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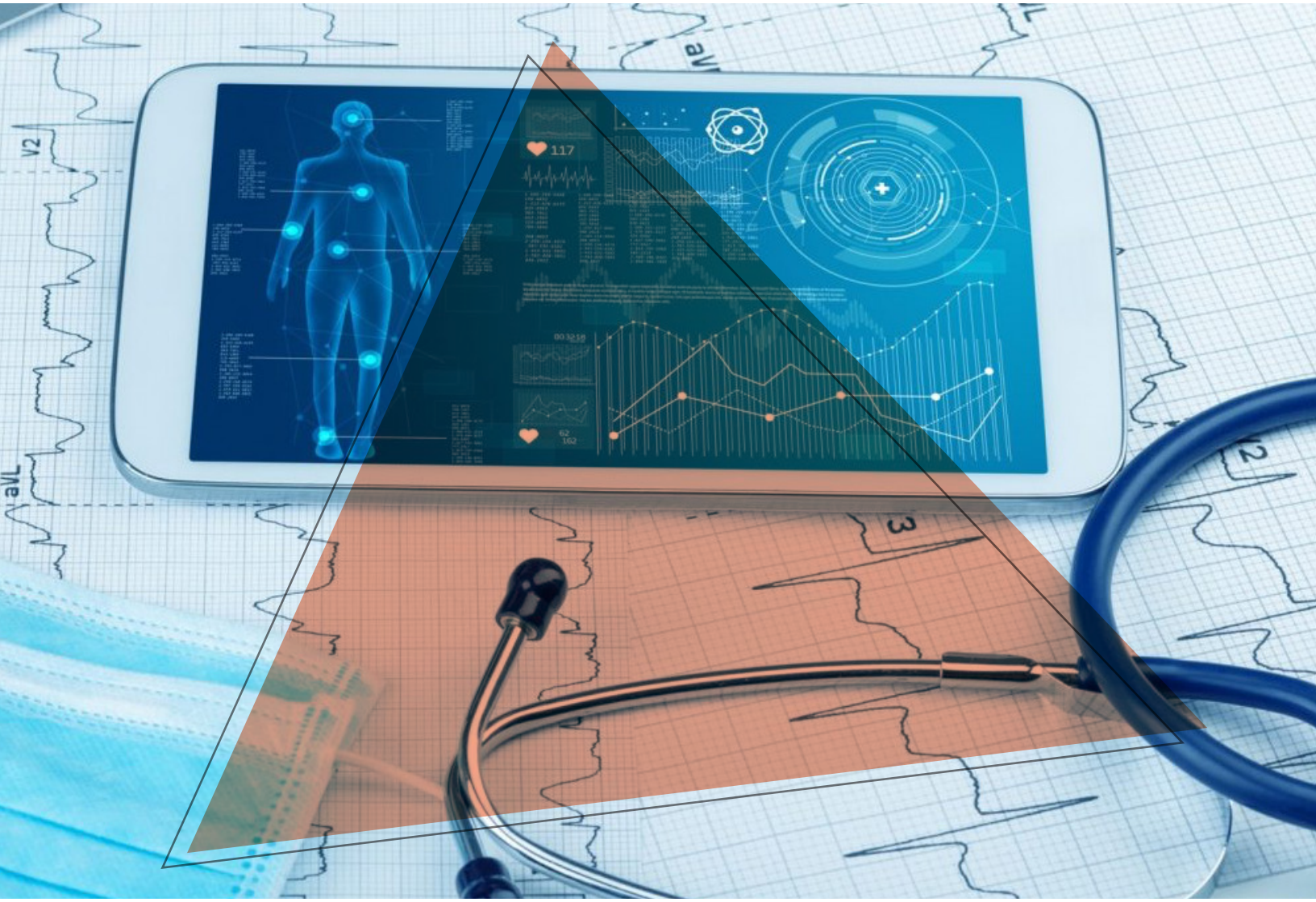

LAUNCHING DIGITAL THERAPEUTICS (DTx)

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Launching Digital Therapeutics Vol 1

Why a Digital Therapeutic Launch is Radically Different than a Pharmaceutical Launch

The rise of digital therapeutics in recent years has been an area for innovation in often 'stale' pharmaceutical therapeutic areas (e.g., diabetes, substance use disorders, incontinence, depression). This has driven the investment, venture funding, and large pharma partnerships in the space (e.g., pioneer Click Therapeutics has publicly disclosed partnerships with large pharma organizations including Otsuka and Boehringer Ingelheim). However, the commercial model to launch these digital therapeutics has yet to be crystallized and has repeatedly resulted in underwhelming launches and provided limited value to patients, providers, and manufacturers. That's because the model needs to be radically different than a pharmaceutical launch in a few key areas. We have identified four areas of focus where manufacturers pursuing digital therapeutics should be exceptionally creative and innovative to successfully bring these assets to market in a commercially viable manner.

1) Establish Clear Provider and Patient Segmentation:

Digital therapeutics are not likely to be applicable to all patients and providers within a specific disease state given the degree of innovation and change in workflow required to prescribe and use. To avoid this pitfall, developing clear market maps and segmentation will be critical to drive appropriate targeting and utilization.

2) Ensure a Comprehensive Evidence Package to Drive Market Access:

Potentially the greatest barrier to the utilization of digital therapeutics has historically been the lack of coverage by payer organizations resulting in poor patient access and high out-of-pocket costs (particularly in the immediate post-launch period). Strong evidence packages paired with unique strategies, partnerships, and contracting will be necessary to break down the market access barriers that currently limit adoption.

3) Design an Appropriately Sized Field Force and Selling Model(s):

Digital therapeutics are in a unique market position that requires significant education to prime the market to integrate these technologies into the treatment paradigm while balancing appropriate reach to target the identified provider segments. A phased approach balancing non-branded disease education alongside general DTx awareness (pre-launch) with a conservative, digitally enhanced sales model can drive a successful launch without the investment typically pursued by traditional therapeutics.

4) Draft a Cohesive Implementation Plan to Limit Provider Burden:

Providers often manage significant workloads and are also unfamiliar with the requirements to prescribe and administer a digital therapeutic. Ensuring products and eRX services are integrated into EMRs to enable easy prescribing will be paramount to successful commercialization of DTx. Furthermore, limiting the requirements for providers to monitor or review data from the application will likely be a driver of use whereas significant provider burden will be highly limiting.

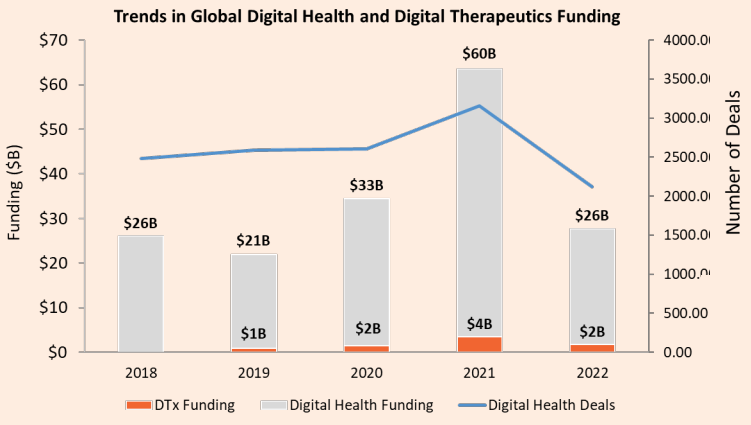
Triangle Insights will publish a series of four insights pieces focused on these key differences in launching a digital therapeutic (DTx) relative to a pharmaceutical product, so that manufacturers entering this space can optimize these important tools and avoid previously experienced commercialization hurdles.

This first piece establishes foundational principles and market trends and then focuses on unique considerations for "Establishing a Clear Provider and Patient Segmentation."

Background: What are digital therapeutics and how do they differentiate themselves from digital health?

Digital health, which broadly encompasses technological solutions that enhance healthcare delivery, has become increasingly popular in recent years. Digital therapeutics (DTx) are evidence-based digital health interventions used to prevent, manage, or treat disease (with or without prescription requirements).

Market Trends: What are the key trends in the digital health and digital therapeutics space?



- *Prior to 2022, DTx funding increased significantly YoY, signaling the promise of the industry.*
- *In 2022, digital health funding, following the trend of the biotech industry overall, dropped to below 2020 funding levels (more than 50% YoY).*
- *Consolidation of the digital health sector increased in 2021 with a record number of M&A deals (~570 total deals), but has since declined by 33% YoY (2021 – 2022).*
- *Example of the impact of shifting market dynamics: Despite Pear Therapeutics' significant venture capital funding, the company filed for bankruptcy and auctioned assets for $6M in the first half of 2023.*
- *Given the evolution of the marketplace for DTx, smart commercialization strategies will be crucial to the overall corporate health and long-term success for digital therapeutic manufacturers.*

Provider and Patient Segmentation: Identifying relevant providers and patients is critical to commercialization success

Because digital therapeutics are making product or marketing claims like that of traditional pharmaceuticals, they are being held to the same clinical efficacy standards. However, DTx face a unique challenge compared to their pharmaceutical counterparts in that physicians exhibit added skepticism of their efficacy because the concept of a DTx is much less mature. Specifically, providers may be concerned about the added complexity of incorporating a digital therapeutic adjunctively or in place of pharmaceutical intervention. Furthermore, there are logistical hurdles (e.g., access to technology and Wi-Fi) that influence provider willingness to prescribe.

Added skepticism may limit prescribing to the most "trustworthy" or "eligible" patient subpopulations (e.g., prescribing to individuals most comfortable with technology or more familiar with smartphone applications, prescribing to younger patients or those with the most incentive to comply [depending on the therapeutic area]). Given these preconceived notions regarding DTx, it will be crucial to establish a market map and associated customer profiles early in the development process.

This segmentation exercise should be performed for both patients and prescribers and incorporate beliefs and behaviors that may influence product utilization. Manufacturers should maximize the strength of the value proposition by targeting clinical evidence generation towards the appropriate segment of patients within the market map. Identifying patients where clinicians have a higher willingness to prescribe, and where there is greater likelihood of clinical success, will enable an appropriate targeting strategy and early wins for DTx manufacturers.

Several digital therapeutic companies have targeted specific patient subsets with positive outcomes to-date. For example, SparkRx created a digital therapeutic specifically for adolescent depression. Adolescent patients are a key demographic that prescribers highlight as having a high likelihood for success with DTx (given their generation's comfortability with technology). In addition, for its Medicare study, Propeller Health required eligible COPD patients to have had at least one emergency department visit or hospitalization, further focusing their efforts to the segment with the greatest motivation to follow-through with therapy. Additionally, in the case of Propeller Health, one could argue that the targeted patient segment is more severe and therefore could demonstrate better outcomes and cost savings (which may, in turn, enable a clearer economic story and better market access).

In summary, early in the development process, digital manufacturers should be sure to establish a clear market map and associated customer profiles for both patients and providers, leveraging underlying behavioral and ethnographic drivers to identify the most likely and appropriate targets. Avoid the trap of "being everything for every patient" to establish a preliminary beachhead into the market and expand appropriately from that point.

Reach out to Triangle Insights Group to learn more about our approach to market segmentation and patient identification and tune in for our next installment in the series focused on strategies to optimize market access for DTx.

Evidence Package Needed to Support Market Access

Data-driven access is optimized with digital therapeutics (DTx) as these products are often designed to track and measure adherence and clinical outcomes. However, there are a few potential challenges with DTx data:

1. Portability given patient privacy concerns,
2. Compatibility of data sources and potential destinations i.e., different medical record systems of various providers and payer databases, and
3. Reliability / integrity of data from patients.

Moreover, the evidence package needed to support access differs from non-digital therapeutics, but if successful, could enhance care delivery in many therapeutic areas. In this second piece from Triangle Insights, we will examine access barriers, posit DTx specific evidence generation improvement, and discuss approaches to launch through unique examples.

While DTx products have been studied through randomized control trials (RCT) resulting in FDA approval, many US government programs have yet to cover or fully recognize the value of DTx. This is partly a coding issue as limited precedence for use of DTx and past reimbursement challenges have stifled the commercial viability of individual products and entire companies. Existing remote therapeutic and patient monitoring (RTM and RPM) codes could be used and billed for services related to digital therapeutics, but reimbursement is often insufficient to cover the cost of these technologies. On the other hand, unique codes like the one AppliedVR received for RelieVRx in the first quarter of 2023 may be viewed as anticompetitive due to narrow or limited use, but are a positive sign towards acceptance of DTx by CMS.

Some payers have developed overall policies not covering any prescription digital therapeutics despite existing evidence. Many commercially available and FDA-approved therapies are considered *"experimental, investigational, and unproven due to insufficient clinical evidence and peer-reviewed medical literature establishing long-term safety, efficacy, and effect on net health outcome."* (Molina Clinical Policy 2023).

To address the reservations of payers regarding DTx effectiveness, the following recommendations may bolster coverage of products already on the market:

- Follow-on studies that are better powered by larger cohorts with comparable control groups to demonstrate statistically significant and meaningful differences in clinical outcomes
- Collecting data over longer periods of time to measure the ability of DTx to impact patient outcomes through positive habit-forming engagement with the technology
- Developing different validated measures or PRO (patient reported outcome) tools than non-digital therapies to support efficacy claims
- Economic studies including cost benefit analyses in relevant patient populations, perhaps leveraging health system partnerships

Appropriately tested and clinically relevant patient assessments through DTx could widen use through broader applicability, support future reimbursement by US government programs, and additional coverage by commercial plans or employers through quantifiable impact. As an example, Freespira, an FDA-cleared treatment that can reduce or stop panic attacks and PTSD symptoms, recently announced a partnership with Lovell® Government Services. As of June 23, 2023, federal healthcare systems including the Veterans Health Administration (VHA) and Military Health System (MHS) can provide access to Freespira's at-home treatment. Freespira was previously studied in partnership with Allegheny Health Network and demonstrated cost benefits resulting in expanded access by Highmark Health plans after a 12-month pilot program in 2017. Access barriers for DTx may be overcome with time, through similar approaches including unique strategic partnerships and different agreements with plans, providers, and even government contracted organizations.

Reach out to Triangle Insights Group to learn more about our approaches to optimizing market access and tune in for our next installment in the series, focused on appropriately-sized field force and selling models for DTx.

Design an Appropriately Sized Field Force and Selling Model(s):

Determining a fit-for-purpose sales strategy based on the specific market conditions associated with a Digital Therapeutic (DTx)

Unique assets require unique solutions. Digital therapeutics often do not reap the benefits of a traditional pharmaceutical field force model at launch as there is limited ability to pull through their efforts due to existing market barriers (e.g., lack of widespread coverage and access at launch). Digital therapeutic manufacturers should seek unique approaches to developing a field force that is fit-for-purpose for digital therapeutics, including pre-approval and non-branded education.

As digital therapeutic manufacturers consider commercialization of their assets, a field force akin to a pharmaceutical launch in the same indication may not be the most suitable approach at launch. There are meaningful differences within the market that initially create limitations for digital therapeutics relative to pharmaceuticals. For example:

- Reimbursement is often delayed for digital therapeutics due to a lack of clear coverage /digital formularies from payers.
- Timing to product integration into ePharmacies and provider workflows can limit the widespread adoption and commercial reach for digital therapeutics.
- Provider awareness of how and when to prescribe digital therapeutics may be more limited than pharmacotherapy.

Given these factors, digital therapeutics may not need a large field force at launch compared to a pharmaceutical launch. Rather, manufacturers should consider targeted and phased alternative approaches to drive commercial success:

- Focus pre-launch on digital therapeutic education amongst relevant providers.
- Initially, target post-launch efforts on key targets and geographies where access is likely attainable closer to launch, before scaling up the sales/field force as access and other infrastructure are enabled.
- Consider hybrid and/or virtual models before and at launch to accomplish key objectives, leveraging lower cost and flexible resourcing.
- Preliminary resources should focus instead on driving reimbursement, ensuring accessible infrastructure (e.g., ePharmacy), and promoting the utility of digital therapeutics to key stakeholders.

More specifically, manufacturers should thoughtfully develop a pre- and post-launch field-facing strategy to 'right-size' and target digital therapeutic entries into the market. For example:

1. **To combat challenges with widespread adoption by key stakeholders, education is required to prime the market through avenues such as targeted MSL engagements or unbranded digital therapeutic awareness.**

Due to a lack of familiarity from key stakeholders (i.e., physicians, payers, regulators), additional investment is required to support the validity of digital tools for therapeutic treatment. To combat this skepticism, digital therapeutic manufacturers have significantly invested in increasing awareness of the product benefits in facilitating better patient care. Organizations like the Digital Therapeutics Alliance allow DTx manufacturers to present a unified voice to support the use case for DTx.

While this advocacy helps to start the conversation with key stakeholders, additional non-branded disease education and non-branded digital therapeutic awareness may be warranted to prime target audiences ahead of launch. These efforts may support earlier utilization as well as product coverage and adoption at launch.

2. **While market access remains a significant barrier for DTx, manufacturers can benefit from waiting to ramp up their field forces until they have successfully achieved widespread reimbursement and appropriate supportive infrastructure (e.g., ePharmacy, integration into provider workflows).**

Immediately pre-launch when market access may be more limited for some DTx, companies can strategically focus their field efforts on predetermined targets where there is a higher likelihood of success (e.g., large centers with robust administrative support, geographies covered by plans with an existing digital formulary). Companies like Akili have utilized this strategy to first drive demand with specific targets and expand sales and marketing initiatives once there is uptake in key prescriber segments.

In addition, smaller, virtual, or hybrid sales forces at launch allow the company to focus efforts on ensuring market access and structural support systems are in place for DTx, while driving appropriate demand that does not exceed coverage and retains resources to scale commercial efforts. Companies can then deploy a larger field force and increase marketing spend, once they have ensured there will be appropriate pull-through and reimbursement.

Significant market access barriers at launch may lead certain physicians to form a negative perception of the asset despite its clinical benefits. Certain early adopters can become champions for the product and may be more willing to go through market access hurdles to drive adoption. Appropriate targeting of these early adopters should be a focus of initial sales and marketing efforts. Strategic execution of the field force deployment ensures stakeholders are accessed at the appropriate time, such that market access will not hinder early perceptions.

In conclusion, balancing product-specific promotion through sales force deployment and pre-launch product agnostic education, all while leveraging a 'right-sized' field force, supports early awareness and drives demand commensurate with the access and ability to get DTx to patients.

Reach out to Triangle Insights Group to learn more about our approach to commercialization strategy and tune in for our next installment in the series, focused on strategies to ensure cohesive implementation for DTx.

Draft a Cohesive Implementation Plan to Limit Provider Burden:

Ensuring Digital Therapeutics (DTx) are easily accessible for patients without needing significant HCP effort to prescribe or monitor enables successful commercialization.

After establishing with HCPs in a data-driven manner that digital therapeutics (DTx) do have real value in patient care, the immediate follow-on step is to confirm that these DTx options can be made available to patients without extensive effort from physicians. Manufacturers have a responsibility to eliminate or reduce the added hurdles faced by already overworked physicians in prescribing DTx today.

The following steps indicate key actions that manufacturers might take to enable successful commercialization:

1. Aim to have DTx products integrated into electronic health records (EHRs) currently used or known by HCPs, therefore ensuring proficiency with previously accepted systems.
2. Provide HCPs instructive guidance through educated product representatives and informative product websites on how to approach prescribing digital therapeutics (DTx).
3. Guide HCPs on how to communicate to patients and caregivers on their role in enrolling in, paying for, and using the prescribed digital therapeutic.
4. Educate HCPs on efficient long-term monitoring of digital therapeutic treatment to enable effective understanding and management of patient outcomes.

While there are few established commercial success examples among digital therapeutics manufacturers, several companies have implemented a clear plan on one or multiple of the steps and are starting to gain traction in HCP and patient adoption.

For example, Akili Therapeutics has organized an effective "How to Prescribe" webpage for its ADHD digital therapeutic, EndeavorRx. The page first lists all the required details for the HCP to include in writing an EndeavorRx script, such as primary ICD-10 code, instructions for patient use, and number of refills. The prescription is then requested to be sent through the HCP's EHR to Phil pharmacy, a technology-enabled pharmacy specializing in digital treatments and managing all EndeavorRx prescriptions.

However, despite HCPs being able to seamlessly use their current EHR, the lack of pharmacy familiarity may still present challenges for HCPs and associated support staff in navigating potential access barriers. The webpage then outlines for the HCP the caregiver's role in enrolling, paying, and activating EndeavorRx after the script's confirmation by Phil pharmacy. Finally, the product prescribing page concludes with simple ways for the HCP to follow-up both during and after treatment to discuss progress and consider product refills. Although Akili is currently struggling to generate revenue as expected, this is likely due to a limited on-label patient population (8–12-year-old ADHD patients) rather than serious missteps in its approach to limit provider burden.

Akili is not alone in this approach. Limbic, another digital therapeutic manufacturer, has developed a similar HCP prescribing support page for its adolescent depression digital therapeutic, SparkRx. Limbic's key addition to its webpage is the inclusion of a demo on how HCPs can offer SparkRx in their practice and use the "Limbic Provider Portal" to monitor patient clinical outcomes and program adherence.

With continued attention and refinement of these provider-support programs, manufacturers will continue to facilitate a gradual increase in HCP adoption of digital therapeutics.

Despite this, DTx commercial success is still distant given the inertia of prescription digital therapeutics to date. However, alternate pathways to broad commercial success are continually being explored by pharmaceutical and digital therapeutics manufacturers. For instance, Welldoc's BlueStar is a digital application used for monitoring purposes and is utilized in active partnerships with Astellas and Roche therapeutics. Although a monitoring device and not a digital therapeutic, BlueStar may serve as an example of a non-traditional route to potential commercial success, given its dual marketing as both a prescription and non-prescription (entirely reducing the role of HCP) digital health solution for diabetes.

In closing, manufacturers have several routes to develop a more cohesive implementation plan to reduce provider burden, ensure ease of DTx prescribing, and build commercial success.

Reach out to Triangle Insights Group to learn more about our approach to commercialization strategy for digital therapeutics.

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