Entering 2020, the promising field of digital therapeutics (DTx) has run up against a classic chicken-and-egg puzzle. Payers who hold the keys to commercial success wish to see real-world outcomes data and evidence of potential cost savings from the use of these new treatments. Yet as long as patients and physicians remain uncertain about reimbursement for DTx, companies will struggle to attract users at a scale that would produce the evidence payers seek.

DTx innovators have begun to deliver unique therapeutic tools to patients, which may also bring relief to resource-strapped health systems. Programs from Pear Therapeutics, Akili Interactive Labs, Click Therapeutics and others have demonstrated an ability to prevent or help manage a variety of medical disorders. Persuaded by data from randomized controlled trials (RCTs), regulators in the U.S. and Europe have approved some of these products to augment or replace more traditional therapies.

Investors, including biopharmaceutical companies, have funneled billions of dollars into DTx. And payers themselves have warmed to the new category. Express Scripts, for example, has launched the industry’s first formulary for digital and mobile health apps and devices.

Nonetheless, the user base for DTx is not growing as quickly as experts once anticipated. And, in recent months, several closely watched DTx companies have encountered pushback from regulators, investors and large pharmaceutical partners—a reminder that the sector is still experiencing birth pains.

Many market observers say physicians won’t recommend DTx to their patients until there is greater clarity around coverage and reimbursement. In fact, DTx are unlike any other medical products. With most prescription drugs, there’s a clear sales chain from manufacturer to wholesaler to retail pharmacy. The doctor then writes a scrip, the patient fills it at the pharmacy and the health plan pays.

But with DTx, who verifies that the patient has downloaded the therapeutic program, and what party adjudicates the claim? How does the payer learn if iterative software updates are having an effect on medical outcomes? What is the process for ongoing collection and assessment of data? Should there be a “digital benefit,” separate from the pharmacy and medical benefits? Early experiments in digital formularies may begin to shine a light on these matters, but many perplexities remain.
What payers think

To better understand how U.S. payers look at the hurdles facing DTx, Syneos Health surveyed 35 pharmacy and medical directors at national and regional managed care organizations, pharmacy benefit managers (PBMs) and payer functions at hospital systems and integrated delivery networks (IDNs). Our research documented a groundswell of payer interest in DTx—but with many asterisks.

In the survey, nearly one-quarter of respondents said they already provide DTx coverage in some form, and an impressive three-quarters said they would do so in the next two to five years. Only 3% said they are unlikely to cover DTx in the foreseeable future.

However, the majority also admitted to considerable confusion regarding DTx. Barely one-half of respondents agreed or strongly agreed that they had a consistent definition of the term, and just 28% strongly felt their organization had a consistent framework for reviewing DTx and making coverage decisions. Is lack of coverage—or uncertainty around reimbursement—limiting DTx utilization? More than half (57%) agreed or strongly agreed that it is.

Organizational understanding of DTx

<table>
<thead>
<tr>
<th>Strongly agree</th>
<th>Agree</th>
<th>Somewhat agree</th>
<th>Neither agree nor disagree</th>
<th>Strongly disagree</th>
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<td>37%</td>
<td>17%</td>
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Expected time to coverage

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<th>Near-term (&lt;2 years)</th>
<th>Mid-term (2-5 years)</th>
<th>Long-term (&gt;10 years)</th>
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<tr>
<td>23%</td>
<td>46%</td>
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Not covering at present, and unlikely to do so

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<td>3%</td>
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Criteria for coverage... and roadblocks

As the DTx field expands, high-quality RWE will be indispensable. But right now, the sine qua non is hitting the bar in RCTs and peer-reviewed literature. “DTx must show improvement in the disease state that is as robust as clinical trials in other therapies,” said one survey respondent at a leading PBM. However, he added, “there is a lack of well-designed studies demonstrating both short- and long-term benefits vs. existing standards of care.”

One possible solution is for DTx developers with a B2B or B2B2C model to integrate their products in the care pathway. A CNS digital therapeutic that’s designed into the health plan’s existing benefit structure might be “administered” by a trusted clinician or pharmacist. The winning model might even be “buy-and-bid,” as with many medicines infused by the physician on-site—only in this case, point-and-click replaces ports and IVs.

Regulators, by and large, are doing what they can to help DTx gain traction. The U.S. Food and Drug Administration created a precertification pathway that simplifies go-to-market strategies for qualified vendors. Similarly, in an effort to increase the user base and expand the pool of real world evidence, Germany’s new Digital Supply Law mandates reimbursement of qualified DTx for a period of one year.

Outcomes in the real world

For many payers, real-world utilization is the crux of the matter. If asked to review the case for coverage of DTx, 94% said real world evidence would be an important evaluation criterion, and 43% of that cohort deemed it “extremely important.”

Utilization is paramount for all classes of DTx, but it presents a particularly tricky barrier for behavioral health-related central nervous system (CNS) conditions, where much of the early DTx strategy and capital formation has concentrated. People struggling with bipolar or major depressive disorder, schizophrenia or substance abuse issues are often protective of their privacy—sometimes in the extreme.

A number of behavioral health DTx companies with business-to-consumer commercial models, such as SilverCloud Health in the U.K., have built real-world user bases of more than 100,000. But others—especially those pursuing a prescription-driven, business-to-business model—have encountered headwinds.

They have found that individuals with serious behavioral health conditions may agree to download programs to their phones and submit to monitoring in a supervised clinical trial setting. But they will react differently in unstructured, real-world settings. Many will balk at texting with an unknown organization, downloading unfamiliar software to a personal device or punching in codes. If such patients don’t activate the programs, there’s no outcomes data for payers to scrutinize.
Addressing urgent needs

Syneos Health’s interviews with payers and developers have highlighted the confusion around how payments for DTx will be made, to whom and for how much. What is the winning formula? “No one knows,” says Akili Senior Vice President Vincent Hennemand. “It will vary depending on the patient population, the unmet need and the product itself.”

Responding to unique regulatory and reimbursement frameworks in different geographic regions only magnifies the challenges. Paris-based DTx innovator Voluntis, for example, cleared its first reimbursement hurdles in Europe while completing U.S. regulatory review of novel software for cancer symptom management and remote patient monitoring.

Partnerships with diverse stakeholders may be the key to innovating amidst so many new variables. That’s why Boston-based AppliedVR has forged alliances with the Department of Veteran Affairs and the Department of Defense, as well as 300 hospitals looking for new ways to help patients cope with pain and anxiety.

Whatever setbacks DTx innovators may face, leaders in the field are driven by the enormity and urgency of unmet medical needs.

Consider clinical depression. Upward of 25 million adults in the U.S. have been on antidepressants for two years or more with little hope of transitioning off the meds. DTx advocates point to data showing that most, with the exception of severely depressed patients, would do just as well on a placebo. DTx solutions that are emerging from pipelines today may finally offer something more meaningful.

On top of human suffering, there are systemwide costs to consider. In the U.S., mental health conditions are responsible for an estimated $89 billion in annual, non-institutionalized spending. As much as $48 billion goes to managing severely depressed individuals classified as “treatment-resistant.” Include conditions such as Alzheimer’s and the annual tally soars to hundreds of billions of dollars.

This is why many healthcare stakeholders are counting on DTx innovators to grapple with market access challenges in an earnest manner. The imperative—especially for innovators with prescription-based models—is to master the idiosyncrasies of reimbursement, anticipate the questions and concerns of payers, and never default to an attitude that says: “If we build it, they will come.” Our payer survey has shed light on some of these concerns. An upcoming whitepaper, “Digital Therapeutics at the Crossroads,” will explore and further analyze those results. We look forward to advancing the conversation in the coming months.

Measured against the enormity of demand for fresh thinking, the birth pains of DTx seem at once inevitable and manageable. The industry has arrived at a crossroad, no doubt. But on each path, the arrows are pointing forward.