DIGITAL THERAPEUTICS FOR MANAGEMENT AND TREATMENT IN BEHAVIORAL HEALTH

The last decade has seen immense changes in digital health, with the expanded use of computing platforms, electronic medical records, mobile applications, and wearable devices in health care. During the COVID-19 pandemic in particular, telehealth expanded access to care for millions of people and was a critical resource to meet the behavioral healthcare needs of individuals with mental health conditions and substance use disorders. Another example of the use of technology to facilitate care is **digital therapeutics** (DTx). DTx are health software intended to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention that has a demonstrable positive therapeutic impact on a patient's health.[1] DTx may be used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes.[2] DTx may or may not require a prescription and are generally considered medical devices subject to regulatory oversight by the Food and Drug Administration (FDA).[3]

Many digital platforms and applications are marketed as behavioral health and wellness interventions. However, other than DTx, few have evidence demonstrating improved behavioral health outcomes. In addition, access to high-quality digital health products can be limited for those who are uninsured or underinsured and who have inadequate broadband access and data plans for smartphone and computer use. All of these factors can result in disparities in the uptake of digital health tools.[4,5] It is therefore important to identify the digital health interventions such as DTx that have an evidence base for both treating and managing mental health conditions and substance use disorders[6,7] and also recognize and address barriers to access.

Key Messages
• DTx can be effective independent or complementary services in the *management and treatment* of mental health conditions and substance use disorders.
• Users should be aware that not all healthcare applications for mental health conditions and substance use disorders have an evidence base for therapeutic use.
• At least five federal agencies have initiatives to develop, research, review, regulate, distribute, and address payment for DTx.
• At this time, few health plans cover prescription digital therapeutics (PDTs), but payers continue to explore and expand this area.
• For DTx to increase behavioral health equity, they must be designed and implemented to account for differences in health and digital literacy and to be culturally and linguistically appropriate, adaptable to variable service settings, and affordable and accessible for all users.
• Continued research is needed on the efficacy of DTx, balanced with ongoing consideration of costs, patient/client privacy, and protection of health data.

Definitions

Digital Health Interventions: Discrete digital functionalities of technology used to achieve health sector objectives.[8] Digital health interventions are typically designed to achieve a specific outcome. They encompass evidence-based DTx but may also include interventions that do not have an evidence base to support their use, such as many wellness apps.

➥ **Digital Therapeutics (DTx):** DTx are health software intended to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention that has a demonstrable positive therapeutic impact on a patient's health.[1] DTx are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes.[2] DTx may or may not require a prescription. DTx are generally considered medical devices subject to regulatory oversight by the Food and Drug Administration (FDA).[3]

➥ **Prescription Digital Therapeutics (PDTs):** DTx in the United States that are cleared or approved (depending upon risk level) for prescription use by the FDA as software-based medical devices intended to prevent, manage, or treat a medical condition. A clinical provider prescribes PDTs, typically to support health claim payment.[9]

Overview of Digital Therapeutics

DTx are part of a spectrum of digital health interventions currently available in behavioral health care (see *Definitions*). DTx are:
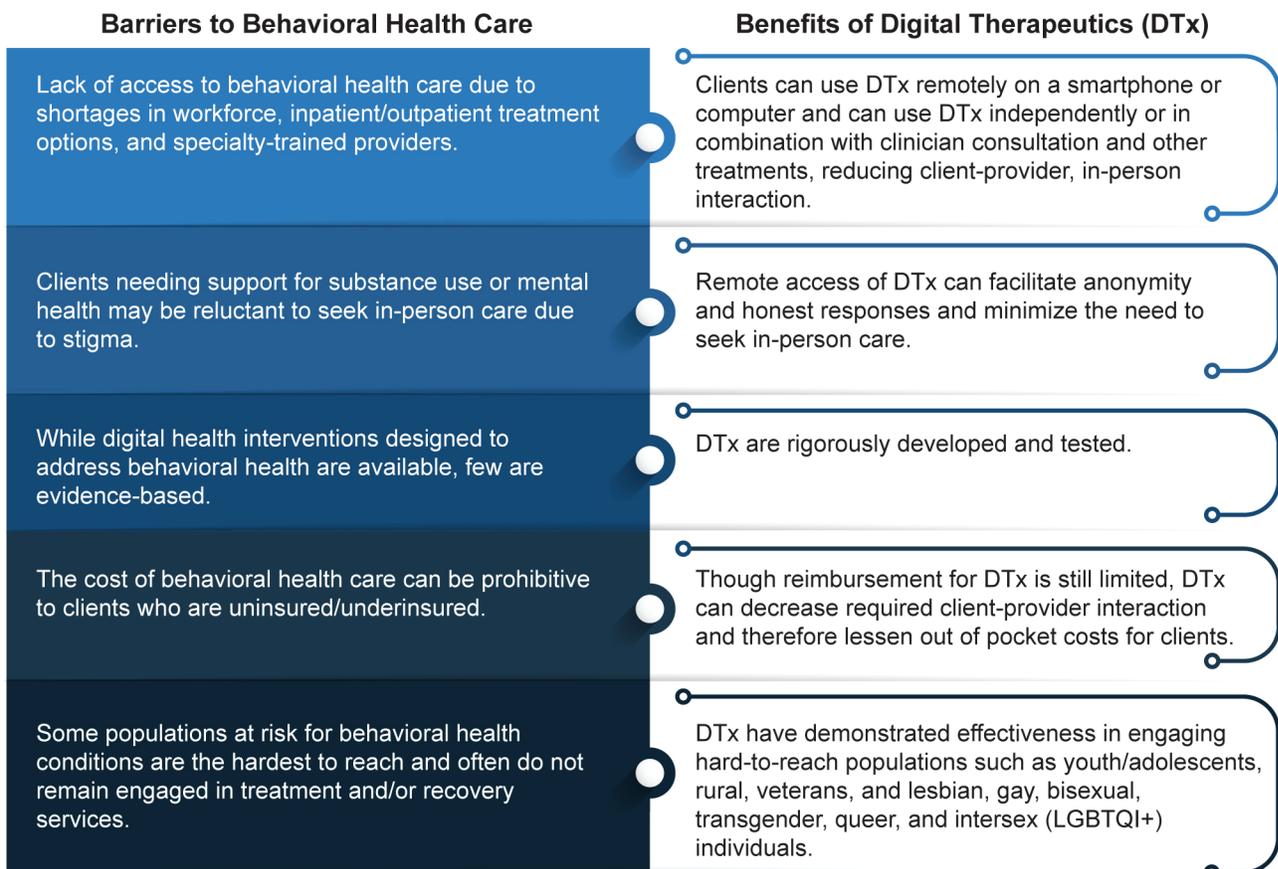
- Currently used to treat or manage mental health conditions or substance use disorders
- Designed and tested rigorously with sufficient scientific and clinical evidence that they improve outcomes in the management and treatment of mental health conditions and substance use disorders
- Able to extend the reach of evidence-based behavioral health treatments (e.g., Cognitive Behavioral Therapy [CBT]) and improve health equity through enabling easier access to patients in their preferred environments
- Accessible via smartphones, tablets, virtual reality headsets, or other devices
- Driven by software that can be used independently or in conjunction with direct clinical care, but are not intended to replace provider-led clinical services
- Designed to maintain client privacy and security protections
- Generally considered medical devices subject to FDA oversight; when cleared or approved for prescription use (depending on the classification and corresponding risks), they can be referred to as PDTs
- In behavioral health, six DTx currently meet the FDA's criteria for PDTs

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Benefits of DTx

DTx have demonstrated benefits in improving access to care, client engagement, and health outcomes while reducing costs for care.[6,7,9,10] They also reduce barriers to behavioral health care for hard-to-treat conditions and hard-to-reach populations, such as youth and those living in rural areas.[9,11,12] In addition, the White House's strategy to address the national mental health crisis specifically notes the importance of bridging the gaps between available services and access for individuals. DTx have the potential to profoundly reduce these gaps, by providing complementary services that may reduce the burden of an already strained behavioral health workforce.

The figure below describes some of the major barriers to accessing behavioral health services and how DTx may address them.

Barriers to Behavioral Health Care Addressed by DTx

Barriers to Behavioral Health Care	Benefits of Digital Therapeutics (DTx)
Lack of access to behavioral health care due to shortages in workforce, inpatient/outpatient treatment options, and specialty-trained providers.	Clients can use DTx remotely on a smartphone or computer and can use DTx independently or in combination with clinician consultation and other treatments, reducing client-provider, in-person interaction.
Clients needing support for substance use or mental health may be reluctant to seek in-person care due to stigma.	Remote access of DTx can facilitate anonymity and honest responses and minimize the need to seek in-person care.
While digital health interventions designed to address behavioral health are available, few are evidence-based.	DTx are rigorously developed and tested.
The cost of behavioral health care can be prohibitive to clients who are uninsured/underinsured.	Though reimbursement for DTx is still limited, DTx can decrease required client-provider interaction and therefore lessen out of pocket costs for clients.
Some populations at risk for behavioral health conditions are the hardest to reach and often do not remain engaged in treatment and/or recovery services.	DTx have demonstrated effectiveness in engaging hard-to-reach populations such as youth/adolescents, rural, veterans, and lesbian, gay, bisexual, transgender, queer, and intersex (LGBTQI+) individuals.

Sources:
Bucci, S., Berry, N., Morris, R., Berry, K., Haddock, G., Lewis, S., & Edge, D. (2019). "They are not hard-to-reach clients. We have just got hard-to-reach services." Staff views of digital health tools in specialist mental health services. *Frontiers in Psychiatry, 10*, 344.

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Jacobson, N. C., Quist, R. E., Lee, C. M., & Marsch, L. A. (2023). Using digital therapeutics to target gaps and failures in traditional mental health and addiction treatments. In *Digital therapeutics for mental health and addiction* (pp. 5-18). Elsevier.

Ostacher, M. J., Fischer, E., Bowen, E. R., Lyu, J., Robbins, D. J., & Suppes, T. (2021). Investigation of a capnometry guided respiratory intervention in the treatment of posttraumatic stress disorder. *Applied Psychophysiology and Biofeedback, 46*(4), 367-376.

Pandian, G. S. B., Jain, A., Raza, Q., & Sahu, K. K. (2021). Digital health interventions (dhi) for the treatment of attention deficit hyperactivity disorder (adhd) in children-a comparative review of literature among various treatment and dhi. *Psychiatry Research, 297*, 113742.

Richardson, S., Lawrence, K., Schoenthaler, A. M., & Mann, D. (2022). A framework for digital health equity. npj *Digital Medicine, 5*(1), 1-6.

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Case Example of DTx Implementation: State of Oklahoma
The Oklahoma Department of Mental Health and Substance Abuse Services uses digital health interventions that include an electronic referral management and client engagement tool to improve continuity of care. They also use a DTx called *Connections App*, an evidence-based smartphone app to support the treatment and recovery of Oklahomans with substance use disorders. Providers are encouraged to use the provider functionality to track client recovery progress, encourage and follow the client's completion of digital CBT lessons, stay engaged with their clients through group discussions or individual messaging, and more. From September 30, 2021 to September 29, 2022, a total of 1,654 Oklahoman service recipients were actively engaged within the *Connections App*.

DTx and the White House Strategy to Address the National Mental Health Crisis
In September 2022, the Department of Health and Human Services (HHS) released the HHS Roadmap for Behavioral Health Integration to advance the President's strategy to address the growing mental health crisis in the United States. Strategy 2 ("Connect Americans to care: Bridge the gap between services the system offers and people's ability to get the care they need") is particularly relevant to expanded use of DTx for behavioral health care and ensuring that individuals receive non-stigmatizing, evidence-based care in the settings where they live, learn, work, and play.

Research, Regulatory, and Reimbursement Considerations for DTx

With increased use of mobile technologies in health care and the relative novelty of DTx in behavioral health, DTx products require further empirical investigation to identify best practices and understand long-term impact. Areas for future research include the impact of DTx in the prevention of mental health conditions and substance use disorders, the safety and effectiveness of various DTx products, and reimbursement strategies to increase access to DTx.

Research and Development

The DTx industry stands to grow exponentially in the coming years with many behavioral health-focused DTx products in the pipeline.[13] Within the National Institutes of Health, the National Institute on Drug Abuse (NIDA) funds a Center for Technology and Behavioral Health (CTBH), with a goal of using science to inform the development, evaluation, and implementation of novel digital health tools for substance use disorders and mental health and other health conditions. This center provides grants to develop DTx that address mental health conditions and substance use disorders. Among these activities, CTBH faculty developed one of most empirically-supported DTx for substance use disorders, which became the first FDA-authorized PDT in the United States, allowing software to be prescribed by clinicians. This DTx has been shown to roughly double abstinence rates when offered as part of substance use disorder treatment, greatly increase substance use disorder treatment retention, and reduce costly emergency department visits and inpatient hospitalizations.[14,15,16,17]

Other examples of CTBH's work include research on DTx to treat anxiety and depression among persons receiving treatment for opioid use disorder (demonstrating a significant reduction in anxiety, depression, and opioid use); a tailored intervention for cannabis use and co-occurring internalizing disorders among sexual and gender minority young adults;[18] and a digital therapeutic for substance use disorders among American Indians/Alaska Natives which increased percent of days abstinent and social connectedness.[19,20]

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CTBH was also the first group to launch a line of digital phenotyping research with individuals in medication treatment for opioid use disorder to evaluate how data captured in everyday life from smartphones/smartwatches can increase our understanding of drug lapse events, medication non-adherence, and treatment dropout. Results indicate that passively collected data from smartphones and wearable sensors can be used to predict future non-prescribed opioid use and other clinically important events with high precision and precise timing.[21,22] These data may inform just-in-time delivery of DTx. Overall, CTBH has had a substantive scientific contribution, impact on the national and international dialogue on the role of clinically-validated digital therapeutics in the treatment of substance use disorders, and impact on the lives of people with substance use disorders. The center has produced over 1000 publications and 87 percent of CTBH publications have been cited in other publications. The center has also supported 100 research grants.

The National Institute of Mental Health (NIMH) is also funding outcomes research to ensure the safety and efficacy of digital health interventions for mental health.[23] Just one example of NIMH-funded research demonstrated that online self-help delivered during the COVID-19 pandemic targeting resilience and coping was effective for long-term alleviation of stress and short-term alleviation of depression symptoms in college students.[24]

The Digital Healthcare Research Program at the Agency for Healthcare Research and Quality (AHRQ) supports research to ensure digital healthcare systems are designed and implemented in ways that improve quality and safety without causing excessive burden for physicians and care teams. The program funds research on the effectiveness of digital healthcare interventions and implementation strategies for their key partners: clients, clinicians, and health systems working to improve healthcare quality and safety.[25]

The Department of Veterans Affairs (VA) also is conducting research and development activities related to DTx. Through VA Mobile Apps, VA has developed several self-help, education, and treatment companion apps to support veterans who have experienced trauma. The apps cover topics such as post-traumatic stress disorder (PTSD), anger, insomnia, alcohol misuse, and smoking, in addition to other healthcare issues. These apps are typically considered digital health interventions rather than DTx, as they align with wellness and self-help tools for prevention.[26,27]

Review and Regulations

While there are over 10,000 apps related to mental health available to the public today, a much smaller number have undergone regulatory review for safety and effectiveness.[28,29] Given FDA's responsibility to conduct safety and effectiveness reviews of medical devices (including software devices), the agency plays an important role in regulating those for DTx. FDA's existing oversight approach considers functionality of the software rather than the platform itself. Consistent with this, the agency plans to only apply its regulatory oversight to software functions that are medical devices and could pose a risk to patient safety if the device were to not function as intended.[3]

FDA Cleared Prescription Digital Therapeutics (PDTs)*

Six examples of DTx that have received FDA clearance for behavioral health treatment

Name	Used to Treat
EndeavorRx	Attention-deficit/hyperactivity disorder
Freespira	PTSD, panic disorder, panic attacks
NightWare	PTSD
reSET	Substance use disorders
reSET-O	Opioid use disorder
Somryst	Chronic insomnia

*Although all six have received FDA clearance, some have been more extensively researched, and long-term outcomes are still being examined.

FDA follows the same clearance and approval processes for DTx as it does for other medical devices.[3,30,31] A Class I medical device presents minimal risk to users, and most Class I medical devices are exempt from premarket review requirements.[3,32] Most medical devices are categorized as Class II, which have a moderate-to-high risk for users and may require a prescription.[3,32] Devices in Class II generally require FDA clearance, rather than full approval, to be marketed and sold in the United States.

DTx used for behavioral health are most commonly Class II. An increasing number of companies seek FDA clearance as part of their business strategy to demonstrate that their product has been reviewed for safety and effectiveness.[33] However, products vary in how extensively they have been researched, and because the field is relatively new, long-term outcomes are still being examined. In addition, certain low-risk DTx are not the focus of FDA oversight and would not require marketing authorization. Several factors related to the software's intended use, including its design, should be considered to determine applicable regulatory requirements. FDA has created a Digital Health Policy Navigator tool to help determine if a product's software functions require FDA oversight.[34]

Reimbursement

Cost is an important consideration in the adoption of a new intervention. Currently, many public and private payers do not cover DTx costs, yet DTx for behavioral health have three primary cost benefits:[13]

1. **Enhanced efficiencies in quality care:** DTx are used as extensions of direct provider care to improve behavioral health outcomes, reducing required face-to-face time between providers and clients while still delivering evidence-based care.[35-37] They can also produce out-of-clinic data to monitor conditions, and in some cases, provide real-time data to health professionals.[6,9] This planning for clinical integration and client engagement is necessary to ensure acceptability, sustainability, and effectiveness of care.[11,38]

2. **Improved retention in care:** Non-DTx health and wellness applications have significant incompletion rates. Behavioral health DTx platforms cleared through FDA have high retention and completion rates, thus reducing the need for ongoing treatment and care.[16,17]

3. **Reduced use of pharmaceuticals:** While DTx use may have associated costs and risks, they have demonstrated reduced pharmaceutical drug use and are not associated with adverse drug interactions or overdoses.[13,39]

Medicare, Medicaid, and Private Insurance Considerations for DTx

There are several reimbursement considerations for DTx. As it relates to DTx, the Centers for Medicare & Medicaid Services (CMS) has issued a new code under the Healthcare Common Procedural Coding System (HCPCS) regarding use of PDTs to facilitate billing for other public and private insurers.[40]

In general, Medicare coverage and payment is contingent on a determination that an item or service: 1) fits within a statutory benefit category, 2) is not specifically excluded from coverage, and 3) is "reasonable and necessary" for diagnosis or treatment.[41] DTx are generally ineligible for Medicare reimbursement under the Durable Medical Equipment Category, so the American Medical Association Relative Value Scale Update Committee recommended that CMS assign a contractor-priced status (a reimbursement rate negotiated with the contractor/payer) for a new HCPCS code describing DTx-related care under the Medicare Physician Fee Schedule. This is due to the vast variability in costs.[42,43]

As of January 2023, only the Massachusetts Medicaid Agency, MassHealth, and Florida's Agency for Healthcare Administration provide coverage under Medicaid for PDTs.[44,45]

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There are an increasing number of private insurers providing coverage for PDTs.[46] Reimbursement pathways for payers to consider include:
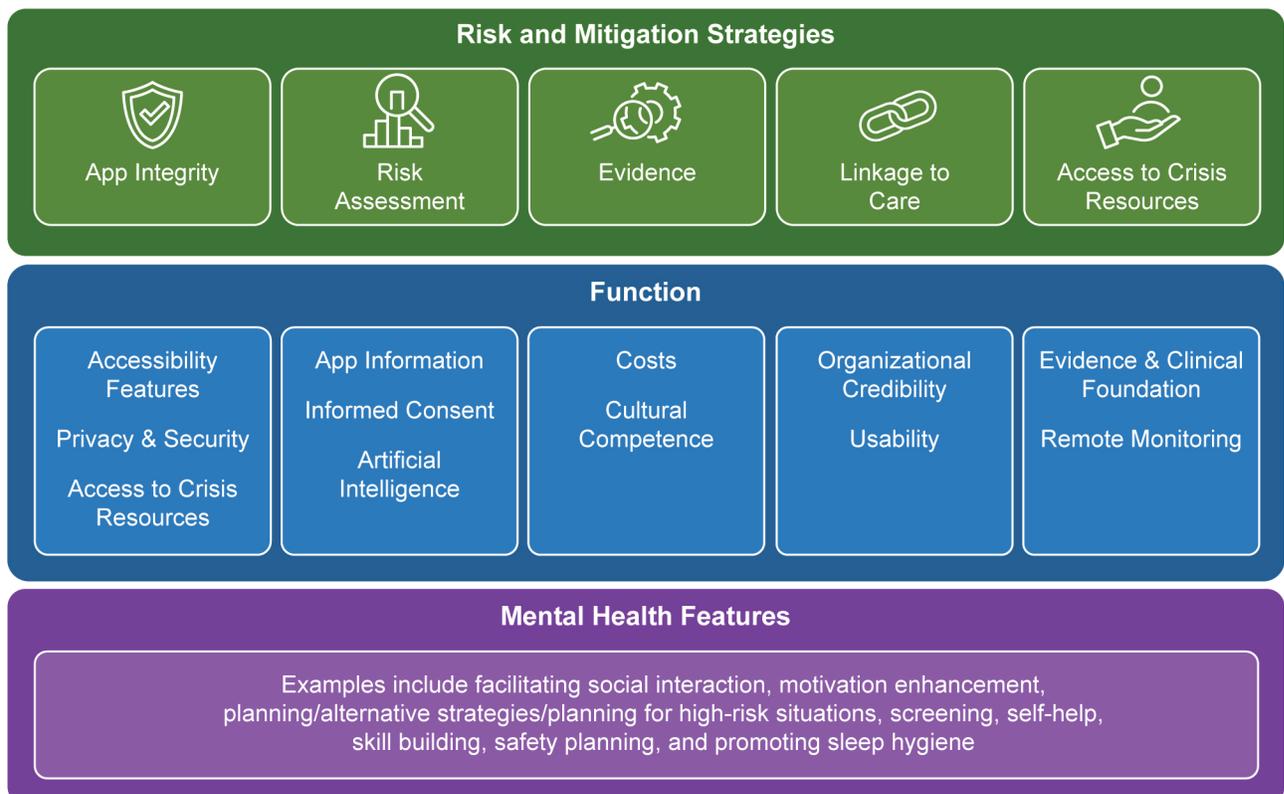
- Value-based payment models
- Flat fee reimbursement
- Subscription fees
- Bundled payments
- Direct contracts among the plan, employers, and prescribers[47]

Alternatively, payers may consider DTx as part of the pharmacy benefit (as most DTx require a prescription) or as a stand-alone benefit.[13]

Considerations for Selecting and Implementing DTx in Care Delivery

There are several important considerations in selecting and implementing DTx in behavioral health settings to ensure successful integration into clinical settings. No established framework for assessing DTx specifically exists; however, a recent report funded by AHRQ established a framework designed for providers and patients/caregivers to assess mental health apps.[48] The *Framework to Assist Stakeholders in Technology Evaluation for Recovery (FASTER)* is designed to assess apps but may have applicability for assessing other types of DTx in behavioral health.

Framework to Assist Stakeholders in Technology Evaluation for Recovery (FASTER)

Risk and Mitigation Strategies

| App Integrity | Risk Assessment | Evidence | Linkage to Care | Access to Crisis Resources |

Function

| Accessibility Features / Privacy & Security / Access to Crisis Resources | App Information / Informed Consent / Artificial Intelligence | Costs / Cultural Competence | Organizational Credibility / Usability | Evidence & Clinical Foundation / Remote Monitoring |

Mental Health Features

Examples include facilitating social interaction, motivation enhancement, planning/alternative strategies/planning for high-risk situations, screening, self-help, skill building, safety planning, and promoting sleep hygiene

Source:
Agarwal, S., Jalan, M., Wilcox, H. C., Sharma, R., Hill, R., Pantalone, E., Thrul, J., Rainey, J. C. & Robinson, K. A. (2022). Evaluation of mental health mobile applications. Technical brief 41. AHRQ Publication, No. 22-EHCO16. https://doi.org/10.23970/AHRQEPCTB41

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FASTER includes 12 multiple choice questions to assess an app's integrity, risk profile, and mitigation strategies that ultimately inform the app's risk level, defined as:

- Risk Level 1: Minimal Risk
- Risk Level 2: Some Risk
- Risk Level 3: Considerable Risk

These questions and associated mitigation strategies are related to:

- **App integrity:** Assesses whether the app can be trusted, based on recent app updates, privacy and security agreements for the user, warnings and disclaimers, and endorsements from government agencies or trusted associations.
- **Risk assessment:** Assesses risks the app poses, based on age of the target audience, ability for the target audience to use the app safely, and whether the app is meant for provider-led care or standalone treatment.
- **Evidence:** Determines whether the app has a solid clinical evidence foundation by looking for scientifically validated evidence of efficacy and whether the app uses an evidence-based strategy (e.g., CBT, Motivational Interviewing, Medication for Opioid Use Disorder).
- **Linkage to care:** Evaluates whether the app facilitates remote monitoring and reporting to healthcare providers who can observe their patients.
- **Access to crisis care:** Evaluates whether the app provides information about emergency resources and consent by legal guardians (for minors) so patients can access emergency/crisis services.[48]

Function
FASTER includes a combination of 48 multiple choice and free text questions to assess the app's functionality. Many of these questions are related to the following:

- **Privacy and security:** Assesses compliance with regulations on protection of health information for adults and minors, data sharing or selling practices, and secure integration with electronic health records, including the Health Insurance Portability and Accountability Act (HIPAA), Children's Online Privacy Protection Act (COPPA), and SAMHSA's 42 CFR Part 2.
- **Accessibility features:** Evaluates ability to use phone accessibility features within the app, and additional accessibility features the app provides.
- **Usability:** Assesses factors such as the availability to use the app offline, app speed and accuracy, available languages, ability to customize, design for target audience, visual appeal, and ability to use intuitively.
- **Remote monitoring:** Evaluates the app's mechanisms for providers to access data, provision of alerts to providers in case of a clinical event, and sharing of data with smartwatches or other technologies.
- **Costs:** Evaluates the business model for the app (e.g., free, freemium [apps that offer in-app purchasing]), estimated annual costs to users, and availability of an HCPCS code for insurance reimbursement.[48]

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Mental Health-Related Features

In the third category, FASTER includes five customizable questions to assess how various aspects of mental health apps enhance or align with therapeutic and wellness goals:

- **Screening:** Efficacy of screening tools within the app (e.g., are they evidence based?).
- **Self-help:** Self-monitoring features (e.g., mood-tracking), psychoeducation, journaling, and sleep hygiene.
- **Planning:** Skill building and safety planning.
- **Social and peer group interaction:** Ability to interact with social and peer groups, as well as family/caregiver support.[48]

FASTER highlights mental health care; however, its assessment questions could also pertain to behavioral health apps that address substance use disorders.

Clinical Integration

While not specifically outlined in FASTER, integrating digital health interventions into clinical care is central to achieving the optimal outcomes these interventions offer.[11,29] Although research is still emerging on incorporating DTx into clinical care, considerations for clinical integration of digital health interventions are applicable to DTx. These include:

- **Provider readiness and training:** Training mechanisms to ensure providers and care staff are informed, engaged, and supported in the adoption and implementation of digital health interventions.[11,29]
- **Multi-system interaction and clinical workflow:** Ease of integration and exchange of data in interoperable formats from DTx to electronic health records, and education for all staff on how digital health interventions will be incorporated into client care.[29]
- **Integration into existing treatment plans:** Communication with clients and providers to determine whether use of digital health interventions is appropriate.[9]
- **Digital liaison:** Integration of a digital liaison or designated staff person to oversee all aspects of digital health interventions to improve client engagement and relieve provider burden.[49,50]

The considerations above highlight ways in which DTx may enhance, but not replace, provider-led clinical services.

Increasing Equity in Digital Therapeutics

Though use of DTx may improve behavioral health outcomes, there are risks related to access, acceptability, and cost that providers and developers must consider to ensure DTx are improving health equity rather than creating more pronounced disparities.[10,51,52]

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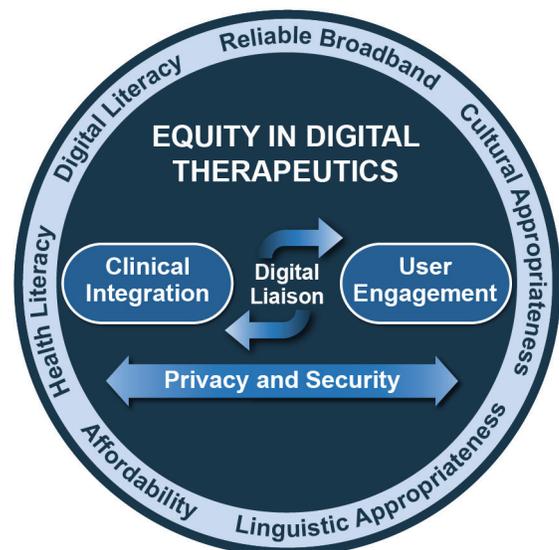
As discussed in the SAMHSA guide *Adapting Evidence-Based Practices for Under-Resourced Populations*, considerations specific to equity in DTx include:

- **Access to technology, broadband, and sufficient data plans:** A primary barrier to using DTx is ensuring access to required technologies and reliable broadband connectivity. Limited access to broadband often impacts individuals in rural areas. Individuals located in urban and suburban areas can experience similar barriers. Some DTx do not require sustained internet access to operate, but it is important to ensure users have multiple mechanisms to access DTx based on their unique needs.[5,10]

- **Digital and health literacy:** Individuals' understanding of common health terminologies and ability to use digital technologies vary greatly and cannot be anticipated simply from a person's age, cultural background, or geographic location. Therefore, it is important that DTx are easily navigable and designed using plain language to overcome possible digital avoidance by those less familiar with these platforms. This is often accomplished through engagement with end-users in the development process.[5,10,52]

- **Cultural and linguistic appropriateness:** When referring a client to DTx, providers should ensure platforms are culturally and linguistically appropriate.[5,10,48] The platforms should include culturally representative examples and vignettes and be available in the individual's native language. Providers should also confirm whether the products have been validated with the user population.[48]

- **Affordability:** To ensure equitable access to DTx, the cost of participation cannot be prohibitive, particularly for those who are uninsured or underinsured or lack access and financial support to smartphones, computers, broadband, and data plans.[4,5,10]

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Resources

The following resources provide additional information on DTx, FDA guidance, and DTx resources developed across federal agencies and other organizations specializing in DTx.

Resource	Lead Agency	Description
AHRQ Center for Digital Healthcare Research	AHRQ	This webpage offers information on AHRQ's Digital Healthcare Research Program, including mission; funded research; research findings; toolkits; and other publications, resources, news, and blogs.
Digital Therapeutics Alliance DTx Value Assessment and Integration	DTx Alliance	The guide provides healthcare providers and DTx developers with a framework to assess digital therapeutics products and their impact in real-world settings.
FDA Digital Health Center of Excellence	FDA	The Center offers a variety of services related to digital health, a network of digital health experts, information on digital health terminology, various medical devices, and more.
FDA Digital Health Policy Navigator	FDA	This tool helps to determine whether a product's software functions require FDA oversight. The page describes what a software function is and relevant laws, guidance, and policies that should be considered.
FDA How to Study and Market Your Device	FDA	This webpage describes a four-step process to market a device: 1) classifying the device and understanding applicable regulatory controls; 2) selecting and preparing the correct premarket submission; 3) preparing and sending the appropriate information for the premarket submission; and 4) complying with applicable regulatory controls, including establishment registration and device listing.
FDA Software as a Medical Device (SaMD): Clinical Evaluation—Guidance for Industry and Food and Drug Administration Staff	FDA	A December 2017 guidance document for FDA staff, developed by the International Medical Device Regulators Forum (IMDRF), that describes the process for clinical evaluation of a software as a medical device (SaMD).
Resources for Mobile Health Apps Developers	HHS Office for Civil Rights	These resources offer guidance to mobile health (mHealth) developers and others interested in the intersection of health information technology and HIPAA privacy and security protections. The resources include interactive tools, health app use scenarios, guidance on the right to access protected health information, on-cloud computing, and HIPAA.

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