Navigating *The Playbook:* Digital Healthcare Edition

Your user guide to *The Playbook:* **Digital Healthcare Edition**

The **opportunities** digital health solutions bring to deliver high-value healthcare.

Industry definitions, classification and **regulation** of digital health solutions.

Your micro-playbooks to digital health solutions

- **AI/ML**
- **AR/VR/MR**
- **Connected Sensor Technology**
- **Digital Therapeutics**
- **Electronic health records**
- **Mobile health applications**
- **Engagement and Social Media**
- **Virtual care**

PRO TIP

Throughout the slides you will see ***'TL;DR'***. This is a common acronym for '***Too Long; Didn't Read.***'

We are acknowledging how busy you are and that a **small chunk of text is easier to digest** than a large portion of text on a slide.

Digital Therapeutics (DTx)

TL;DR

DTx are new care modularity tools that deliver care through high quality software programs

What is the difference between **DTx vs PDT?**

- **DTx** are evidence-based therapeutic interventions that are driven by high quality software programs to prevent, manage, or treat a medical disorder or disease.

  PDTs are a subset of DTx. **In the US, PDTs** deliver similar to DTx and are:
  - **authorized** by the FDA (i.e., cleared or approved) with approved directions for use;
  - undergo **rigorous evaluation** for safety and effectiveness in clinical trials with clinically-meaningful results;
  - **prescribed** and initiated by a licensed healthcare practitioner.

- **Deployed throughout the compendium of care delivery** for a range of purposes including chronic disease management, mental health, addiction and sleep medicine, oncology, neurology, and more. Newer areas include ophthalmology and female health

Applications

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://dtxalliance.org/wp-content/uploads/2021/01/DTA_DTx-Definition-and-Core-Principles.pdf
https://dtxalliance.org/understanding-dtx/product-library/

Realizing the potential value of DTx and PDTs for evidence-based therapeutic interventions

Opportunities to create value for patients, providers and healthcare systems

Produce **novel medical intervention** that is driven by software

Maximize patient engagement by engaging end users in product development and usability processes

Collect, analyze, and **apply real world evidence** and/or product performance data

Providing meaningful insights on **personalized goals** and outcomes to patients and providers

Provide convenience care outside doctors office, outside clinic hours, etc

Deliver high quality therapies **to underserved populations**

Providing therapies in **various languages,** such as English, Spanish, Arabic, German, and French

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://dtxalliance.org/wp-content/uploads/2021/01/DTA_DTx-Definition-and-Core-Principles.pdf

The missing pieces of the digital therapeutics that still needs to be addressed

Although the clinical safety profile of DTx to date is low risk, the surveillance of the clinical efficacy and safety of these new tools still need to be considered in real-world setting. Market access pathways and reimbursement are vital to the adoption and success of DTx in mainstream healthcare, yet these are still nascent. Better collaboration among digital innovators and payors, providers, and pharmaceutical is necessary to continue forward progress.

Challenge

Clarity on what quality, sufficient clinical evidence is and what's needed to support clinical decision making

Challenge

Challenges in **pricing, regulations, and reimbursement** prevents access to novel treatments

Challenge

Low translatability of solutions from controlled to real world settings

Challenge

High **adoption barrier** due to lack of implementation infrastructure

Challenge

Lack of standardization of evidence for underlying therapeutic outcomes

Challenge

Lack of skilled workforce to support initiation and deployment

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://www.statnews.com/2021/12/29/digital-therapeutics-pear-health-payers/

Outlook on the DTx regulatory landscape in US

- DTx are most **commonly regulated under Software as a Medical Device (SaMD)** framework, developed by the International Medical Device Regulators Forum (IMDRF). Learn more about SaMD:
  - SaMD Definitions
  - SaMD Framework for Risk Categorization
  - SaMD Application of quality system
- **DTx clearances** are usually granted by the FDA Center for Devices and Radiological Health.
- In wake of Covid-19 we have seen FDA also **allowing** certain digital health products focused on psychiatric conditions to **go-to-market temporarily.**

UNITED STATES Regulatory

Category Name	Medical Device—includes Software as a Medical Device (SaMD) and Software in a Medical Device (SiMD)		
Responsible Regulatory Agency	Food and Drug Administration (FDA), specifically the Center for Devices and Radiological Health (CDRH)		
Product Risk Classifications	**Exempt Medical Devices** Class I Exempt, Class II Exempt, or Enforcement Discretion (including COVID-19 public health emergency (PHE))	**Class II** Pre-market Notification 510(k) or De Novo pathways	**Class III** Premarket Approval (PMA)
Regulatory Review	Exempt from a marketing submission: Most Class I and some Class II devices are 510(k) exempt devices, but must register and list. Enforcement discretion devices may not be required to register and list. Enforcement discretion is a risk-based decision by FDA to decline enforcing certain regulatory requirements and is not specific to a classification.	510(k): Marketing submission required to demonstrate substantial equivalence to predicate device. General controls are required. Special controls may also be required, which may require a clinical trial (see regulation to determine requirements). De Novo: Marketing submission required to demonstrate reasonable assurance of safety and efficacy. General controls are required. Prospective clinical trial generally required.	PMA: Most stringent market submission application to demonstrate safety and effectiveness. General controls are required. Prospective clinical trial generally required.
Pre-Submission Opportunities	513(g) can be submitted to confirm the regulatory pathway, but is not required: *Timeline: 60 days* *Cost: $2,530 small business* / $5,061 standard*	Pre-submission strongly recommended, especially for De Novo: *Timeline: 70 days* *Cost: no charge* 513(g) may be submitted to confirm regulatory pathway. Breakthrough Devices request may be possible for highly innovative products: *Timeline: 60 days* *Cost: no charge*	Pre-submission strongly recommended. Pre-IDE should be submitted for feedback on significant risk clinical studies. 513(g) may be submitted to confirm regulatory pathway. Breakthrough Devices request may be possible for highly innovative products.

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://dtxalliance.org/wp-content/uploads/2022/01/US-Regulatory-and-Reimbursement-Pathways.pdf

SPOTLIGHT

The opportunity: novel approaches for evidence generation to support broad acceptance of DTx

THE LANCET
Digital Health

Viewpoint

Advancing digital health applications: priorities for innovation in real-world evidence generation

Ariel D Stern, Jan Brönneke, Jörg F Debatin, Julia Hagen, Henrik Matthies, Smit Patel, Ieuan Clay, Bjoern Eskofier, Annika Herr, Kurt Hoeller, Ashley Jaksa, Daniel B Kramer, Mattias Kyhlstedt, Katherine T Lofgren, Nirosha Mahendraratnam, Holger Muehlan, Simon Reif, Lars Riedemann, Jennifer C Goldsack

In 2019, Germany passed the Digital Healthcare Act, which, among other things, created a "Fast-Track" regulatory and reimbursement pathway for digital health applications in the German market. The pathway explicitly provides for flexibility in how researchers can present evidence for new digital products, including the use of real-world data and real-world evidence. Against this backdrop, the Digital Medicine Society and the Health Innovation Hub of the German Federal Ministry of Health convened a set of roundtable discussions to bring together international experts in evidence generation for digital medicine products. This Viewpoint highlights findings from these discussions with the aims of (1) accelerating and stimulating innovative approaches to digital medical product evaluation, and (2) promoting international harmonisation of best evidentiary practices. Advancing these topics and fostering international agreement on evaluation approaches will be vital to the safe, effective, and evidence-based deployment and acceptance of digital health applications globally.

The health innovation hub of German Ministry of Health (hih) and DiMe released global priorities highlighting global best practices and a roadmap for the continued methodological advancements necessary for the acceleration of DTx innovation.

In 2019, Germany's DVG act created a **regulatory and reimbursement pathway** for various digital health applications including DTx in the German market. The **"Fast-Track" pathway** set the legal framework for **doctors to prescribe** certain categories of digital health applications (known by their German acronym, **DiGA**), while evidence demonstrating a positive healthcare effect is still being collected.

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://www.thelancet.com/action/showPdf?pii=S2589-7500%2821%2900292-2

Examples of regulated DTx in the German market

- **Positive effects of care** for DTx under the DiGA may be **defined as either**:
  1. **A medical benefit** (i.e., a therapeutic improvement by positively influencing patient-relevant endpoints such as quality of life, reduction in disease duration, improved survival), or
  2. **Patient-relevant improvements in structure and process**, such as adherence, better coordination of treatment processes, health literacy, patient safety, patient autonomy, etc.

- Access the full DiGA directory here
- Information for DiGA users here
- Information for service providers here
- Information on the Fast Track application here

An example of an early digital health application that completed the Fast-Track process is the digital therapeutic Elevida (GAIA; Hamburg, Germany), a digital health application for individuals with multiple sclerosis who also suffer from fatigue. For this product, evidence of positive care effects was generated from a randomised controlled trial of 275 patients with multiple sclerosis with fatigue. The trial compared the use of the Elevida application as well as standard multiple sclerosis care (the intervention group) with standard multiple sclerosis care alone (the control group). A significantly lower Chalder Fatigue Scale score was found in the intervention group compared with the control group after 12 weeks (the primary survey time endpoint) and differences were also detectable at 24 weeks.[13]

Many analogous products have gone through other regulatory approval processes internationally. For example, reSET (Pear Therapeutics; Boston, MA, USA) had the first de-novo approval of a digital therapeutic by the US Food and Drug Administration.[14] In the case of reSET, real-world evidence observational studies have been used to examine efficacy and product usage. Other examples include the use of BlueStar (Welldoc; Columbia, MD, USA) for people with diabetes and EaseVRx (AppliedVR; Los Angeles, CA, USA) for treating pain.

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://www.thelancet.com/action/showPdf?pii=S2589-7500%2821%2900292-2, German Digital Healthcare Act (Digitale–Versorgung–Gesetz or DVG)

Case study: Managing PTSD, panic disorder, and panic attack with digital therapeutics

The Challenge:

In the US, **17.1 million people** have frequent **panic attacks** and **8.7 million** people have **PTSD** (Post-traumatic stress disorder). PTSD is **significantly higher in the Veteran population** with as high as **30% of** Veterans diagnosis of PTSD**.**

The Approach:

Freespira® FDA-cleared DTX that normalizes exhaled **CO2 and Respiratory Rates** (RR) in a single **28-day at-home treatment**. Guided, **twice-daily (17-minute)** treatments use a sensor sampling the patient's exhaled air (measure CO2 levels & RR).

These physiological markers are displayed in real-time on a tablet as visual feedback along with **rising and falling audio tones** to teach patients how to **normalize respiration rate** and expired CO2 levels.

The Result:

- **89%** Clinically significant **symptom reduction**
- **50%** in **remission** at 6 months
- **41% decrease in suicidality**
- **29% decrease in depression**
- **77%** increase in treatment **adherence**
- **91% satisfaction** rate

Source: DiMe-VHA The Playbook: Healthcare team analysis, Ostacher, M.J., Fischer, E., Bowen, E.R., Lyu, J., Robbins, D.J., and Suppes, T. Journal of Applied Psychophysiology and Biofeedback, September 1, 2021, https://www.ptsd.va.gov/understand/common/common_veterans.asp

Patient's story with Freespira®

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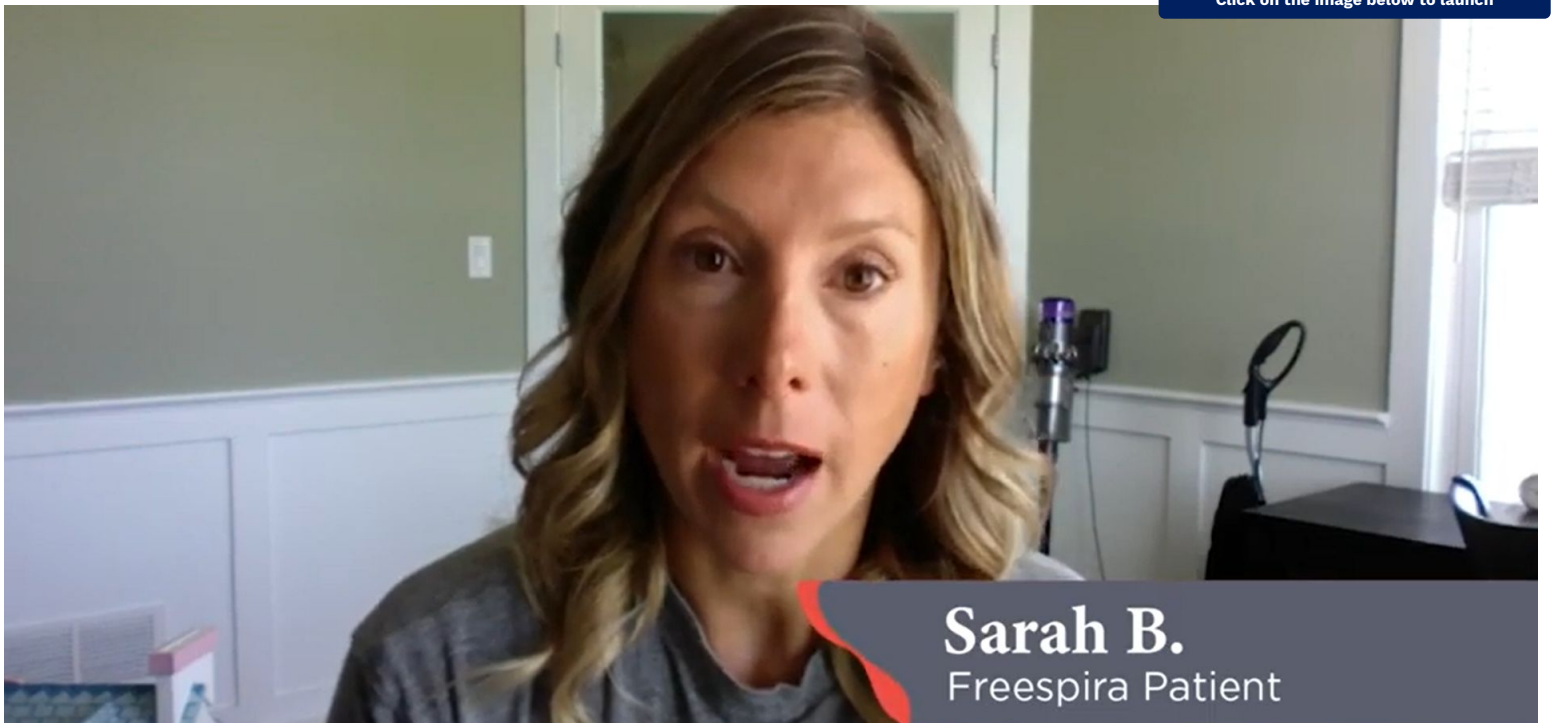

Source: DiMe-VHA The Playbook: Healthcare team analysis, View the video https://youtu.be/Vg-uH8h0CgA

LEARN FROM THE EXPERTS

Source: DiMe-VHA The Playbook: Healthcare team analysis, https://youtu.be/BU4y9ENxshI