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The Evolving Landscape of Prescription Digital Therapeutics for Mental Health in the COVID-19 Era

EXECUTIVE SUMMARY AND OUTLINE

Prescription digital therapeutics (PDTx) is an emerging category of evidence-based treatment gaining traction as demand for remote solutions to treat mental health needs has accelerated in the COVID-19 era. Unlike wellness, telepsych or disease management apps, PDTx products pursue clearance through regulatory bodies in order to support their claims, akin to medical devices. In this whitepaper, Marwood explores how the defining features of PDTx in the larger digital health space impact market access considerations from a payor and provider perspective. Marwood also provides strategic guidance regarding market access pathways that could lead to widespread coverage and adoption of PDTx products, such as the Category I Common Procedural Terminology (CPT) code. Sections include:

I. Introduction

Accelerated in part by the growing demand for remote solutions to treat mental health needs, and the exacerbation of such needs caused by our current public health crisis, prescription digital therapeutics (PDTx), an emerging category of evidence-based treatment, has been gaining traction. To understand the potential value of PDTx, it is important to grasp where the category fits in the larger digital health landscape and the market access considerations therein.

"Digital health" encompasses a wide range of software solutions used across the wellness and healthcare industries, including mobile health, health information technology, devices, sensors and wearables, remote patient monitoring, medication management, telehealth, and PDTx. In late 2019, several industry coalitions, including the Digital Medicine Society (DiMe), Digital Therapeutics Alliance (DTA), HealthXL, and NODE.Health, collaborated to better align their organizations on the distinctions between various digital health categories. A summary of their definitions is provided below (Figure 1).

PDTx offers medical interventions that leverage software to prevent, manage, and/or treat medical disorders or diseases. PDTx products that target mental health issues may share similarities with other digital health and digital medicine platforms, such as wellness apps (i.e., Noom and Omada Health) or telepsychiatry platforms with interactive software tools (i.e., TalkSpace and Happify Connect). However, while wellness, telepsych, or disease management apps may have peer-reviewed studies and be covered by payors PDTx products pursue clearance through regulatory bodies in order to support their claims, akin to medical devices and thus require more robust standards of clinical and real-world evidence.

	Digital Health	Digital Medicine	Digital Therapeutics
Definition	Digital health includes technologies, platforms and systems that engage consumers for lifestyle, wellness and health-related purposes; capture, store or transmit health data; and/or support life science and clinical operations	Digital medicine includes evidence-based software and/or hardware products that measure and/or intervene in the service of human health	Digital therapeutics (DTx) products deliver evidence-based therapeutic interventions to prevent, manage, or treat a medical disorder or disease
Clinical Evidence	Typically do not require clinical evidence	Clinical evidence is required for all digital medicine products	Clinical evidence and real-world outcomes are required for al DTx products
Regulatory Oversight	These products do not meet the regulatory definition of a medical device and do not require regulatory oversight	Requirements for regulatory oversight vary. Digital medicine products that are classified as medical devices require clearance or approval. Digital medicine products used as a tool to develop other drugs, devices or medical products require regulatory acceptance by the appropriate review division.	DTx products must be reviewed and cleared or certified by regulatory bodies as required to support product claims of risk, efficacy and intended use

Figure 1: *Taxonomy of Digital Therapeutics, a subset of Digital Medicine, which in itself is a subset of Digital Health, as defined by the Digital Therapeutics Alliance.*

II. Telepsych and Test Balloons in PDTx

Digital health in the form of telepsychiatry has been accessible for decades, but adoption was initially slowed by barriers such as state-by-state regulations, payer coverage, provider acceptance, and lack of electronic health record interoperability. In 2011, less than 1% of addiction treatment providers in the US offering cognitive behavioral therapy (CBT) were using telemedicine.[1] Now, in the time of COVID-19, remote CBT solutions are the standard of care, be it via telephone, video conference or texting. Utilization of, and investment in, telepsychiatry has grown rapidly over the last decade and may soon eclipse in-person counselling.

[1] Molfenter T, Capoccia VA, Boyle MG, Sherbeck CK. The readiness of addiction treatment agencies for health care reform. Subst Abuse Treat Prev Policy. 2012;7:16.

PDTx Mechanisms of Action: Utilizing Existing Smartphone Technology

Most PDTx platforms focus on indications with a strong behavioral component — using the device's existing input and output systems to capture, analyze, and transmit medical interventions. Because the input vehicle is generally a smartphone or tablet, the common PDTx application components conform to the specifications of modern smartphones. The aim of these input and output mechanisms is to replace or augment existing treatments like counseling, devices or drugs.

Input Mechanisms	
Keyboard	Collect patient's behavioral or cognitive status by administering tests/quizzes (mood, cognition, memory, familial recognition, concentration)
Accelerometer	Measure dexterity or steadiness (stretching, range of motion tests)
Microphone	Audio analysis (voice quality, shakiness)
Camera	Visual analysis (photos, video)
Auxillary	Input devices attached to phone

Output Mechanisms	
Screen and Speaker	Deliver content (blogs, tips, FAQs, videos)
Chat	Patient communications (professional coaching, peer-to-peer support)
Notifications audio and tactile (vibration)	Adherence prompts (inactivity, sleep, diet)
Auxiliary	Output devices attached to phone

Inset Figure: *Smartphone input and output mediums for PDTx applications.*

With the rise of telepsychiatry – and telehealth more broadly – came a rising interest in how these platforms might leverage a digital interface to provide added value to patients, payors, and providers. In September 2017, Pear Therapeutics' reSET became the first PDTx cleared by the FDA (**Figure 2**). reSET is a 90-day prescription-only treatment that provides patients with CBT in coordination with outpatient therapy to treat alcohol, cocaine, marijuana, and stimulant substance use disorder (SUD). A year later, at the height of the opioid crisis, Pear received FDA clearance under the Expedited Access Pathway for reSET-O, a similar product to reSET but one that targets opioid use disorder (OUD) in combination with medication assisted treatment (MAT). These products were the first test balloons for FDA-cleared software-based treatments in the behavioral health space.

In contrast, Talkspace, a leading telepsych platform that emphasizes text-based communication, launched a digital employee assistance program (Digital EAP) in April 2020 that offers a range of mental health resources in addition to therapy. As part of this offering, Talkspace partnered with Happify Health, a provider of FDA cleared and non-FDA cleared digital therapeutics, to include Happify Connect, a mental health support tool, in their Digital EAP suite (**Figure 2**).

	TalkSpace with Digital EAP / Happify Connect	reSET
Addressable Patient Population	Adults	SUD patients
Category	Digital Medicine	Digital Therapeutic
CBT	√	Yes, but adjunct to direct counseling
Interactive Lessons	√	√
Encouragement Through Rewards	√	√
Quizzes	√	√
Tracking Patient's Mood/ Triggers/Cravings etc.	√	√
Medication Management Reminders	√	√
Clinician Prescription and Monitoring	Sometimes	All of the time
FDA Clearance	×	√

Figure 2: *Comparing TalkSpace's Digital EAP with Pear's reSET.*

Happify Connect "blends scientific research from positive psychology, CBT, and mindfulness with a gamified approach." While the product neither has FDA clearance, nor markets itself as a PDTx, it, and the broader Digital EAP suite, shares similar features to reSET. However, the latter's leverage of substantiated clinical data toward regulatory clearance and targeting of a narrower patient population has implications both to provider and payor.

Another more recent PDTx case study is Akili Interactive's digital therapeutic, EndeavorRx. This app-based video game was FDA cleared in June 2020 as a prescription treatment for children with attention deficit hyperactivity disorder (ADHD). While many marketed video games may claim to improve focus or attentiveness, EndeavorRx has FDA validated clinical trials to support their claims. Notably, the clinical trials for EndeavorRx used the same clinical endpoint (the Attention Performance Index – a composite score from the Test of Variables of Attention) that is used to evaluate the efficacy of pharmaceuticals prescribed for pediatric ADHD, like methylphenidate. Thus, not only are PDTx platforms at times competing with their unregulated digital health counterparts, they may also compete with pharmacologic interventions.

In determining commercialization strategy, a key question is market access. Although some digital health platforms implying therapeutic benefit lack the same evidentiary rigor and

regulatory validation as PDTxs (i.e., EndeavorRx and reSET), they target a much wider patient population. While the broader approach may help win employer and payor contracts piecemeal in a saturated market, it may also lead to barriers in gaining the widespread, technology-specific coverage and reimbursement seen of efficacious pharmaceuticals and medical devices.

Although PDTx may start narrow, by rigorously targeting each FDA-cleared indication, a time may come when every mental health need has an easily accessible PDTx to address it. Thus, the broad-based approach of currently marketed digital health alternatives may one day be replaced by precision digital therapies tailormade and clinically validated for specific psychiatric indications and profiles. Additionally, the value of these therapies may be reflected in increased platform-specific reimbursement rates. Though PDTx is still in its infancy and the payor landscape is still indeterminate, there is plenty of reason to anticipate enhanced public and private payor enthusiasm, particularly in light of our current public health crisis. We explore some potential avenues toward favorable PDTx coverage and reimbursement decisions in the US below.

III. Commercial Payor Coverage and Reimbursement Dynamics

Historically, there has been more openness to digital health solutions among private payors. This is due, in part, to the fractured nature of the commercial payor market and their reliance on employer sponsorship. Unlike public payors, private payors are better able to create partnerships and pilot programs with digital health solutions. Their employer sponsors are similarly eager to find plans for employees that incentivize wellness and access to comprehensive mental health services. However, the adoption of these digital health solutions by private plans does not go through the same institutional review process as other more conventional therapeutic products.

Marwood believes that while payors have a general understanding of PDTx, their organizations have yet to define them and lack the operating procedures to consistently review them. Given that the category is in its infancy and PDTx volume and consequent budget impact is exceptionally low, it is no surprise that payors and their organizations remain relatively unprepared to evaluate PDTx with the rigor and uniformity of pharmaceuticals or medical devices. To date, while there is talk of reviewing PDTx via existing Pharmacy & Therapeutics (P&T) or Medical Technology (Medical Policy) committees, there still lacks budget justification for a third separate committee focused exclusively on PDTx.

One of the current key challenges to coverage decisions under the current payor infrastructure is lack of data. Real world evidence is valued highly by payors to address questions regarding clinical evidence and patient adherence. Thus, skepticism towards clinical trials for PDTx products are grounded in their experience with associated trials that are rarely designed with an active comparator arm, most notably a currently covered pharmaceutical or device. Without this frame of reference, comparisons are difficult. Furthermore, adherence to this new class of therapy is difficult to judge by clinical trials where optimized patient populations

are closely monitored. Consequently, real-world evidence or payor-associated pilot programs would be helpful to payors to determine if the PDTx improves patient outcomes in a cost-efficient manner. Economic evaluations would be another important aspect required, so that payors would be able to better evaluate these technologies. Medical data that demonstrates savings from decreased hospital admissions, decreased drug use, better adherence, or other measurable outcomes would need to be presented.

Digital health formulary approaches have begun to develop; however all of the listed digital health products so far lack FDA clearance. For example, Express Scripts announced in December 2019 that it had selected its first 15 products to include in its digital health formulary, which aid in the management of some of the most common chronic conditions. Express Scripts picks which digital health products to include based on their clinical effectiveness and usability. Clients can pick which tools they want to include in their plan from the formulary, instead of sorting through the thousands of apps that are currently on the market.

Marwood will continue to monitor this formulary to see how it adapts to the ramp-up in market launches of FDA-cleared PDTx products, but it seems reasonable to assume they will be included. Formularies could play an instrumental role in the accumulation of PDTx real-world evidence and could expedite the adoption of PDTx products. However, the true best-case scenario for widespread PDTx coverage and adoption could be achieved through the Centers for Medicaid & Medicare Services (CMS).

IV. CMS Coverage & Reimbursement Dynamics

Marwood believes that CMS could play an instrumental role in the advancement and adoption of PDTx. From molecular diagnostics to implantable medical devices, CMS is known to be more deferential to the FDA's review of clinical trials relative to private payors. This indicates a favorable coverage environment for FDA-cleared PDTx products. Additionally, unlike private payors, CMS is able to assign products and services specific codes that are standardized at the national level under the Healthcare Common Procedure Coding System (HCPCS).

For those PDTx products that require practitioner involvement, a HCPCS Category I common procedural terminology (CPT) code is the optimal route, as these codes are assigned a nationally standardized reimbursement rate through the AMA-RUC (American Medical Association Relative Value Scale Update Committee). Additionally, the formation of a new product-specific Cat I CPT code sets a national coverage precedent which private payors are more likely to adhere to and bill for. Typically, as these determinations are made in light of a new technology's differentiation, these Cat I CPT codes may be the optimal route for PDTx products to receive widespread coverage and higher reimbursement than other digital health alternatives. Additionally, the standardization of a Cat I CPT code allows for more efficient collection and analysis of real-world evidence.

However, obtaining a product-specific CPT code is a complex process involving independent review from the American Medical Association (AMA) CPT Editorial Panel. As such, a comprehensive value strategy is necessary. For more information on the critical components of a comprehensive value strategy, inquire through the contact information provided below.

Notably, most PDTx HCPCS codes that have already been approved by CMS relate to remote patient monitoring or add-on features to durable medical equipment (e.g. continuous glucose monitoring). Some examples include:

- **T1505**, electronic medication compliance management device, include all components and accessories, not otherwise classified
- **A9999**, miscellaneous durable medical equipment supply or accessory, not otherwise specified
- **E1399**, durable medical equipment, miscellaneous, provide the sorts of catchall pathways necessary for apps seeking a durable medical equipment approach to reimbursement

Apart from pursuing product-specific Cat I CPT codes, there are two additional pathways toward creating simpler reimbursement mechanisms for app-related treatments, though they are less likely to capture the full value of PDTx products. First, the existing durable medical equipment codes could be clarified to include apps. Although they are already being used in some cases for this purpose, they are at the discretion of the insurer. Second, there may be a need for a treatment-related equivalent to the brief emotional/behavioral assessment code 96127. Such a code could be used to cover automated app-based treatment conducted in a standardized fashion rather than automated app-based screening.

V. Easing Administrative and Provider Burden

To overcome the linkage between procedure-based reimbursement and physician work, malpractice, and practice expenses, PDTx app developers have been pursuing FDA regulatory clearance via the same rigorous clinical assessments that are required for Class II medical devices. However, when apps are treated as prescription devices or drugs, they may only be billed by individuals with prescribing authority. This poses a barrier to widespread adoption, as states vary in their willingness to grant various nonphysician health care providers – from nurse practitioners to psychologists – the ability to prescribe, and in some cases, grant only partial prescribing authority. As a result of the limitations on prescribing authority, the majority of psychologists are unable to prescribe apps. Notably, as Marwood has engaged KOLs from national psychiatry associations, it remains unclear, even among their leadership, how prescribing will play out.

In light of these considerations, the US Food and Drug Administration (FDA) issued its *Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency*, on April 14, 2020. In the policy, the FDA announced its intent to exercise enforcement discretion with respect to certain regulatory requirements — i.e., the 510(k), registration and listing, and unique device identifier

requirements, among others — for digital health therapeutic devices for psychiatric disorders during the public health emergency.

Practically, this means that the FDA does not intend to apply or enforce medical device requirements for these products during the public health emergency, though it remains to be seen how they will restructure enforcement and regulatory oversight when our current crisis has subsided. However, the question remains whether companies will bypass these requirements for expediency or continue to pursue FDA clearance as a means of signaling value and validation to payors.

VI. Conclusion

Despite easing of regulatory hurdles, rigorous clinical evidence will be required to convince stakeholders, whether investors, payors, physician societies, or the industry at large of the value of PDTx. This includes the development of evidence dossiers toward payor negotiation of reimbursement and contracting, strategic evaluation of partnership, and distribution strategies, as well as an understanding of the federal landscape steering both approval and reimbursement of PDTx. As a leading healthcare-focused advisory firm, Marwood advises digital therapeutics developers in strategizing market access and managing product lifecycles, which allows them to leverage direct insight into payor policy and intra-institutional dynamics.

About the Authors

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Marwood Group is a healthcare advisory firm offering strategic consulting services, with expertise advising healthcare investors in conducting market diligence, strategizing market access and managing product life cycles leveraging direct insight into federal and state policy as well as intra-institutional dynamics.

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