Digital Therapeutics:
Combining Technology and Evidence-based Medicine to Transform Personalized Patient Care
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Introduction

While the term “digital therapeutic” may sound futuristic, these therapies are already a reality. As this new category of medicine continues to be integrated across the healthcare ecosystem, digital therapeutic (DTx) products will increasingly influence the way healthcare is delivered and consumed across the world.

In order for patients, healthcare providers, and payers to better understand and have confidence in these groundbreaking products, the Digital Therapeutics Alliance (DTA) is spearheading the development of foundational industry definitions, best practices, and frameworks.

There is a growing number of digital therapeutics on the market today that are being developed in accordance with internationally-recognized design, quality, and manufacturing standards. Through our ongoing efforts, DTA encourages the development of products that directly address patient needs, are safe and effective, demonstrate positive clinical and health economic outcomes, and influence the delivery of healthcare in a meaningful way.

This paper provides the definition of a digital therapeutic, in addition to core principles, industry-wide best practices, and examples of DTx products currently on the market or under development. Over the coming months, DTA will further explore and identify best practices and correlating standards in the areas of product quality and design, clinical validation, patient utilization, and regulatory oversight.

DIGITAL THERAPEUTICS ALLIANCE

Founded in 2017, the Digital Therapeutics Alliance (DTA) is a non-profit trade association of industry leaders and stakeholders engaged in the evidence-driven advancement of digital therapeutics. DTA maintains an international industry focus and is headquartered in the United States.

Mission

DTA exists to broaden the understanding, adoption, and integration of clinically-validated digital therapeutics into healthcare through education, advocacy, and research.

Vision

DTA works to enable expanded access to high quality, evidence-based digital therapeutics for patients, healthcare providers, and payers in order to improve clinical and health economic outcomes.
Digital Health Landscape

To understand the value of digital therapeutics, it is first important to explore the distinction between digital health and digital therapeutics. The term “digital health” describes all technologies that engage patients for health-related purposes; as such, it encompasses a wide range of products used across the wellness and healthcare industries.

Digital therapeutics form an independent category of evidence-based products within the broader digital health landscape. Digital therapeutics are distinguished from other digital health categories through their primary function of delivering software-generated therapeutic interventions directly to patients to prevent, manage, or treat a medical disorder or disease.

Digital therapeutics are distinct from pure-play adherence, diagnostic, and telehealth products. However, while their principal focus is on delivering direct therapeutic interventions, DTx products possess the unique ability to incorporate additional functionalities into a comprehensive portfolio of synchronous products and services. This includes potential integration with mobile health platforms; the provision of complementary diagnostic or adherence interventions; the ability to pair with devices, sensors, or wearables; the delivery of interventions remotely; and integration into electronic prescribing, dispensing, and medical record platforms.

The expanding digital health landscape includes products such as:

**Mobile Health (mHealth)**
- Wellness, fitness trackers, and nutrition apps
- Consumer health information
- Medication adherence apps

**Digital Therapeutics**
Digital therapeutics deliver evidence-based therapeutic interventions to patients to prevent, manage, or treat a medical disorder or disease.

**Examples provided on page 6.**

**Health Information Technology (HIT)**
- Electronic medical record systems
- Electronic prescribing and order entry
- Consumer health IT applications

**Devices, Sensors, and Wearables**
- Wearable and wireless devices
- Biometric sensors
- Diagnostic products

**Personalized Healthcare**
- Patient reported outcomes
- Predictive analytics
- Clinical decision support

**Telehealth**
- Telemedicine virtual visits
- Remote patient monitoring
- Remote care programs

Sources provided on page 14.
Defining Digital Therapeutics

Thought leaders across the digital therapeutics industry, supported by the Digital Therapeutics Alliance, collaborated to develop the following comprehensive definition:

*Digital therapeutics (DTx) deliver evidence-based therapeutic interventions to patients that are driven by high quality software programs to prevent, manage, or treat a medical disorder or disease. They are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes.*

*DTx products incorporate advanced technology best practices relating to design, clinical validation, usability, and data security. They are reviewed and cleared or approved by regulatory bodies as required to support product claims regarding risk, efficacy, and intended use.*

*Digital therapeutics empower patients, healthcare providers, and payers with intelligent and accessible tools for addressing a wide range of conditions through high quality, safe, and effective data-driven interventions.*
Digital Therapeutic Products

The types of interventions being delivered by digital therapeutic products across the industry are as diverse as the disease states being addressed. As the DTx field grows, patients, providers, and payers can expect to see an increasingly comprehensive network of therapy options for physical, mental, and behavioral disease states.

Examples of digital therapeutics on the market or under development include:

- Combined software and hardware program to improve asthma and COPD control and optimize healthcare utilization
- Digital therapeutic utilizing adaptive sensory stimulus software for the treatment of ADHD delivered through an engaging video game experience
- Digital sleep improvement program featuring Cognitive Behavioral Therapy (CBT) techniques
- Digital therapeutic used as an adjunct to standard, outpatient treatment for Substance Use Disorder (SUD)
- Digital therapeutic engaging individuals with Type 2 diabetes, hypertension, and obesity, and their providers, to improve self-management and outcomes
- AI-based digital diagnostics and personalized therapeutics for pediatric behavioral healthcare
- Neurologic Music Therapy to address motor, speech, and cognitive dysfunction caused by neurologic disease or injury
- Digital delivery of physical exercises, behavioral therapy, and education for chronic back pain patients
- Personalized digital program to help people prevent the onset of diabetes and other chronic diseases
- Intervention tool to train cognition in concussion patients
- Basal insulin dose calculator for adults with Type 2 diabetes
Role in Healthcare

Accounting for the diversity of products across the DTx industry, individual digital therapeutics have the potential to:

➢ Provide patients, providers, and payers with novel therapy options for unmet medical needs
➢ Be used independently or in conjunction with other therapies
➢ Enhance and support current medical treatments
➢ Reduce reliance on certain pharmaceuticals or other therapies
➢ Integrate into medical guidelines and best practices

Product Categories

Each digital therapeutic corresponds to one of four categories based on its intended use and official product claims:

➢ Address a medical condition
➢ Manage or prevent a medical disorder or disease
➢ Optimize medication (an individual medication or class of pharmaceuticals)
➢ Treat a medical disease or disorder
Developing Industry Standards

The direct delivery of personalized treatment interventions to patients places digital therapeutics in a unique position, one full of additional responsibility and promise. Given the diversity of interventions being delivered by digital therapeutics and the types of disease states addressed, it is important for all products to adhere to industry-adopted core principles and best practices.

Core principles all digital therapeutics must adhere to:

- Prevent, manage, or treat a medical disorder or disease
- Produce a medical intervention that is driven by software, and delivered via software or complementary hardware, medical device, service, or medication
- Incorporate design, manufacture, and quality best practices
- Engage end users in product development and usability processes
- Incorporate patient privacy and security protections
- Apply product deployment, management, and maintenance best practices
- Publish trial results inclusive of clinically-meaningful outcomes in peer-reviewed journals
- Be reviewed and cleared or approved by regulatory bodies as required to support product claims of risk, efficacy, and intended use
- Make claims appropriate to clinical validation and regulatory status
- Collect, analyze, and apply real world evidence and product performance data
Considerations around the safety and quality of digital therapeutics are of highest importance as adoption by patients, providers, and payers continues to grow. Building on the core principles that all digital therapeutic products must meet, industry leaders are working to establish best practices related to the design, manufacture, validation, and regulation of these products.

Industry-adopted best practices for digital therapeutics include:

### Product Design, Development, Manufacture

- Incorporate data-driven and informed interventional pathways.
- Compliance with international and national certifications and standards.
- Establish and adhere to quality systems to ensure that products consistently meet applicable requirements and specifications.
- Design the product using a human-centered approach, accounting for the user’s core needs, the user environment, and device interface.

### Clinical Validation

- Product must be subject to adequate and well-controlled clinical investigations that establish the product as safe and effective.
- Completion of one or more clinical studies, including an adequately-powered Randomized Control Trial (RCT) in the target patient population.
- Clinical studies are approved by an Institutional Review Board and registered in a recognized Clinical Trials Registry before study begins, as appropriate to clinical claims.
- Publication of trial results inclusive of clinically-meaningful outcomes on the stated primary outcome in peer-reviewed journals (prior to or following regulatory review).
- Conduct ongoing analysis and application of real world evidence and product performance data to ensure continued safety and effectiveness of product.
- Collect and analyze real world behavior data to optimize the product for better engagement, implementation, and adherence.

### Product Security and Maintenance

- Pass and obtain appropriate security and vulnerability certifications, including standards-based guidelines to safeguard data at rest and in-transit through proper authentication, encryption, and other methods.
- Ensure compliance with all applicable electronic Protected Health Information (ePHI) regulations.
- Monitor changing external security environments, with a focus on how to protect patient and customer private information.
- Employ a system that identifies, monitors, and addresses adverse events to detect and correct problems in a timely manner.

### Regulatory Oversight

- Be compliant with oversight provided by each national regulatory agency or notified body, including review of safety and efficacy medical claims.
- Register with the applicable regulatory agency or notified body in each jurisdiction the product is being used.
- Be compliant with regional manufacturing requirements.
- Ensure that product claims are appropriate to clinical validation, regulatory status, and marketing authorization.
- Adhere to labeling and advertising regulations under appropriate authorities, including all labels and other written, printed, or graphic matter accompanying or associated with the product.
Digital Therapeutic Product Categories

Each category of digital therapeutics displays varying degrees of product claims, requirements for regulatory oversight, patient and provider access, and integration with concurrent therapies.

Note: All digital therapeutic products must adhere to industry-adopted core principles (page 8) and best practices (page 9).

<table>
<thead>
<tr>
<th>PRIMARY PURPOSE OF THE PRODUCT:</th>
<th>ADDRESS A MEDICAL CONDITION</th>
<th>MANAGE OR PREVENT A MEDICAL DISORDER OR DISEASE</th>
<th>OPTIMIZE MEDICATION</th>
<th>TREAT A MEDICAL DISEASE OR DISORDER</th>
</tr>
</thead>
<tbody>
<tr>
<td>To support product claims of risk, efficacy, and intended use:</td>
<td>Regulatory enforcement discretion (without explicit oversight)</td>
<td>Third-party validation of efficacy and safety claims by regulatory or equivalent national body</td>
<td>Third-party validation of efficacy and safety claims by regulatory or equivalent national body</td>
<td>Third-party validation of efficacy and safety claims by regulatory or equivalent national body</td>
</tr>
<tr>
<td>Product claims related to a medical disorder or disease:</td>
<td>No efficacy claims regarding a medical disorder or disease</td>
<td>Low to medium risk claims (e.g., reduce rate of disease progression)</td>
<td>Medium to high risk claims (e.g., improve efficacy of adjunctive therapies)</td>
<td>Medium to high risk claims (e.g., direct efficacy claims on clinical outcomes)</td>
</tr>
<tr>
<td>Clinical evidence generation:</td>
<td>Clinical trials and ongoing evidence generation required</td>
<td>Clinical trials and ongoing evidence generation required</td>
<td>Clinical trials and ongoing evidence generation required</td>
<td>Clinical trials and ongoing evidence generation required</td>
</tr>
<tr>
<td>Patient access to product:</td>
<td>Direct-to-Consumer (Prescription not required)</td>
<td>Over-the-Counter OR Prescription required</td>
<td>Over-the-Counter OR Prescription required</td>
<td>Prescription required</td>
</tr>
<tr>
<td>Relationship to concurrent therapies:</td>
<td>Works independently OR Indirectly supports another therapy</td>
<td>Monotherapy OR Directly supports a concurrent treatment</td>
<td>Directly supports a concurrent treatment</td>
<td>Monotherapy OR Directly supports a concurrent treatment</td>
</tr>
</tbody>
</table>
Global Reach of Digital Therapeutics

The core principles and best practices described in this paper apply to digital therapeutic products regardless of their country of origin or use. Every digital therapeutic product should meet each of the industry core principles and incorporate best practices related to product quality, design, manufacture, security, clinical validation, and regulatory oversight.

As a class, digital therapeutics have vast potential to establish a significant global presence given their ability to:

- Deliver high quality, evidence-based therapies to underserved and under-diagnosed populations.
- Make effective, patient-centered treatments accessible and scalable at relatively low units of cost.
- Support healthcare teams in countries with varying degrees of health care infrastructure.
- Transform how patients and populations manage medical conditions and engage in their healthcare.

Companies planning to launch DTx products in multiple regions and countries must consider a range of factors spanning from language and cultural relevance, to optimal integration in the current healthcare landscape, in addition to country-specific regulatory requirements.

In order to support the development of digital therapeutics on a global scale and build public and professional trust, it is necessary to consider:

**Legislative & Regulatory Environments**

Regulatory bodies and national health systems across the world are beginning to identify ways to evaluate and regulate digital therapeutics, striking a balance between access to new therapies while simultaneously ensuring product safety, effectiveness, and quality.

**Recommendation:** It is important for consensus to form on a set of internationally-recognized standards for this new class of medicine. Such standards will ensure consistency in the way digital therapeutics are understood, evaluated, and trusted by patients, providers, and payers.

**Global Infrastructure**

From an infrastructure perspective, digital therapeutics have the ability to scale with relative ease given the broad use of personal devices across populations and growing access to internet services.

**Recommendation:** Collaborations within countries between digital therapeutic companies, technology and service providers, pharmaceutical manufacturers, national health systems, academic institutions, patients, and provider groups can lead to the creation of local, regional, and national roadmaps to better operationalize and commercialize digital therapeutics.

**Cross-cultural Acceptance**

There is a need across this growing industry to establish a standard for "DTx-equivalence" regarding the way digital therapeutic outcomes apply to various settings and are translated across different cultures, languages, and national borders. This process aligns with the principle of drug bioequivalence.

**Recommendation:** Industry leaders should develop best practices and standards to demonstrate consistency across digital therapeutic development processes, clinical outcomes, and equivalence across multiple cultures, languages, and national borders.
Benefits of Digital Therapeutics

Digital therapeutics are demonstrating meaningful benefits for stakeholders across the spectrum of healthcare delivery. Continued evolution in the field will result in expanded therapeutic targets and interventions for patients, caregivers, healthcare providers, and payers.

Demonstrated benefits for **patients and caregivers** include digital therapeutics’ ability to:

- Deliver reliable, evidenced-based interventions with a high control of quality
- Increase access to therapies that are clinically demonstrated as safe and effective
- Personalize care based on individual patients’ needs and abilities
- Administer therapeutic interventions in an engaging and convenient way
- Provide care independent of a patient’s schedule and in the privacy of their own environment (e.g., home, office, on-the-go, etc.)
- Reduce stigma associated with the delivery of certain traditional therapies
- Provide patients, caregivers, and select healthcare providers with secure progress updates on personalized goals and outcomes
Benefits for healthcare providers and health-systems include digital therapeutics’ ability to:

- Increase access to novel treatment options for patients with unmet medical needs
- Integrate into healthcare delivery systems in accordance with industry best practices and guidelines
- Be prescribed to patients by qualified healthcare providers independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes
- Provide secure data regarding patient engagement and response to therapy that is integrable into provider portals and clinical data warehouses
- Enable intelligent data-driven care management and clinical decision making
- Deliver clinically-proven therapies that provide patients with effective self-management therapeutic options
- Expand access to evidence-based medical therapies locally, nationally, and globally

Benefits for public and private payers include digital therapeutics’ ability to:

- Improve clinical and health economic outcomes at the patient and population levels for a large range of physical, behavioral, and mental disorders and diseases
- Facilitate analysis of population health outcomes
- Provide ubiquitous access to evidence-based treatment options for conditions that previously have been untreated or undertreated by traditional medications and therapies
- Increase patient population exposure to effective and engaging treatments without potentially requiring an equivalent workforce expansion
- Decrease the economic burden of medical conditions by reducing overall costs
On the Horizon

The growth of the digital therapeutic industry will be dramatic over the next 18 months, resulting in major impacts for users, organizations, and the healthcare industry.

**Patients and caregivers** should expect digital therapeutics to:

- Provide new treatment options for a broad spectrum of medical disorders and diseases
- Deliver highly engaging and interactive therapeutic interventions, while providing actionable insights
- Demonstrate improvements to existing care pathways
- Increasingly be covered by payers, employers, and national providers

**Public and private payers** should expect digital therapeutics to:

- Deliver clinical, service efficiency, and health economic benefits
- Achieve commercial scale through partnerships between DTx companies and industry partners
- Demonstrate improved clinical and health economic outcomes at patient and population levels
- Receive coverage similar to existing medicine and therapies

**Healthcare providers and health-systems** should expect digital therapeutics to:

- Integrate as value-added therapies into official clinical guidelines and existing care management pathways
- Operate in tandem with complementary therapies and other DTx programs through increasing levels of connectivity
- Incorporate into healthcare prescribing, data management, and distribution systems
- Increase patient safety and improve practice efficiency

**Legislative and regulatory bodies** should expect digital therapeutics to:

- Incorporate internationally-recognized standards and best practices relating to product design, quality, manufacture, and privacy
- Demonstrate safety, efficacy, and cost effectiveness based on the principles and practices of evidence-based medicine
- Be accepted as an independent class of medicine, equivalent to, or as an effective adjunct to, pharmaceuticals and other treatments

**Sources**

4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3938085/
Ongoing Work

Given the growing significance of digital therapeutics (DTx) in patient care and the rapid expansion of this industry, the Digital Therapeutics Alliance (DTA) convenes thought leaders to establish foundational industry-level validation, operational, value, and regulatory best practices and frameworks. DTA members collectively promote the need to apply evidence-based approaches to the development, manufacture, utilization, and support of high quality, patient-centered digital therapeutics.

DTA members and partners are committed to safeguarding DTx product quality and integrity across the industry, while simultaneously encouraging the development of therapies that are highly engaging, interactive, and meaningful.

The integration of digital therapeutics into healthcare is no longer a theoretical conversation. Following this inaugural paper, DTA will further develop best practices and frameworks that directly support the design, validation, utilization, and regulatory oversight of digital therapeutics across multiple cultures, languages, and national borders.
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