



Hui Xue, Kirsten Westhues, Mike Joyce, Olivier Leclerc

Digital therapeutics

Preparing for take-off

Understanding the obstacles to the adoption of digital therapeutics is key to understanding how they might be overcome

Digital therapeutics have made much progress over the past decade, harnessing technology to supplement or potentially replace traditional clinical therapy. Some devices complement traditional treatment by helping patients manage their condition, including informing when and how much medication to take. And some offer alternative treatments to drugs, such as sensory stimuli delivered through a tablet computer to manage insomnia or depression.

Importantly, digital therapeutics tend to target conditions that are poorly addressed by the healthcare system today, such as chronic diseases or neurological disorders. In addition, they can often deliver treatment more cheaply than traditional therapy by reducing demands on clinicians' time. And all the while more evidence is emerging to demonstrate their value in clinical terms. For instance, the US Food and Drug Administration (FDA) recently approved a mobile application to help treat alcohol, marijuana, and cocaine addiction, citing clinical trials that showed 40 percent of patients using the app abstained for a three-month period, compared with 17.6 percent of those who used standard therapy alone¹ (see sidebar, "What is the value of digital therapeutics?").

¹ Mukherjee, Sy, "FDA clears the first-ever mobile app to treat alcohol, marijuana, cocaine addiction," *Fortune*, September 14, 2017, <http://fortune.com/2017/09/14/fda-alcohol-marijuana-cocaine-mobile-app>.

So why have digital therapeutics not yet joined the mainstream in healthcare? Why are more physicians not prescribing digital therapies, and more patients not using them? And why are pharmaceutical companies not investing more in digital therapeutics R&D, preferring to test the water with relatively small investments in partnerships and acquisitions?

We believe the potential of these new treatments is being restrained by two obstacles. First, to its detriment, digital therapeutics as a segment is often not distinguished from the digital health and well-being market, which includes anything from sleep trackers to fitness apps. Second, the incentives for providers, payors, and pharmaceutical companies to adopt digital therapeutics are not well aligned.

Understanding these obstacles is key to overcoming them and gauging when digital therapeutics will take their place as an integral part of modern medicine.

Obstacle 1 – Distinguishing digital therapeutics from the health and well-being market

Hundreds of millions of dollars have been invested in digital wellness technology, with more than 318,000 health-related apps available to date.² But it is hard to separate those that merely pass the minimum technical requirements for download from an app store from those that are not only safe, but also have proven therapeutic value. Indeed, some have fallen foul of regulators because of unsubstantiated claims about clinical benefits, helping instill doubts about digital therapeutics in the minds of consumers and healthcare professionals alike. As Peter Hames, CEO of Big Health, a digital medicine company, says, “We are in the ‘quack medicine’ era of digital therapeutics, where there’s a huge morass of solutions of incredible variance of quality, and there isn’t yet a really established set of criteria.”

A definition of digital therapeutics, grounded in clinical evidence and sufficient to meet the standards of regulators, would therefore help build confidence in the technology, separating it from general digital wellness in the same way that pharmaceuticals are separated from supplements. The definition might include the following requirements:

- Completion of a number of studies among the target population, conducted by independent principal investigators and replicated at multiple sites and/or with different investigators, with trial results (including clinically meaningful outcomes) published in a peer-reviewed journal
- One or more multi-center, randomized, controlled trials
- Ongoing clinical research in the target population involving collection and analysis of real-world evidence to assess safety and effectiveness.

Such a definition would assure all stakeholders – including advocacy groups, patients, practitioners, and investors that want to back not just app sales but medical advances – that devices referred to as digital therapeutics met high standards of safety, effectiveness, and value.

² IQVIA Institute report, “The Growing Value of Digital Health,” November 2017.

What is the value of digital therapeutics?

Years ago, an optimistic answer to this question might have been “We don’t know yet.” Now, interest is emerging in the clinical studies that show the value of digital therapies, particularly in disease areas that benefit from continuous patient engagement.

We see two distinct segments of digital therapeutics emerging. The first consists of therapies that extend the value of traditional pharmaceutical treatments, through companion software providing adherence management and personalized treatment recommendations, for example. The second segment consists of therapies that potentially could replace traditional pharmaceuticals.



Digital companions

Voluntis, a medtech company, creates digital companions that empower people to self-manage their treatment or treatment symptoms in remote collaboration with their healthcare teams. Its disease-specific companions optimize the value of medication therapies in diabetes and oncology. Using an app, a patient can document daily observations on their smartphone. The app then gives the patient instant recommendations about dosage, changes to behavior, or when to call a physician. In the meantime, it shares the patient’s data with healthcare professionals, via a dedicated Web app, enabling them to intervene between visits if necessary and prepare for the next examination. Voluntis has clinical evidence to support its companions’ effectiveness and has received FDA clearance and the CE Mark for Insulia, its digital companion for people with type 2 diabetes.



Replacement therapies

An example of a replacement therapy is Akili, which is building clinically validated treatments for neurological and psychiatric conditions to be deployed on personal devices such as tablets or smartphones.

Akili’s digital therapeutic is a software-based, algorithmically powered sensory stimulus delivered through an action video game interface on a tablet. Rather than serving as an extension of a conventional therapy, the company says the device could potentially be a primary treatment for ADHD¹, depression, Alzheimer’s disease, and traumatic brain injury, reducing or eliminating the need for pharmaceutical or face-to-face therapy.

The treatment targets the brain’s interference-processing system. During the interaction, the game deploys real-time interventions that adapt as a person continues through the game. All the while, it collects data that can be used to tailor therapy, track progress, and continuously improve the product. Some other companies in this area include Big Health, whose Sleepio product targets insomnia with cognitive behavioral therapy, and MindMaze, which is developing a stroke recovery therapy.

¹ “Akili achieves primary efficacy endpoint in pediatric ADHD pivotal trial” (<https://www.akiliinteractive.com/news-collection/akili-achieves-primary-efficacy-endpoint-in-pediatric-adhd-pivotal-trial>), December 4, 2017.

Regulators will play a crucial part. Their evaluation of products signals to consumers and industry what is safe and effective and what is not. FDA's Center for Devices and Radiological Health is thoughtfully taking steps to encourage innovation and inform consumers. The creation of its Digital Health unit was a significant step. Under its leadership, FDA has begun to think of how it must judge the quality of software differently than how it judges the quality of traditional drugs and medical devices to accommodate the distinctive nature of digital health technology and its compressed cycle of commercial innovation. What followed was the announcement of its Pre-Cert for Software Pilot Program.³ The program will help FDA create a framework to review a technology developer without necessarily waiting for its finished product to appear, with the aim of certifying companies that meet certain criteria in design, development, validation, and maintenance. Success of the pilot will hopefully lead to further guidance to software developers it regulates and in doing so enable a faster pace of innovation for products that can differentiate themselves from the "me too" noise of digital health.

Obstacle 2 – Misaligned incentives in the healthcare ecosystem

Digital therapeutics companies face challenges working in the traditional value chain of healthcare providers, payors, and pharmaceutical companies because incentives currently are misaligned.

Providers

Believers in the power of digital therapeutics think that one day prescriptions for apps will be as widespread as they are for pills. But for apps to be widely adopted, they will have to be oriented as much to the provider as to the patient.

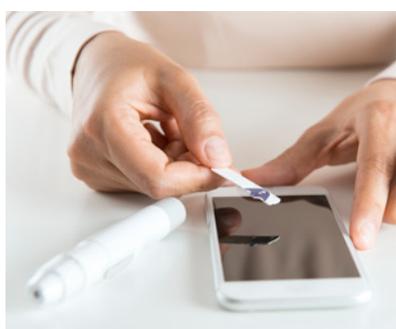
Many digital therapies currently require changes to provider processes. For example, if an app tracks dosage and patient-reported symptoms, a provider is usually expected to do something with the data produced. The data requires analysis, and analysis requires time. Where capacity is constrained, physicians can regard additional data as more of a nuisance than an aid. How can a general practitioner who has only 15 minutes with a patient sift through daily records? As Vidya Raman-Tangella, head of United Healthcare's Innovation Center of Excellence, warned recently, "You have to give [clinicians] the right information, at the right time, for the right purpose. Don't flood them with information."⁴ A typical general practitioner with 500 patients could have dozens of equivalent data streams for different conditions and patients. The analytical underpinnings must exist to process the large amount of data and make it actionable.

Some apps such as BlueStar®, WellDoc's diabetes management system, have already evolved to try to make providers' lives easier. If technology can help physicians spend less time collecting data and more time discussing solutions with patients, it is likely to drive adoption. In the United Kingdom, for example, constraints on general practitioners caused by overwhelming demand for their services is leading clinical commissioning groups to prioritize digital therapies that save physician time or shift demand to other healthcare professionals.

³ Gottlieb, Scott, "FDA announces new steps to empower consumers and advance digital healthcare," FDA Voice, July 27, 2017.

⁴ Comstock, Jonah, "To increase adoption, digital therapies need to fit into patients' and doctors' lives," MobiHealthNews, <http://www.mobihealthnews.com/content/increase-adoption-digital-therapies-need-fit-patients%E2%80%99-and-doctors%E2%80%99-lives>.

The go-to-market model is complicated, however, by the fact that incentive structures differ within health systems. Where general practice is private, or in public payor systems that contract to private providers, physicians might have less interest in shifting demand elsewhere or in recommending digital tools – such as Sleepio, a Big Health app that targets insomnia using cognitive behavioral therapy – that might disintermediate them. As Hames says, “behavioral interventions can be very, very low clinical risk, and deliberately open up a new care pathway of delivery mechanisms that don’t necessarily require a doctor or health professional, and that instead can rely upon self-referral.”



Helping patients and providers

BlueStar®, WellDoc’s FDA-approved diabetes management system, is available through an enterprise software license or on prescription. The system is marketed as supporting clinicians’ decisions, providing them with patient management information and recommended treatment modifications based on actual trends and patterns. It also helps patients by offering in-app individualized tips on how to manage their condition. Clinical trials have demonstrated the system can reduce HbA1c by two points.

Payors

As with all modern therapies, reimbursement is vital if digital therapeutics are to become mainstream, which means progress toward their adoption will depend upon the incentives and priorities of payors.

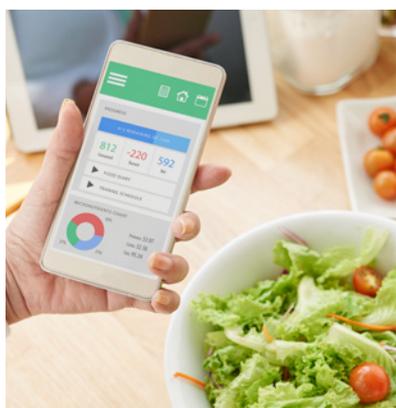
Private health insurers, for example, will want to know that covering a new therapy will offer clear improvement in quality outcomes. If it can lead to better management of conditions, help control adverse events of unmanaged chronic conditions, close gaps in care, etc., then they will consider paying for it. The problem is proving measurable and material outcomes that are clearly tied to the new approach and can be captured by the insurer in an adequate timeframe. Some of the chronic diseases targeted by digital therapeutics companies fester for years before requiring costly treatment. In the case of type 2 diabetes, the real drivers of cost – such as stroke, amputation, and the need for dialysis – are long-term consequences that might occur 20 years after the onset of the disease. Yet individuals in the United States typically remain with a private health insurer for between five and ten years.⁵ The incentive for a payor to invest in any therapy to prevent diabetes, let alone a relatively new digital one, when the return is likely to be captured by another organization, could be low.

Employer health plans or single-payor systems might be better targets for companies offering digital therapies. Employers have a larger net in which to capture savings, as their incentives include protecting against productivity loss, which is influenced by absenteeism and employee morale.

⁵ Davis, Jerel, Ma, Philip, and Sutaria, Saumya, “The microeconomics of personalized medicine,” McKinsey Quarterly, February 2010.

Meanwhile single-payor systems, such as government schemes that provide insurance for life, absorb the long-term risks with patients so have an incentive to pay for therapies that might mitigate them.

Experimentation with alternative payment methods has brought some success, though. Omada Health offers an online coaching program to prevent chronic disease that uses an outcome-based payment model. In general, however, therapies that target conditions such as insomnia – where impact is relatively immediate and the cost can be compared directly to alternative treatments, such as sleeping pills – likely have an easier path to reimbursement. Therapies with little real-world evidence to support actuarial claims will need time and significant investments to establish their worth. In the case of chronic disease, it could take decades to complete the necessary longitudinal studies.



An alternative payment model

Omada’s online coaching program to prevent chronic diabetes uses an outcome-based payment model, whereby Omada is paid only if employees sign on to the program and achieve results, such as targeted weight loss. Omada commissioned studies that show a positive return for employers after two years. With more than 45,000 patients in March of 2016¹, it was the largest federally recognized provider of diabetes

¹ Omada health press release, “Medicare Will Cover Diabetes Prevention Program for At-Risk Seniors,” March 23, 2016.

Traditional pharmaceutical companies

One reason pharmaceutical companies have been slow to invest is the difference in approaches to R&D. On average, it takes at least ten years for a pharmaceutical product to complete its journey from discovery to the market, and the average cost to shepherd it through this process is USD 2.6 billion.⁶ Digital solution innovators move more quickly. Their devices require the latest technologies coupled with a user-centric, iterative design process, which means their R&D teams must adopt an agile approach, welcoming and incorporating fresh feedback on ever-evolving user preferences. Approaching R&D in this way is a skill that many pharmaceutical companies would have to build in order to compete in delivering digital therapies.

Another disincentive is the pharmaceutical model itself. In most countries, patents give drug manufacturers 20 years or more of protection from generic competition. Regulators do not afford the same protection to devices. Competitors can avoid infringing design patents and enter the market quickly by making incremental changes to the technology they use. Add to these factors the massive differences in manufacturing and distribution, and producing digital therapeutics starts to look very different from producing pharmaceuticals.

⁶ PhRMA, “Biopharmaceutical research & development: The process behind new medicines.”

Nonetheless, digital therapeutics could also present a huge opportunity for pharmaceutical companies, transforming the way they develop or market products. Collecting real-world evidence in support of patient outcomes and economic value has long been a challenge for those seeking market access for their products. But digital therapeutics offer insights into how medicine is consumed and real-time data on its impact. Companion sensors can tell a drug company how patients react to its medicine, which could influence R&D, or indicate when a relatively low-grade therapy is ineffective, proving to physicians and payors that more robust treatment is needed.

A number of pharmaceutical companies see these use cases playing out imminently. For this reason, many, if not most, true digital therapeutic companies have attracted at least one investor or partner from the sector. Roche, for example, recently purchased mySugr, which seeks to treat diabetes. In the long term, more pharmaceutical companies may well have their own digital therapeutic lines. But in the short term, partnerships may be the most likely way forward, especially for digital devices that act as extension therapies by using data and patient engagement to offer insights into the effectiveness of those therapies. GlaxoSmithKline, which has partnered with digital therapeutics company Propeller Health to manufacture a “smart” inhaler for treating asthma and COPD, said the data the device generated would help it improve patient care while reducing the complexity and cost of clinical trials.⁷



The opportunity for digital therapeutics to address important health conditions is obvious, but the path toward widespread adoption of them is arduous and will likely be longer than many in the industry had hoped. Solutions to the main challenges are beginning to evolve, though, as understanding grows of the need for defined standards of safety and efficacy, for collaboration between digital innovators and payors, providers, and pharmaceutical companies, and for swifter regulatory approval. A potentially potent new driver of modern medicine can then be unleashed.

⁷ Comstock, Jonah, “GSK ventures into connected inhaler space with Propeller Health deal,” *MobiHealthNews*, December 1, 2015.

