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We Make Digital Health Work

DIGITAL THERAPEUTICS Primer

1. Introduction

Digital Therapeutics (DTx) are evidence-based software solutions that manage, prevent, and treat various mental and physical diseases and disorders. There are many digital health apps, but DTx solutions are differentiated by needing clinical evidence to provide evidence they are safe and effective. They often, but not necessarily, include integration with data from personal health monitoring devices or wearables.

Over the last twenty years, innovative digital health solutions have exploded taking advantage of the proliferation of smartphones and the ever-growing list of wearables, with digital therapeutics playing a pivotal role in driving that expansion.

This Primer aims to provide a comprehensive overview of digital therapeutics and examine its potential benefits and challenges.

Healthcare providers across the globe are leveraging the capabilities of personal health monitoring devices (wearables) and digital therapeutics to treat medical conditions like asthma, obesity, chronic pain, diabetes, dementia, and depression.

Such devices can collect vast amounts of physiological data on patients in real-time, broadening treatment options in ways that were unfathomable just a few short decades ago.

Millions of people across the country deal with poor health conditions due to a confluence of physiological and psychological problems. Digital therapeutics, through proper usage, can help to improve those health functions, optimize patient care interventions, and produce positive, long-term outcomes.

2.Regulations

Developments in digital therapeutics began in earnest in the late 90s, when researchers began exploring the potential of using technology to improve healthcare outcomes outside of a typical healthcare setting.

This unique medical concept involved using mobile health (mHealth) applications and often wearables to track health data and provide patients with personalized health information from the comfort of their homes.

These new software-based therapeutics have been regulated as devices, but the FDA regulatory organizations are striving to create better methodologies that can respond more quickly to the pace of change possible with software.

While Food and Drug Administration (FDA) guidance on software existed in the 1990s, particularly for testing and validation, in the early 2000s, they focused on the unique aspects of the software.

In 2005 they released guidance on software in medical devices (SiMD) which focused on software design, testing, and evaluation. This was the bases for guidance around Software As a Medical Device (SaMD), which overlaps significantly with DTx.

Implementation of the 21st Century Cures Act in 2016 further accelerated the development of guidance in support of digital therapeutics. It helped streamline the regulatory approval of novel solutions with the Breakthrough Devices Program.

The Breakthrough Devices Program

This program was created to give patients and doctors quick access to novel medical devices that may be able to diagnose or treat life-threatening or permanently crippling diseases or ailments more effectively. The program's goal is to hasten the creation, evaluation, and review of these devices while upholding the FDA's strict safety and efficacy requirements.

Manufacturers (software developers) can participate in the program if they meet certain requirements, such as offering a more accurate diagnosis or treatment for ailments or diseases that are life-threatening or irreversibly debilitating, and there are no recognized or cleared alternatives. The program further stipulates that the device must have the potential to be a breakthrough technology and offer a significant clinical advantage over currently available therapies or diagnostic choices.

The advantage of being classified as a Breakthrough device allows for early and regular communication with the FDA throughout the development and review processes, which can assist in identifying and resolving any difficulties as soon as they arise. The initiative also offers a faster evaluation procedure, which might hasten the time before these gadgets are available on the market.

A program that allowed manufacturers (software developers) to interact more closely with the FDA and received a prioritized review of their submission if they were deemed a Breakthrough Device. The goal was to facilitate getting products to market faster in underserved medical conditions.

In 2017, the FDA published the Digital Health Innovation Action Plan (**link**), whose purpose was to reimagine how the FDA approach regulatory oversight of digital health, including DTx.

It was recognized that an approach based on hardware was not sufficient for the rapid pace of software development, and a new approach was required to meet the demands of the market and to ensure the safety of the population.

This action plan launched the Software Precertification Pilot Program. The goal was to pre-qualify a number of software vendors, which had software development practices based on industry standards, such as 21 CFR Part 820 QMS Requirements and the ISO13485 Quality Management System and demonstrated a strong culture of quality and excellence.

In 2019, nine (9) companies were enrolled, but the small number of vendors and limitation of regulatory oversight afforded to the FDA limited the outcome of the program.

In 2022 the FDA ended the pilot study. It was recognized a new regulatory paradigm is required to adequately support the fast pace and flexibility of SaMDs and DTx solutions, and to fully implement such a program legislative change would be required.

FDA Key Findings Report

3.Cybersecurity

As software is used increasingly as a medical device, the inherent risk of a cybersecurity threat or attack becomes elevated.

While cybersecurity of medical devices and DTx have always been a concern, over the last few years the US government and FDA have renewed their focus on cybersecurity and mitigating the risk of an attack.

As early as 2005, the FDA published guidance documents for connected medical devices (**link**). In 2022, the FDA released new draft guidance, Cybersecurity in Medical Devices: Quality System Considerations (**link**) which focuses on software in devices as well as DTx products.

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The key to a good cybersecurity risk management plan is to follow the guiding principles of the industry standard ISO 14971 Risk Management Process – establish a plan, analysis, evaluate, and control.

The analysis phase of the software solution should identify the core components, the system boundaries and data flows. Once the scope is identified, the vulnerabilities can be identified and categorized for a level of risk.

Based on the level of risk strategies to eliminate or mitigate that risk can be determined. There are numerous strategies for threat modeling and determining risk within the cybersecurity risk analysis process.

Key Considerations

1. Cybersecurity is part of a Quality Management System.
2. A specific Cybersecurity focused risk analysis should be conducted to identify risks, potential vulnerabilities and approaches to eliminate and/or mitigate the risk to an acceptable level.
3. Continually monitor and adapt to new cybersecurity risks and vulnerabilities.
4. Establish an incident response plan to quickly address any incidents.
5. Be transparent and share information with the industry to improve the overall level of safety.
6. Maintain records of cybersecurity activities and provide them to the FDA on request.
7. Train users and staff on cybersecurity and how to report and respond to incidents.

Cybersecurity risk management is not a single activity. It is an ongoing process of evaluating risk and being aware of cybersecurity signal intelligence. New risks are discovered each day. In 2021, US legislation was passed mandating vendors supply a Software Bill of Materials (SBOM) with their products (**link**). This extends to the FDA, which now requires the same information.

An SBOM is defined as “a formal, machine-readable inventory of software components and dependencies, information about those components, and their hierarchical relationships.” by the National Telecommunications and Information Administration (NTIA). This spawned an industry around monitoring an SBOM and providing software vendors with known vulnerabilities related to their products.

The MITRE Corporation maintains a list of Common Vulnerabilities and Exposures (CVE) (link) that is publicly available. These new monitoring products evaluate the contents of an SBOM against the CVS listing and can notify vendors of new risks.

DTx solution developers also need to consider US HIPAA, HITECH, and FTC regulations as well as individual state legislation like California Consumer Privacy Act (CCPA) and Massachusetts Data Privacy Law (MIPSA) among others when developing solutions.

HIPAA is usually broadly recognized in the US when a covered entity is involved, but lesser known is that the FTC has privacy guidelines that must be adhered to even if a covered entity is not involved.

These regulations address technological concerns but also, mandate guidelines and processes for how data is handled by the people within the organizations.

And don't forget, GDPR must be considered if doing business in the European Union.

HHS Adopted Standards

Covered entities are defined in the HIPAA rules as:

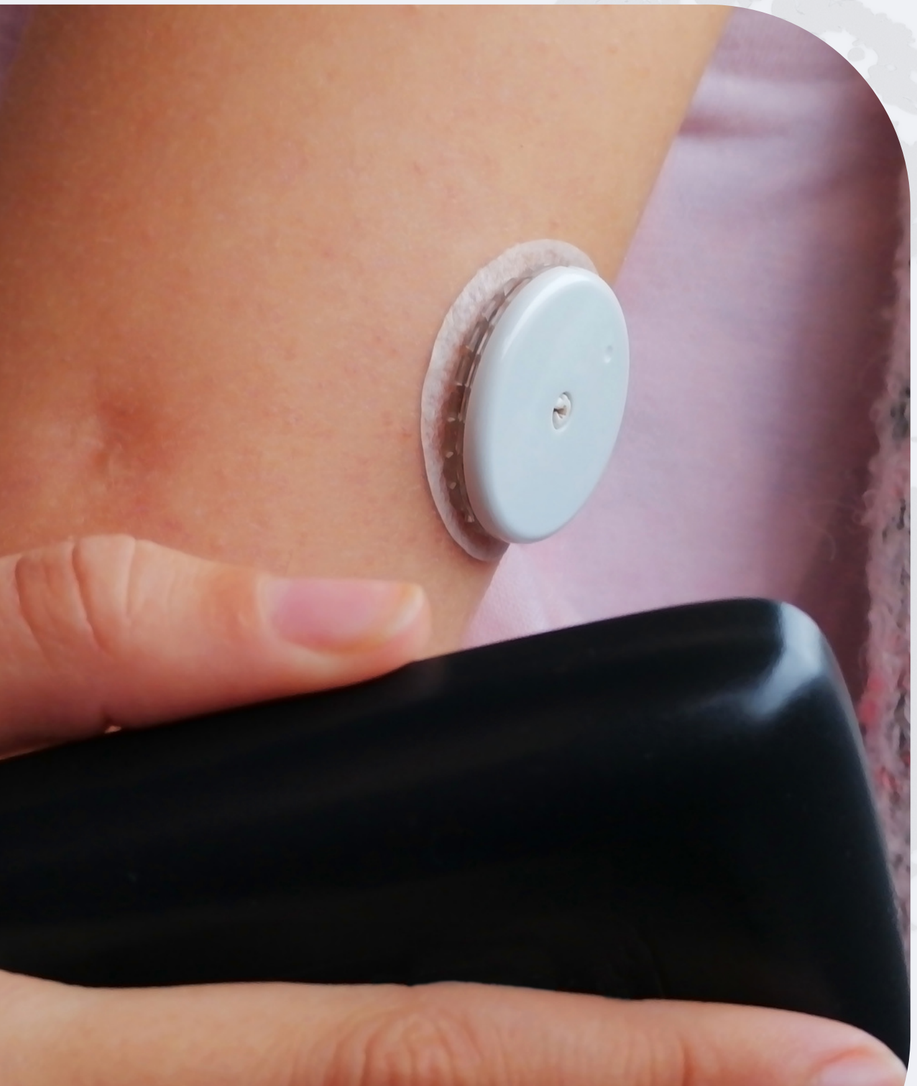
1. health plans
2. health care clearinghouses
3. health care providers who electronically transmit any health information in connection with transactions for which HHS has adopted standards

4.Opportunities and Benefits of Digital Therapeutics

Digital therapeutics have helped reshape and move healthcare out of the office. Differentiating itself from telehealth as a more tactile and self-governing approach to remote healthcare, the most significant benefit of digital therapeutics is accessibility.

A diabetes patient can use their continuous glucose monitor to track their blood glucose in real-time, or a patient can interact with therapist-like artificial intelligence (AI) to help manage and lessen their depressive symptoms.

These products present new opportunities for patients to manage their health as they go about their daily lives, saving them unnecessary doctor visits, improving their long-term health outcomes, reducing hospitalizations, preventing expensive medical interventions, and providing physicians with a more flexible workflow.



The use of DTx improves adherence to treatment regimens by providing accountability between the patient and the healthcare provider. If a patient is not responding to medication, with the right monitoring, the doctor can know if the patient is taking the medication as prescribed.

In the case of people with diabetes, are they taking their insulin correctly?

By having the physical device track the patient’s glucose and insulin taken, the information doesn’t have to be manually entered, so improves overall accuracy and timeliness.

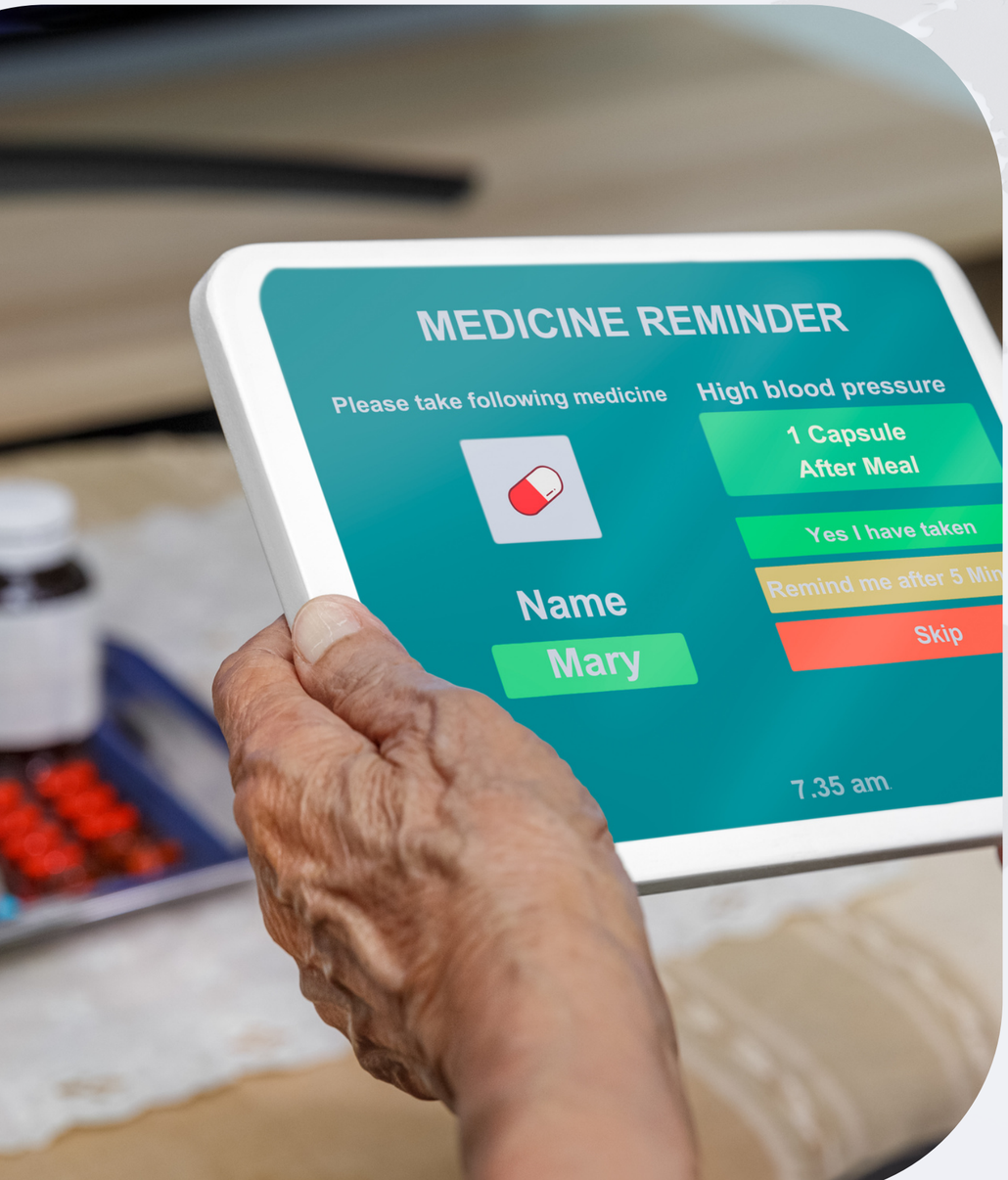
Through increased adherence and better feedback, improved treatments become available, therapies can be updated/advanced faster, and patient outcomes improve.

Improved patient outcomes result in reduced costs to the healthcare system. A healthcare provider is still often an integral component of patient care, but DTx is becoming more and more advanced reducing the need for human intervention.

Because of the direct feedback loop with a patient, research to develop and understand whether a solution is working properly becomes even more important.

Remote patient monitoring allows research to more closely monitor patients and better understand the impact of a particular drug or medical intervention.

It’s also easier for subjects to participate by reducing or eliminating the need to be physically close to a research center or disrupt their day by visiting the research site.



For Your Consideration

Physical medications are easy to take. Or are they? Medication non-adherence is a well-documented issue. From not filling a prescription, forgetting or just not taking the medication as prescribed for either lack of understanding, side effects, or just plain forgetfulness, there are a variety of issues leading to non-adherence. This impacts the efficacy of the treatment and reduces positive patient outcomes.

Consider a DTx where the patient must use the therapy over the course of several weeks to months or interact with it multiple times a day, patient engagement becomes a major component of the DTx design. The level of effort required to be compliant with the therapy is increased, but due to the digital nature of the therapy, the opportunities and approaches to track and engage the patient are significant.

While solutions and strategies exist, it can be challenging to understand whether a patient has taken physical medication. With a digital approach, patient interaction can be tracked against the desired usage patterns, and increasing levels of engagement can be employed from simple reminders on a smartphone to text messaging or at an extreme a call from a healthcare provider who has been alerted to lack of engagement.

5.Reimbursement

DTx insurance reimbursement is the gold standard business model, but it is challenging and will remain so for some time.

Some European countries like Germany (Link) are ahead of the game, and countries like France, Belgium, and Italy are looking to replicate the German model which it fast tracks reimbursement after regulatory approval. The EU is also driving forward with establishing standards.

The US with our more complicated healthcare ecosystem still needs much work and acceptance. It's an area ripe for forward-thinking risk-based models such as pay-for-performance or outcomes-based payments since DTx can often generate real-world data to use as a basis.

The US healthcare ecosystem is diverse as is its reimbursement system of public and private payors. One must consider government programs such as Medicare/Medicaid, Department of Defense - military and VA, Bureau of Indian Affairs, state programs, and private insurance.

It is a challenge for any one of these entities to provide reimbursement for a DTx. First, it must be cleared or approved by the FDA, and then the Centers for Medicare & Medicaid Services (CMS) must establish a billing code (HCPCS) for it to be reimbursed.

Petitioning and working with CMS to create a new billing code can take years.

Fortunately, the current administration has advocated for expanding access and coverage for Digital Therapeutic Treatments. A proposed bill Access to Prescription Digital Therapeutics Act of 2022 (link) is in the works, but has not yet been voted on.

This bill provides for Medicare and Medicaid coverage of prescription digital therapeutics (i.e., software applications that are used to prevent, manage, or treat medical conditions.

The Centers for Medicare & Medicaid Services must establish a Medicare payment methodology for payments to manufacturers that takes into account certain factors (e.g., ongoing use); manufacturers must report specified information about private payors, subject to civil penalties.)

It would greatly advance the cause for reimbursement and increase the availability of DTx. In 2022, CMS did issue a new HCPCS code, A9291, for prescription digital behavioral therapy, "Prescription digital behavioral therapy, FDA cleared, per course of treatment."

While helpful, CMS did not propose federal coverage or introduce any reimbursement rates which introduces a new challenge.

Public and private payors typically set a reimbursement rate per code, with various modifiers, but only having one code for many DTx options is a pricing challenge. The use of different DTx solutions will have different cost structures, so only having one code remains challenging. DTx providers will likely have to negotiate independently with payers to get adequate reimbursement.

Outside of the federal system, several states, Massachusetts and Oklahoma, have announced plans to cover digital therapeutics and Highmark, a commercial health plan, announced last year they would cover eight FDA-approved digital therapeutics.

Hopefully, other states and commercial payors will follow in their footsteps.

For Your Consideration

A key driver for any product is generating market share. Achieving FDA approval and reimbursement for a DTx is a challenging task that can take more than a year. Is there a model where the DTx provider creates a non-prescription version of their products that can be sold directly to the consumer?

Pricing and uptake in the B2C space have their own challenges. Still, this approach could help increase market share, generate evidence of improved outcomes, and help convince payors or companies to cover the user of the DTx once the prescription version is approved and reimbursement rates are achieved.

6.Accessibility and Equity

Digital health tools are not equally available to all as reported by a recent WHO analysis (**Link**). Their research shows often those with poor health are least likely to have new DTx available to them.

Numerous potential reasons for this lack of equity in use are cited including language barriers, lack of access to technology, age, and education. Access and use skews to a younger, more educated population, but this can be addressed.

While there are potential solutions that may help address accessibility, they remain fairly tentative. Language and cultural challenges can be overcome, and there are market challenges. Can a DTx company find a viable financial model to provide a product to smaller markets with the regulatory and reimbursement challenges? One first has to question the size of the market – is it really small or just challenging?

It may seem smartphones are ubiquitous, and everyone has high-speed internet at home, but this is not always the case. They are essential to digital health, and the success of digital therapeutics and disparities need to be addressed for the benefit of all. In the US various initiatives are underway by commercial internet providers and the government to subsidize access. This has become apparent in light of the COVID pandemic.

Parents should not have to park in a restaurant parking lot so their kids can do homework. Advocates are calling for high-speed internet access to be declared a basic human right, maybe it's time.

General awareness of the available solutions and their benefits needs to be increased among healthcare providers, patients, and the general public through education, training, marketing, and outreach efforts to help drive further expansion in the field. Increasing insurance coverage and establishing viable reimbursement rates will increase the willingness and capability of the market to expand awareness.

7. The Future of Digital Therapeutics

Digital Therapeutics is barely entering the toddler stage, but the US market size was valued at $1.48 billion in 2021 and is projected to reach $10.5 billion by the end of the decade (**link**).

Technology and available therapies will continue to develop at breakneck speeds. Regulatory challenges keeping pace with the rate of change are being addressed and while not solved show promise. Reimbursement rates present a different challenge, but are also being quickly addressed.

The advance of technology will continue. New therapeutics will be created and with the rise in healthcare consumerism and shift to value-based care and outcomes-based payment models the future of DTx is bright.

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A Digital Therapeutics Solution That's Right For You

Have an idea for a digital therapeutic, but not sure where to start?

Do you have lots of data and not sure what to do with it, access it, or manage it?

Don't have the necessary data, but need it for regulatory or commercial purposes?

Are you asking what is ISO 13485, ISO 62304, and ISO 14971, threat modeling, testing vs validation?

That's Where ESTENDA Comes In!

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We, at Estenda, have twenty years of experience in digital health/therapeutic solution design, development, testing, and validation. Estenda is ISO 13485-certified and experienced with the challenges of creating digital therapeutics and the regulatory process. We can create sophisticated, custom software and data analytic solutions for you.

We work with you to understand your passion, your needs, and your business model, and with our experience in software design, development, and delivery in digital health/therapeutics, craft a solution that works for you, your patients, and your customers.

Whether you need a scalable software-as-a-service (SaaS) platform for weight loss management or a digital solution to help diabetes patients better manage their glucose, Estenda will bring your digital health ideas, data, and projects to life.

If you’re interested in learning more or if you have a custom software or data analytics project in mind, we’d love to hear from you. Click the Contact Us link or reach out to RJ or Luke!

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