence for approvals—both for wellness and the treatment of psychiatric conditions. In the interim, it will be important for psychiatrists to evaluate the evidence for the DTx they would like to leverage in their practice, whether or not the FDA has cleared them.

Delivery of DTx
FDA regulatory classifications of DTx for psychiatric disorders have specified that these products should be distributed by prescription only. However, restricting access to DTx with particularly safe profiles contradicts many of the central goals behind DTx development. It is
critical to consider which providers will be able to offer DTx to patients. With few exceptions (eg, the US Army), the only providers with prescription privileges are medical doctors and nurse practitioners. However, mental health care is provided by a broader range of professionals.

Most FDA-cleared DTx have been designated as adjunctive rather than stand-alone treatment, despite the fact that many DTx have been developed as stand-alone interventions and have shown clinical benefits without serving as an adjunct to in-person care. Requiring adjunctive care may be appropriate for some DTx, but denying individuals with low or moderate levels of psychiatric symptoms the opportunity to benefit from stand-alone DTx when risks are minimal seems misguided.

The majority of DTx have not been cleared by the FDA because they fall under other categories of oversight that do not require premarket clearance. In many cases, digital tools marketed as wellness products leverage the same clinical interventions (eg, CBT) that are simultaneously cleared by the FDA as prescription-only products. Given the large number of individuals who do not meet formal criteria for a diagnosis but experience clinical levels of distress nonetheless, a more granular approach to evaluation may be appropriate.

To provide additional guidance for psychiatrists and patients, it would be helpful for the FDA to establish a clearance status for DTx that is similar to an OTC designation. Although some DTx carry inherent risks, unnecessary restrictions on access to low-risk DTx are a bigger risk to consumers.

**Reimbursement of DTx**

Broadly speaking, there are 2 central challenges impacting the development of routine reimbursement pathways for DTx: reimbursement for the DTx itself and reimbursement for coordinating care.

There is currently no standard pathway for reimbursement for DTx; instead, DTx tend to be purchased by patients directly.2 If providers or patients cannot be reimbursed for the cost of DTx via the insurer, then the reach of DTx will be limited to patients who can pay out of pocket. The most comprehensive solution would be to establish a new DTx benefit category under Medicare; however, this change would require an act of Congress.

Reimbursement for coordinating care surrounding DTx is not straightforward. Under the current system, 4 Current Procedural Terminology (CPT) codes for remote physiologic monitoring treatment management services (99453-99458) have been used for some DTx. However, the October 2020 editorial meeting of the American Medical Association (AMA) seems to have established a new group of codes titled remote therapeutic monitoring services and remote therapeutic monitoring treatment management services. The change in a key word, from *physiologic* to *therapeutic,* may make these codes available to a broader scope of DTx, including those that target mental health and substance abuse.30

**Concluding Thoughts**

As we move into a new era of DTx for mental health, regulatory and reimbursement structures and processes must be modernized to reflect the treatments they oversee. As psychiatrists and other mental health providers learn to integrate DTx into patient care, it is critical to advocate for policies that broaden the accessibility and acceptability of these innovative and effective tools.

**Dr Doss** is a professor of psychology at the University of Miami. **Dr Weingardt** is chief executive officer of Audacious Digital Health. **Dr Lindhiem** is an associate professor of psychiatry at the University of Pittsburgh. **Dr Timmons** is an assistant professor of psychology at Florida International University. **Dr Jones** is a professor in the Department of Psychology and Neuroscience at the University of North Carolina at Chapel Hill.

Dr Comer is a professor of psychology at the Center for Children and Families at Florida International University. Dr Carl is vice president of clinical development & medical affairs at Big Health Inc.

**REFERENCES**


8. Medicare Program; Medicare Coverage of Innovative Technology (MCIT) and Definition of “Reasonable and Necessary.” Delay of Effective Date. Final Regist. 2021;218(64):268-26854.


As the need grows for equitable, accessible, and affordable mental health treatment, digital therapeutics—app-based treatments—show promise for filling these gaps, particularly to target anxiety. The high prevalence of anxiety disorders “vastly exceeds the capacities of mental health services” to provide treatment for all those affected.1

Anxiety has risen since the beginning of the COVID-19 pandemic. The US Census Bureau reported that adults were 3 times more likely to screen positive for anxiety disorders in 2020 compared with 2019 (31% vs 8%). A cross-sectional survey of individuals conducted in China February 2020 found the prevalence of generalized anxiety disorder (GAD) to be 35.1%; a meta-analysis found an average anxiety prevalence of 32% during the pandemic (17 studies, n = 63,439).2,3 A study of patients diagnosed with COVID-19 between January and August 2020 (n = 62,000+) found that 1 in 5 patients with no psychiatric history received a new mental health diagnosis, with the greatest health risk being for anxiety disorders.4

Digital therapeutics can be designed to specifically target a behavioral or psychological mechanism of action, and they can be developed with user-centered design principles to maximize engagement. However, to date, very few digital therapeutics have been tested for efficacy, and even fewer have been studied regarding mechanism of action. There seem to be 2 categories of digital therapeutics emerging: those that are commercially developed with little supporting evidence or plans for evaluation and those with academic or government backing (and often not easily available to consumers).1 The former has the advantage of maximizing curb appeal: Resources can be devoted toward developing engaging user experiences using the latest design techniques, and companies can push a digital therapeutic to market rapidly. Scientists have developed evidence-based digital therapeutics, yet few are publicly available. They appear more slowly than their commercial counterparts, and those that do appear usually fail to attract users and user engagement.5 However, both face the same fate: No matter how shiny an app is, it still takes time to run rigorous clinical trials to determine efficacy (and mechanism).

John Torous, MD, Digital Section Editor for Psychiatric Times™ and chair of the American Psychiatric Association’s Smartphone App Evaluation Task Force, put it bluntly when interviewed for an article on digital therapeutics in Nature: “Right now it almost feels like the Wild West of health care.”6

How can the busy health care clinician keep up-to-date on the latest trends, determine which digital therapeutics are evidence based, and give informed answers when patients ask which apps to use? Is there enough evidence for prescribers to pull out their proverbial digital prescription pad to recommend an app-based treatment for anxiety?

After considering the recent literature, there are a few questions clinicians should consider.

**Judson Brewer, MD, PhD**

Dr Brewer is an associate professor of psychiatry at the Warren Alpert Medical School of Brown University, executive medical director of behavioral health at Sharecare Inc, and author of Unwinding Anxiety. Twitter: @judbrewer. He owns stock in, and serves as a paid consultant for, Sharecare Inc, the company that owns the Unwinding Anxiety app described in this article. The financial interest has been disclosed to and is being managed by his institution, Brown University, in accordance with its Conflict of Interest and Conflict of Commitment policies.

---

**Treatment at Your Fingertips: Cautious Optimism for Digital Therapeutics to Treat Anxiety**

---

**Dr Brewer** is an associate professor of psychiatry at the Warren Alpert Medical School of Brown University, executive medical director of behavioral health at Sharecare Inc, and author of Unwinding Anxiety. Twitter: @judbrewer. He owns stock in, and serves as a paid consultant for, Sharecare Inc, the company that owns the Unwinding Anxiety app described in this article. The financial interest has been disclosed to and is being managed by his institution, Brown University, in accordance with its Conflict of Interest and Conflict of Commitment policies.

---

8  Psychiatrist Times™ supplement  August 2021
Why Should There Be an Effect? What Mechanism Is Being Targeted?

A good place to start is to consider if a digital therapeutic is mechanistically based. Although many apps assert that they are scientifically based, very few live up to this claim. The National Institutes of Health established a common fund program called the Science of Behavior Change (SOBC) to focus on mechanisms of change in behavioral interventions as a way to both strengthen intervention development and “increase rigor, transparency, and dissemination of common terminology, methods, and measures.”7 The basic idea behind SOBC is to measure if a behavioral intervention engages a hypothesized mechanism of change and if engaging that target leads to change in a health outcome. If this approach sounds similar to that taken for the development of any new drug, it should, because it is. It was modeled after the experimental medicine approach. However, a significant research-practice gap exists in the digital mental health field, especially in the field of anxiety interventions.4

Findings of a recent study looking at the frequency of evidence-based treatment elements in apps for anxiety showed that the most commonly included elements were psychoeducation (53%), relaxation (47%), meditation (41%), and mindfulness (29%) (Figure).4 Yet, the inclusion of an element does not automatically translate to targeting a specific mechanism or therapeutic benefit. Another recent review found that 67% of apps for anxiety lacked involvement of any health professional in their development, and just 4% had been empirically evaluated.5

This unfortunate lack of focus on mechanism is not due to an absence of information on how anxiety can develop and be perpetuated. For example, decades-old research has suggested potential mechanisms of action, such as targeting worry-driven negative reinforcement, yet only recently have these been incorporated into digital therapeutic development.20–24

Who Is the Studied Population?

With apps that can reach thousands, and even millions, of potential patients, it is much easier to collect data from a convenience sample, look for reductions in some type of scale, and then claim it to be an evidence-based treatment for anxiety. However, there is a world of difference between someone who is mildly anxious (after all, who is not these days?), and someone with mild to moderate symptoms of anxiety, individuals in the United Kingdom’s National Health System (NHS) and “who may be eligible and require iCBT” as part of the Improving Access to Psychological Therapies (IAPT) program.15 Additionally, 2 studies of app-based mindfulness training for anxiety (Unwinding Anxiety) have used GAD-7 scores of ≥ 10 as a minimum cutoff for inclusion of anxious physicians and individuals with GAD, respectively.15,16 Taken together, these results suggest that the majority of studies are drawing convenience samples from nonclinical populations, and that can lead to problematic inferences on the efficacy and utility of digital therapeutics in individuals with moderate to severe anxiety—those that would be most likely to seek or be referred to treatment—unless they have been specifically studied in these populations.

What Is the Evidence? Is There a Clinically Relevant Reduction in Symptoms?

Popularity does not equal evidence for efficacy. A number of app-based programs have put a primary focus on increasing their user base rather than developing digital therapeutics for anxiety. Although there is nothing inherently wrong with this approach—it is just a different focus—seeing a lot of individuals use an app can lead to a false sense of efficacy. Most studies to date are small pilot studies, often run by the app developers rather than by independent researchers, and the results have yet to be replicated. Additionally, many studies are run relative to wait-list

“Right now it almost feels like the Wild West of health care.”
—John Torous, MD

August 2021 Psychiatric Times™ supplement
control groups. Although this is better than no control group, it does not assess basic confounding components that are covered by a treatment as usual control group, such as receiving some type of treatment and expectancy effects (which, if performed well, will include the usual clinical care delivered by their therapist or doctor).

As previously mentioned, only a few published studies have examined digital therapeutics in individuals with moderate to severe anxiety: 1 in the general population (mainly recruited from users who were already signed up for the app Pacifica) with baseline GAD-7 scores of between 5 and 14; 1 (iCBT) in the UK’s NHS in individuals with baseline GAD-7 scores of ≥ 8; 1 (Unwinding Anxiety) in anxious physicians with baseline GAD-7 scores of ≥ 10; and 1 (Unwinding Anxiety) in individuals with GAD with baseline GAD-7 scores of ≥ 10.13,15-17

In the first study, a randomized controlled trial that compared the Pacifica app to a wait-list control, only 35% of the app and 47% of wait-list participants completed the study. A composite anxiety score, using an average score of standardized GAD-7 and Depression and Anxiety Stress Scale-21 (anxiety component) scores, showed a statistically significant drop in both groups after 4 weeks (wait-list control, 0.23 composite point; Pacifica, 0.66 composite point), which was reported as statistically significantly different. In the second study, a randomized controlled trial of iCBT (Silvercloud) vs wait-list control, individuals in the iCBT group showed a statistically significant 35% reduction in GAD-7 scores at 8 weeks (baseline, 12.7; 8-week follow-up, 8.2) relative to a 15% reduction in the control group (baseline, 12.7; 8-week follow-up, 10.8). Retention was 82% and 76%, respectively.

In the third study, a single-arm trial of the Unwinding Anxiety app, anxious physicians demonstrated a statistically significant reduction in GAD-7 scores of 48% and 57% after 1 and 3 months, respectively (baseline, 11.5; 1-month, follow-up, 6.0; 3-month follow-up, 5.0). Retention was 60%.

In the fourth randomized controlled trial looking at Unwinding Anxiety vs treatment as usual (TAU), individuals randomized to Unwinding Anxiety showed a statistically significant 67% reduction in GAD-7 scores (baseline, 12.0; 2-month follow-up, 3.0) relative to a 14% reduction in the TAU group at 2 months (baseline, 13.0; 2-month follow-up, 10.0). Retention was 88% for the Unwinding Anxiety group and 100% for the TAU group.

**How Risky Is This App For My Patient?**

When prescribing a medication or suggesting that a patient try a behavioral treatment, we fall back on the ideals of the Hippocratic oath that we took at the beginning of medical school: First, do no harm. Although digital therapeutics do not carry the traditional

---

**FIGURE. Characteristics of Apps for Anxiety**

<table>
<thead>
<tr>
<th>Element</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoeducation</td>
<td>53%</td>
</tr>
<tr>
<td>Relaxation</td>
<td>47%</td>
</tr>
<tr>
<td>Meditation</td>
<td>41%</td>
</tr>
<tr>
<td>Mindfulness</td>
<td>29%</td>
</tr>
<tr>
<td>Lacked involvement of any health professional during its development</td>
<td>67%</td>
</tr>
<tr>
<td>Empirical evaluation</td>
<td>4%</td>
</tr>
</tbody>
</table>
adverse effect risk profile of a medication, it is important to approach information in a parallel manner: Ingesting information is not free of unintended consequences. For example, a review of apps for bipolar disorder found the presentation of information that could lead to harm (eg, encouraging individuals to drink liquor to help them sleep during manic episodes). Additionally, privacy is a concern, as apps can easily collect personal information ranging from symptoms to geolocation.

**Key Takeaways**

Digital therapeutics have the potential to live up to their promise: Mechanistic and evidence-based treatments that can be widely disseminated at low cost. To date, very few have demonstrated efficacy, and these studies would benefit from replication and extension of their findings. As clinicians consider recommending app-based treatments, it is important to stay abreast of emerging study results, and as they evaluate apps for their patients, they must keep those aforementioned important questions in mind (Table).

**REFERENCES**


**TABLE. Important Questions to Consider When Evaluating an App**

1. What is the proposed mechanism, if any?

2. How anxious is the population that was studied?

3. Are the reported changes in anxiety clinically meaningful?

4. Is the treatment safe (eg, developed by credible teams that include clinicians)?
According to some estimates, close to one-third of adults in Western countries regularly experience difficulties with sleep. Additionally, approximately 10% of adults meet DSM-5 diagnostic criteria for insomnia disorder, which is characterized by difficulties falling or staying asleep at least 3 days per week for at least 3 months, along with impairment in daytime functioning or well-being. Additionally, approximately 10% of adults meet DSM-5 diagnostic criteria for insomnia disorder, which is characterized by difficulties falling or staying asleep at least 3 days per week for at least 3 months, along with impairment in daytime functioning or well-being. Beyond sleep difficulties and associated daytime complaints, individuals with insomnia are at increased risk of developing mental disorders (eg, depression, anxiety, substance use disorders) and physical health conditions (eg, type 2 diabetes, cardiovascular disease, and hypertension). It is not surprising, then, that the burden of insomnia is significant and individuals with insomnia report a lower quality of life than their healthy-sleeping counterparts.

The Potential of DTx
Internet- and smartphone-delivered treatments, termed “digital therapeutics” (DTx), are ideally situated to provide a solution for overcoming the dissemination and access barriers. Chieflly, DTx decouple treatment from the requirement to work directly with a mental health care professional. It also makes treatment flexible and scalable, as access to the internet and devices are its only limiting factor (and even that may one day be an obsolete consideration). Plus, many patients with insomnia turn to self-help more readily than to professionals, making DTx an ideal access point.

Digitally-delivered CBT (dCBT) can take 1 of 3 formats: 1) web- and smartphone-based tools to support ongoing psychotherapy with a clinician; 2) dCBT packages implemented by the consumer outside of a therapy context but guided by regular input from a clinician, ie, guided dCBT; and 3) fully automated dCBT requiring no support from clinicians. Of these, fully automated CBT is the most promising option for addressing access to CBT-I; these programs can completely transcend the limitations in provider availability, offer immediate access, and negate any reluctance patients
may have to working with a therapist. For these reasons, it is the only form of dCBT that could be scaled to implement treatment guideline recommendations to use CBT-I as first-line therapy.

To fully realize the ambitious aim of digital solutions, attention to technical expertise and the infrastructure of big tech collaborators is required. DTx are successful and scalable only if they 1) guarantee an intuitive, engaging, and adaptive user experience; 2) can be updated, monitored, and repaired easily as needed; and 3) are capable of managing tremendous amounts of data securely. If the aim is to make CBT as accessible and acceptable as pharmacotherapy, clinicians and patients need not (and should not) be satisfied with digital solutions that fall short of this goal. Technological rigor must be matched by empirical rigor, ensuring only those treatments with the very strongest evidence base are carefully translated to a digital format.

A number of dCBT programs have been developed; the 2 most widely known and fully automated programs are Sleepio and Somryst (previously called SHUTi). Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs. Sleepio is delivered via their website and has an accompanying smartphone application; Somryst was historically delivered via their website and is now available via a smartphone application. Both deliver content and exercises across 6 sessions over a flexible timeline, and content remains available to suit the patient’s needs.

### TABLE.

**Components of CBT for Insomnia**

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep hygiene</td>
<td>Information and education on lifestyle factors (eg, caffeine intake, alcohol use) and environmental factors (eg, noise, temperature, light) that can influence sleep.</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>Techniques to target and address thoughts and beliefs about sleep that interfere with sleep and increase sleep-related arousal.</td>
</tr>
<tr>
<td>Stimulus control</td>
<td>Instructions to strengthen the association between the bed and sleep and break associations between the bed and wakefulness.</td>
</tr>
<tr>
<td>Sleep restriction therapy</td>
<td>Systematic restriction and standardization of time in bed to consolidate sleep and increase sleep drive.</td>
</tr>
<tr>
<td>Relaxation techniques</td>
<td>Progressive muscle relaxation, autogenic breathing, and guided imagery to help reduce sleep-related anxiety.</td>
</tr>
</tbody>
</table>
dCBT will involve many more products following a similar route.

**Examining Effectiveness**

The efficacy of dCBT-I is supported by a large and growing evidence base. In randomized controlled trials, both guided and fully automated dCBT interventions have demonstrated medium to large effect sizes on a range of outcomes including insomnia severity, sleep efficiency, total sleep time, and sleep onset latency. Additionally, dCBT interventions consistently outperform the behavioral therapy equivalent of placebo (imagery-based procedures), wait-list, sleep hygiene, and usual care controls. dCBT has also been shown to improve sleep in a wide variety of populations, including individuals with subclinical sleep complaints, pregnant women, and individuals with comorbid medical and psychiatric disorders. The durability of effects for dCBT is promising, with these improvements being maintained up to a year and beyond. Based on these findings, there is an emerging consensus that dCBT produces effects comparable to face-to-face therapy.

Notably, the effects of dCBT-I extend beyond better sleep. Studies have consistently shown reductions in anxiety and depression symptoms in addition to other areas of mental health, and that effects are likely mediated by improvements in insomnia symptoms. Benefits have also been observed in terms of quality of life, physical health, and workplace productivity; effects on physical health and workplace productivity are, again, likely mediated by reductions in insomnia. It is critical, therefore, to continue exploring how dCBT could be integrated in behavioral medicine, rehabilitation, and other nonpsychiatric health care settings in order to best meet the needs of those seeking insomnia therapy and for whom insomnia may not be their presenting complaint but who could nonetheless benefit from intervention.

Scaling dCBT has the potential to be significantly more affordable than scaling in-person services. Even guided dCBT is more cost-effective than traditional CBT-I, and we can expect that fully automated dCBT would offer yet more cost efficiency. To illustrate, my colleagues and I recently evaluated the estimated monetary benefits of Sleepio in terms of treatment costs and downstream effects of treating insomnia, such as improved workplace productivity. We found fully automated dCBT to be more cost-effective than pharmacotherapy and traditional individual and group therapy for insomnia, yielding an estimated net monetary benefit of $681 per individual over 6 months.

Consider, finally, another methodological advantage of dCBT for insomnia, or any digital therapeutic for that matter: the ease of disseminating digital interventions permits conducting research with sample sizes at least an order of magnitude larger than face-to-face RCTs (eg, recent trials of Sleepio randomized 1711 and 3755 participants respectively). Researchers have the freedom to ensure that study populations are broadly representative and generalizable or narrowly specified to meet the scientific need. This means that the evidence base for dCBT may be able to grow faster, and with greater rigor and granularity, than that of medication or face-to-face therapy.

It is worth noting, however, that dCBT will not be a panacea for all. Some individuals will still require face-to-face CBT-I with a trained clinician or sleep medicine specialist, and some will require medication management. Nevertheless, dCBT has the advantage of providing access at scale to evidence-based CBT-I and, therefore, is well-positioned to be part of a stepped-care model of insomnia treatment that is consistent with treatment guidelines.

**Future Research Directions**

To responsibly harness the tremendous potential of dCBT for insomnia, it is important to recognize where more research is needed. Although we can confidently say that dCBT is advantageous in a general sense, the picture must be sharpened in a number of ways. To date, there have been very few noninferiority trials comparing dCBT to in-person CBT-I, and those that have been carried out have reported mixed results. In addition, a systematic exploration of the variables moderating and mediating response to dCBT is important, especially in figuring out how best to fine-tune treatment delivery to meet the needs of patients with insomnia. Factors likely to affect treatment effectiveness include facility with digital applications in general, inclination to access treatment or self-help generally, and the tendency to have difficulty engaging with treatments and adhering to treatment regimens.

We also need to compare different means of disseminating and implementing dCBT at scale (eg, as PDTs vs self-help, with and without the involvement of providers known to the patient, and across different settings). Demonstrating real-world cost-effectiveness will be critical.

Even with the overarching aim of maximizing automation, it will nonetheless be essential to identify conditions under which judicious use of sleep experts is incrementally beneficial. It is also important to consider that some individuals who pursue dCBT treatment may have conditions that require evaluation and treatment by a health care provider. While this consideration applies to a wide range of medical conditions, a few notable examples include the following: obstructive sleep apnea, narcolepsy, major depressive disorder, anxiety disorders, mania, substance use disorders, and endocrine disorders associated with sleep disturbance. It
will be important to identify ways to incorporate some means of identifying individuals with such conditions and motivating them to engage in appropriate evaluation/treatment into digital platforms. Finally, recognizing that pharmacotherapy remains the most widespread intervention for insomnia to date, it is important to explore how dCBT-I might be implemented in combination with pharmacotherapy, or as a means of reducing reliance on medication. Only with these questions in mind can we meaningfully leverage the power of dCBT to bring clinical practice in line with the best available guidelines for treating insomnia.

**REFERENCES**

34. August 2021

**Psychiatric Times™ supplement**
MEET THE FIRST AND ONLY
FDA-APPROVED PRESCRIPTION VIDEO GAME

A clinically-validated treatment for inattention in children with ADHD

Our proprietary and patented 
Selective Stimulus 
Management Engine 
(SSME™) technology targets each patient’s key neural systems related to attentional control in the brain.

Proven efficacy and safety profile in
600+ PATIENTS across 5 CLINICAL STUDIES

Learn more and see the data at 
HCPENDEAVORRX.COM

Indication and Important Safety Information

The EndeavorRx® app is a digital treatment indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD and should be considered for use as part of a therapeutic program. Patients who engage with EndeavorRx may not display benefits in typical behavioral symptoms, such as hyperactivity.

The most common side effect observed in children in EndeavorRx’s clinical trials was a feeling of frustration, as the game can be quite challenging at times. No serious adverse events were observed with its use.

Copyright ©2021 Akili Interactive Labs, Inc. All rights reserved. Akili, EndeavorRx, Akili Care, ADHD Insight, Insight, as well as the logos for each, are trademarks or registered trademarks of Akili Interactive Labs, Inc. Other trademarks are trademarks or registered trademarks of their respective owners.