REAGAN-UDALL FOUNDATION for the Food and Drug Administration

Advancing Digital Mental Health Innovation:

COMMUNITY PERSPECTIVES SUMMARY REPORT

REAGAN-UDALL

FOUNDATION

for the Food and Drug Administration

ABOUT THE REAGAN-UDALL FOUNDATION FOR THE FDA

The Reagan-Udall Foundation for the FDA (Foundation) is an independent 501(c)(3) created by Congress to advance regulatory science to help the U.S. Food and Drug Administration accomplish its mission. The Foundation manages a suite of programs that assist the FDA to engage with external stakeholders and that facilitate evidence generation, improve public understanding of the FDA, deliver more accessible health information to the public.

FUNDERS:

The Commonwealth Fund

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APPENDICIES

List of Abbreviations

AHIP	America's Health Insurance Plans
AHRQ	Agency for Health Research and Quality
AI	Artificial Intelligence
AMA	American Medical Association
APA	American Psychiatric Association
ARPA-H	Advanced Research Projects Agency for Health
ASTP/ONC	Assistant Secretary for Technology Policy and Office of the National Coordinator for Health Information Technology
CDC	Centers for Disease Control and Prevention
CFPB	Consumer Financial Protection Bureau
CMS	Center for Medicare and Medicaid Services
CMMI	Center for Medicare and Medicaid Innovation
DHCoE	Digital Health Center of Excellence
DIME	Digital Medicine Society
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EKG	Electrocardiogram
FDA	U.S. Food and Drug Administration
FSA/HSA	Flexible Spending Account / Health Spending Account
HRSA	Health Resources and Services Administration
IRS	Internal Revenue Service
ML	Machine Learning
NIDA	National Institute on Drug Abuse
NIH	National Institute of Health
NIMH	National Institutes of Mental Health
OHT-5	Office of Neurological and Physical Medicine Devices
ONC	Office of the National Coordinator for Health IT
OPEQ	Office of Product Evaluation and Quality
RCT	Randomized Controlled Trial
RWD/RWE	Real-World Data/Real-World Evidence
SAMHSA	Substance Abuse and Mental Health Services Administration
SUD	Substance Use Disorder
TAP	Total Product Life Cycle Advisory Program
VC	Venture Capital

Executive Summary

The Reagan-Udall Foundation for the FDA organized a workshop titled "Advancing Digital Mental Health Innovation.[a]" Participants identified strategies to stimulate investment and foster innovative development in digital mental health tools, while also addressing regulatory science and process challenges that hinder digital health innovation.

With more than one in five Americans experiencing mental illness[1,2] and a ratio of just one provider to every 350 Americans[3], the demand for effective treatment is far outpacing supply. The advent of digital technologies for mental and behavioral health holds promise for improving access and affordability of diagnosis, treatment, and monitoring of mental health disorders. While FDA has provided guidelines and resources for conducting studies and effectively marketing digital health devices within the evolving regulatory landscape, many developers of mental and behavioral health report confusion and challenges.

On May 21, 2024, the Foundation convened an invitation-only, half-day workgroup meeting attended by representatives of industry, mental health professionals, and patients, in which participants articulated challenges facing mental health interventions and discussed potential solutions. The viewpoints reflected in the discussions and in the resulting report are those of the attendees.

a This activity is a Foundation project supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of an award of $75,000 of federal funds (60% of the project) and by $50,000 from non-governmental sources (40% of the project). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA, HHS, or the U.S. Government. For more information, please visit FDA.gov.

Key challenges identified included the following:

- Healthcare professionals, patients, and users lack information to make informed care decisions
- Mental and behavioral health industry includes new entrants to federal regulatory oversight
- Conflation between review for FDA marketing authorization and payor reimbursement
- Rapidly evolving landscape requires regulatory flexibility
- Distinct efforts spanning multiple federal agencies leads to perceived inefficiencies

Potential solutions discussed included the following:

- FDA and NIH should continue leading collaborative efforts to expand clinical measures and best practices in clinical trial design for digital mental health tools
- FDA should strengthen its proactive approach to educating digital health product developers
- Non-government organizations could play a bigger role in supporting mental and behavioral health stakeholders
- FDA should consider enabling greater flexibility in mental and behavioral health submissions
- Government agencies should enhance collaboration through continued interagency task force efforts for digital mental health tools

Regulating digital health products is inherently challenging, and the unique aspects of mental health disorders add an additional layer of complexity. There are opportunities for improvement through better communication, collaboration, and an adaptive regulatory approach. Addressing these challenges can lead to more efficient pathways for the development and implementation of digital mental health tools, ultimately benefiting all stakeholders and improving mental health outcomes for patients.

Introduction

The Reagan-Udall Foundation for the FDA and The Commonwealth Fund, with input from the U.S. Food and Drug Administration (FDA), organized the "Advancing Digital Mental Health Innovation" workshop in which stakeholders identified strategies to spur investment and foster innovative development in digital mental health tools for assessment, diagnosis, and intervention, with a focus on clinically meaningful endpoints. The project aspired to identify and help solve both regulatory science and process challenges to digital innovation, with a particular focus on the FDA's role

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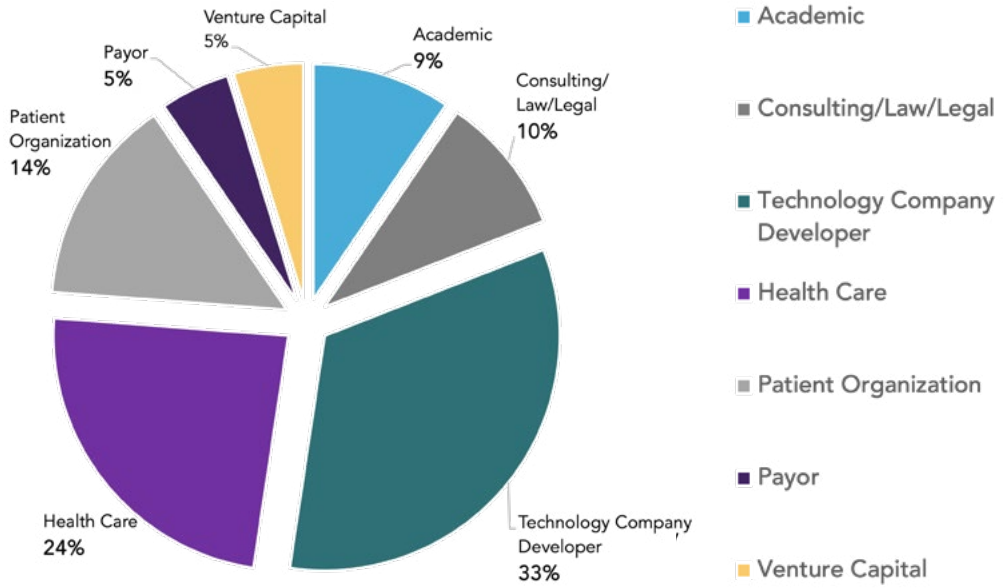
To achieve these objectives, the Foundation sought input from a diverse group of experts and stakeholders across the digital mental health ecosystem, including leaders in digital therapeutic development, alongside clinicians, patient advocates, payors, researchers, and representatives from mental health non-profits (*See Figure 1*). This report targets a broad spectrum of stakeholders essential to advancing mental health innovations. It is intended for industries investing in developing digital health tools, the payors crafting reimbursement strategies, clinicians seeking effective treatments, policymakers shaping healthcare regulations, researchers gathering evidence to support digital mental health interventions, and patients seeking proven solutions. Additionally, the findings and recommendations are directed towards regulatory bodies such as the FDA and other government agencies responsible for overseeing and supporting innovation in healthcare.

Through collaborative efforts and strategic engagements, this initiative aims to foster an environment conducive to innovation, regulatory advancement, and improved patient outcomes in the mental health domain.

FIGURE ONE

Advancing Digital Mental Health Innovation Discussants by Sector



Methods

On Tuesday, May 21, 2024, the Foundation convened an invitation-only, half-day workgroup meeting in which participants articulated current challenges facing mental health interventions, particularly focusing on digital solutions. (Observers included representatives from the FDA, the Commonwealth Fund, and Commonwealth Fund collaborators.) Prior to the meeting, the Foundation asked attendees to provide written suggestions for potential solutions to help ensure discussions were focused on identifying solutions.

This document captures the discussion of the May meeting, submitted solutions, and related conversations. Note that this project was not intended to reach consensus on topics but rather to capture, and share, the input of a range of stakeholders.

Background

Demand for Digital Mental Health Solutions

It is estimated that more than one in five Americans, including adults[1] and children ages 3-17[2], are currently experiencing mental illness. Recent survey data indicates that more than 25% of U.S. adults report having taken medication and/or received counseling or therapy, while an additional 11% report not receiving necessary counseling or therapy in the most recent four-week period.[3] Access to care and treatment varies significantly due to factors such as geography, payor coverage, health literacy, and income, all of which influence a person's ability to obtain appropriate care for a mental health disorder. For example, providers of traditional treatment options, such as cognitive behavioral therapy, may not be accessible to individuals in rural areas or to patients with limited insurance coverage. Additionally, the ongoing shortage of mental health professionals affects access to care, with a ratio of just one provider to every 350 Americans as of 2022[4].

The advent of digital technology holds promise for improving access and affordability of diagnosis, treatment, and monitoring of mental health disorders. The field of digital mental health is experiencing rapid growth, fueled by a nearly tenfold increase in venture capital funding in the broader digital health space over the past decade and consistently topping the list of top-funded clinical indications since 2020. Despite this explosion in development, substantial barriers to availability and adoption of digital mental health tools remain[7] and robust clinical evidence is limited.

Digital Health Technologies for Mental and behavioral health

Developers of digital health technologies for mental and behavioral health (mental and behavioral health) face unique challenges and often lack prior experience navigating FDA regulatory pathways—navigating FDA requirements simply was not required for other digital products they may have developed. In addition, for some start up developers, the expense of an unplanned clinical trial, especially if developing for a specialized, higher need

population, may exceed the resources available to companies, resulting in abandoning product development. All companies entering the healthcare space should generate valid scientific evidence on their product or intervention in order to have confidence in its safety and efficacy; regulatory review and payor coverage typically require robust levels of clinical evidence based on specific intended uses and device types.. This evidence could also serve as a competitive advantage for this subset of products, especially in driving clinical adoption. But not all digital mental health products are routinely regulated by FDA and thus face different levels of scrutiny.

For mass market digital mental health products that fall outside the FDA-regulated subset of digital mental health tools, evidence of effectiveness may not typically serve as a competitive differentiator in the marketplace. Most consumers do not demand upfront evidence of the product's efficacy before using it, unlike health care professionals who may seek out such evidence. As a result, very few mental and behavioral health are marketed based on clinical evidence[8]. Of the roughly 20,000 mental health apps available on major platforms, only a handful have been reviewed by FDA[9]. And for those consumers who look at evidence—and health care professionals seeking it—locating evidence that might differentiate products in a crowded marketplace is challenging.

Unlike other modern digital health technologies, like wearable electrocardiograms (EKGs) and continuous glucose monitors that were preceded by conventional medical device models and later adapted for consumer technology platforms, many mental and behavioral health are initially designed as consumer-facing applications. The developers of these technologies may come from information technology fields, such as computer engineering and app development, rather than clinical research or biomedical engineering. This tech-focused culture, which prioritizes rapid experimentation and frequent iteration, contrasts sharply with traditional regulatory and clinical development approaches. While medical device culture also involves iteration, the tech-centric culture accelerates experimentation even further. As a result, concepts well known to clinical researchers, such as good clinical practice and informed consent, may be unfamiliar to these organizations.

The digital mental health space includes a wide array of tools spanning the entire continuum of care—from diagnosis to treatment and monitoring. (*See Figure 2*) These tools include applications such as screening surveys, gaming approaches, medication reminders, mood trackers, and digital journals. The sheer volume and wide variety of these tools makes it challenging for clinicians to identify and select the appropriate tool for the right purpose at the right time.

Additionally, the scope of professionals engaged in supporting individuals' mental health extends beyond clinicians to include non-clinical social workers, clergy, community health workers, peer supporters, and other—all of whom tend to be under-resourced. These care professionals and community caregivers often lack the experience, training, and resources necessary to make mental and behavioral health product recommendations based upon regulatory and/or reimbursement status.

FIGURE TWO

Potential Uses for Digital Health Technologies for Mental and Behavioral Health

Note: These examples are illustrative and not intended to be comprehensive

Finally, the large number of individuals affected by mental health disorders combined with varying access to care raises important questions about the risk-benefit analysis of mental and behavioral health. Specifically, in the context of lower risk mental and behavioral health interventions, it is worth considering whether any care is preferable to no care and how perceptions of risk and benefit may shift depending on access to traditional care. This consideration plays a crucial role in evaluating the safety and effectiveness of mental and behavioral health in improving mental health outcomes, and the technology's ability to demonstrate cost-effectiveness, meaningful clinical improvement, and potential to reach underserved populations.

Current Regulatory Approach

Digital health tools utilized in mental and behavioral health care include a wide range of technologies, some of which are the focus of FDA's regulatory oversight and others that are not. The FDA approach to the regulation of medical devices, including medical device software, is risk-based and least burdensome. It focuses on intended use and the function of software rather than the platform it operates on, and evaluates the benefits and risks of products through a review of valid, scientific evidence.

The FDA has regulatory authority over medical hardware and software functions that meet the definition of a device in the federal Food, Drug, & Cosmetic Act[10] , including those software functions that are intended for the diagnosis and treatment of mental health disorders. Some software functions are not devices and therefore not subject to FDA authority (for example, video conferencing software functions intended to help patients communicate with health care professionals via telehealth).

Other software functions may meet the definition of a medical device, but because they pose a lower risk to the public, FDA has said that it intends to exercise enforcement discretion over these devices (see guidance listed below for further explanation and examples). FDA focuses its regulatory oversight of mental health-related digital health technologies on a subset that includes software functions that are medical devices and whose functionality could pose a risk to a patient's safety if the device were to not function as intended (for example, software intended to provide computer-based behavioral therapy). FDA guidance and other resources provide more information about its oversight approach, including questions a developer can consider about their products that would inform their development and marketing, and many examples of each of the types of digital health technologies mentioned above.

The FDA's Office of Neurological and Physical Medicine Devices, Office of Product Evaluation and Quality (OHT-5), Office of Product Evaluation and Quality (OPEQ), and the Digital Health Center of Excellence (DHCoE), within the Center for Devices and Radiological Health develop and implement policies for the FDA's regulatory approach to mental health-related digital health technologies, including FDA review of digital health devices and its coordination of related activities. OHT-5 is the primary review division formental and behavioral health.

For devices requiring oversight and for companies who aim to determine whether their devices require FDA oversight, the FDA created programs and resources to help developers navigate the complexities of digital mental health device review. These resources include guidelines, guidance documents, and programs and resources to assist product developers seeking to bring a regulated device to market, including:

- FDA Digital Health (DH) Policy Navigator[b]
- How to Study and Market Your Device[c]
- Medical Device Development Tools [d]
- FDA Guidances with Digital Health Content [e]
- Medical Applications and General Wellness: Policy for Low Risk Devices[f]
- Total Product Life Cycle Advisory Program (TAP)[g]
- Medical Device Coverage Initiative[h]
- Activities to Support Medical Device Innovators [i]
- FDA Digital Health Center of Excellence [j]
  - Among other roles, the Digital Health Center of Excellence manages a general email inbox to answer inquiries from investigators and developers seeking non-binding feedback related to digital health content. Response time is typically within two weeks[k]..

Although this information is public, available programs may not be fully known to, or understood by, product developers. As raised by participants in the May discussion, even with the availability of this information, the regulatory process itself appears lengthy, uncertain, and resource-intensive to developers to developers.

Key Challenges

This section explores five distinct challenges identified by meeting participants as impacting mental and behavioral health innovation and adoption. In addition to these distinct challenges, a common theme of difficulty defining clinical measures and agreed-upon endpoints for mental health research appears repeatedly across various challenges. This is a concern that affects not only digital solutions but extends more generally to clinical research in this field.

b https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-policy-navigator
c https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/how-study-and-market-your-device
d https://www.fda.gov/medical-devices/medical-device-development-tools-mddt
e https://www.fda.gov/medical-devices/digital-health-center-excellence/guidances-digital-health-content
f https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-wellness-policy-low-risk-devices
g https://www.fda.gov/medical-devices/how-study-and-market-your-device/total-product-life-cycle-advisory-program-tap
h https://www.fda.gov/about-fda/cdrh-innovation/medical-device-coverage-initiatives-connecting-payors-payor-communication-task-force
i https://www.fda.gov/about-fda/cdrh-innovation/activities-support-medical-device-innovatorsi Digital Health Center of Excellence | FDA
j https://www.fda.gov/medical-devices/digital-health-center-excellence
k https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-frequently-asked-questions-faqs

Healthcare professionals, patients, and users lack information to make informed care decisions

Healthcare professionals, patients, and users often struggle to evaluate mental and behavioral health to make informed decisions about how to use them in clinical practice and the relevance of FDA review or clearance of a particular mental and behavioral health in this context remains unclear. According to a report from the Meadows Mental Health Policy Institute, "Confusion about when [mental and behavioral health] warrant regulation is one reason these tools are underutilized in clinical care." Meeting participants echoed the Meadows report observation: healthcare professionals are uncertain about the necessity and implications of FDA review—if or when a product needs to be cleared, what it means if a product is not cleared, or how to verify whether a product has received clearance. This uncertainty hampers their ability to confidently recommend or prescribe digital health products to their patients. In turn, the lack of demand for, or understanding of, clinical evidence reduces the incentive for mental and behavioral health developers to generate such evidence, which serves to reinforce the status quo of limited information.

Healthcare professionals also face challenges in evaluating the appropriateness of a solution for a specific patient. If a product is cleared by the FDA, clinicians may access information regarding the indications in the "Indications for Use" section of the labeling. Although locating that information may be challenging, it is, at least, explicitly documented. For products that do not require clearance, however, accessing such information is far less clear—and identifying those products that are supported by clinical evidence (and locating that evidence) becomes a challenging and time consuming process. Additionally, a healthcare professional's ability to determine the most suitable product for a specific patient hinges on their capacity to assess its effectiveness. This requires broader understanding of both the relevant clinical endpoints and agreed upon definitions of clinically meaningful change, which remain a challenge more broadly in mental health treatment.

It can also be difficult for healthcare professionals to determine whether a product is a covered service under a patient's health insurance plan. This uncertainty makes it difficult to recommend digital mental health products with confidence that they will be accessible to a given patient. At the same time, patients and other users of mental and behavioral health also face considerable challenges. This population exists along a wide continuum, ranging from those who inherently trust the recommendations of app stores to highly skeptical healthcare consumers. While the average American may be familiar with the FDA as a stamp of approval on traditional medical devices and therapeutics, they may not grasp the nuances of regulatory

requirements in the digital health domain. Consumers of mental and behavioral health do not have access to clear and reliable sources of information about the safety and efficacy of these products. This affects their ability to make informed decisions about their use of mental and behavioral health that might impact their health.

These challenges for both healthcare professionals and consumers are exacerbated by the sheer number of mental and behavioral health options available on the market, making it nearly infeasible to evaluate and select the most appropriate tools quickly and efficiently in a clinical setting. This lack of centralized information organized in a clear, accessible format for informed decision-making poses significant barriers to effective care.

Mental and behavioral health industry includes new entrants to federal regulatory oversight

Although there is a clearly defined digital health review pathway within FDA, developers in the digital mental health sector report finding it difficult to determine whether regulatory oversight is required for a specific product or feature, as well as when and how to engage with the FDA (See Figures 3 and 4). For example, some developers expressed uncertainty about the necessity of conducting clinical trials and may not allocate funding for such research in their development plans. This uncertainty is particularly common among developers without prior experience with regulated products. Clinical trials—particularly those associated with regulatory pathways—are complex, costly endeavors, often exceeding the expertise or resources of many developers. This ambiguity contributes to confusion and reluctance among developers, potentially stifling innovation.

Conversely, regulatory agencies may not fully understand the areas of uncertainty that developers face, as they are accustomed to working with larger, well-resourced industry players that have significant clinical experience and know how to engage stakeholders to gain the needed information and clarity. This traditional dynamic does not align well with the needs of smaller mental and behavioral health developers that often lack the resources and experience to navigate the regulatory landscape independently.

This disconnect leads to confusion and frustration for both regulators and industry, hindering the effective introduction of innovative digital mental health products to market.

Conflation between review for FDA marketing authorization and payor reimbursement

Although the regulatory review and payor reimbursement[I] processes are distinct, confusion remains regarding this relationship. Close correlation of these statuses for traditional therapeutics, such as medication, has led some to incorrectly believe that a direct relationship exists between FDA clearance/approval and health insurance reimbursement. In the United States, marketing authorization and payor reimbursement of a marketed drug or device are not mutually inclusive. Misconceptions and misunderstandings about reimbursement can result in unrealistic or unsustainable business models that result in preventable market failures.

A common misconception among developers, healthcare professionals, and patients is that FDA clearance or approval of an intervention automatically translates to reimbursement by the Centers for Medicare & Medicaid Services (CMS) in the Medicare and Medicaid health insurance programs, which often influences reimbursement across the broader payor ecosystem. Likewise, it is incorrect to assume that all products reimbursed by insurance have received FDA clearance. Further, the existence of coverage determination or development of reimbursement codes does not necessarily correspond with payor reimbursement. This leads to unrealistic expectations and significant misunderstandings about health insurance payor reimbursement. A recently proposed CMS CY2025 rule, released after this workshop, would provide Medicare coverage for FDA cleared mental and behavioral healths, but it is a novel payment method yet to be utilized and tested by developers.

Although payor determinations may explicitly link the two processes, the criteria and authority for regulatory approval and reimbursement remain distinct. As a result, certain products may be covered by insurance without undergoing the FDA approval process and vice versa. This is particularly true with mental and behavioral health, where only a subset require regulatory review and a relatively wide range of tools are covered by payor plans. This challenge extends beyond CMS, as evidentiary standards and processes for individual payors may differ.

Developers often feel frustrated by the need to develop different sets of evidence for regulatory and reimbursement purposes. Many developers assume that obtaining FDA clearance will automatically secure insurance reimbursement, not realizing that they must also meet the specific evidence requirements set by individual payors. Others may understand the unique data and evidence requirements but struggle to find a single approach that can meet multiple needs. The demand for differing approaches to evidence generation creates an additional burden, complicating the development and commercialization process for digital mental health products.

Rapidly evolving landscape requires regulatory flexibility

The existing regulatory framework governing medical devices created by federal law was not originally designed to handle the rapidly evolving digital technologies that exist today. The need for the FDA to adjust to a changing technological landscape without authority to implement changes to the review process could introduce significant challenges for the development and regulation of digital mental health tools. The changing landscape, fueled by the exponential growth in computing power, internet connectivity, and mobile device adoption, creates opportunities for rapid advancement in research while simultaneously placing significant demands on FDA resources. Further, meeting participants believed the FDA's regulatory framework defined by federal law limits its ability to respond swiftly to the changing technology landscape.

Development and adoption of new technologies, in particular artificial intelligence (AI), is rapidly accelerating. But data collected in mental health research, which provides the basis for AI models and is the real-world data (RWD) most often used in FDA contexts, tends to be more complicated and heterogeneous compared to other treatment areas. For example, many mental health professionals do not interact with health care payors, so mental health interventions are not always reflected in payor claims databases, a potential data source for AI. Similarly, mental health treatment, particularly in the case of private-pay-only professionals or facilities, is often captured in medical records separately from a patient's other health care records. This complexity underscores the importance of the FDA's ability to adapt to the changing landscape to better define its expectations for regulatory submissions, including the use of AI, RWD, and real-world evidence as both an input for mental and behavioral health solutions and as a basis for mental and behavioral health studies.

Distinct efforts spanning multiple federal agencies leads to perceived inefficiencies

Multiple stakeholders across the federal government work independently and collaboratively to address challenges in this area (e.g., FDA, the National Institute of Mental Health, National Institute on Drug Abuse, Office of the National Coordinator for Health Information Technology, Agency for Healthcare Research and Quality, Substance Abuse and Mental Health Services Administration, Advanced Research Projects for Health). However, their unique mandates necessitate different approaches and evidentiary standards. The meeting attendees believed that this unintentionally results in various inefficiencies impacting developers, healthcare professionals, and patients.

Agencies have not aligned on defining appropriate research and clinical endpoints for mental health disorders—a challenge that extends beyond the scope of studies involving mental and behavioral health. For example, the National Institute of Mental Health (NIMH) and the FDA can have different measurement criteria and approaches, such as in substance use disorder (SUD) treatment. This misalignment leaves researchers and developers uncertain about what constitutes improvement and how to measure it, complicating the development and evaluation of mental health treatments.

Furthermore, as noted earlier, the data required for FDA review (i.e., safety and effectiveness) are not necessarily the same or sufficient for CMS review (i.e., reasonable and necessary), leading to a lack of joint pathways for submission. Developers often find themselves in a position where they must generate different sets of evidence to satisfy the distinct requirements of each agency, as highlighted in a previous section regarding regulatory and reimbursement status confusion. Lack of awareness among developers about payor coverage and evidentiary requirements for payors leads to challenges in adoption of these technologies.

The challenges are exacerbated by the fact that multiple stakeholders across the federal government work independently to address issues within the digital mental health space. Agencies such as the FDA, NIMH, National Institute on Drug Abuse (NIDA), Assistant Secretary for Technology Policy and Office of the National Coordinator for Health Information Technology (ASTP/ONC), the Agency for Healthcare Research and Quality (AHRQ), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Advanced Research Projects Agency for Health (ARPA-H) all play roles. However, their independent efforts can lead to fragmented and uncoordinated approaches—or at least the perception thereof.

This siloed organizational structure, while necessary for the functioning of a large federal government, creates inefficiencies for private industry. This can lead to significant barriers to the development and adoption of digital mental health tools, as well as implementation of comprehensive strategies to address mental health challenges.

Potential Solutions

FDA and NIH should continue leading collaborative efforts to expand clinical measures and best practices in clinical trial design for digital mental health tools

To advance mental health research and improve the development of digital mental health tools, the FDA, NIH, and other key government and clinical research stakeholders, including patients and healthcare professionals, should continue to invest in a collaborative effort to identify the full scope of meaningful clinical measures and patient reported outcomes related to mental health and define best practices for research. This initiative would create a comprehensive framework for defining effectiveness and safety in mental health treatments and would help align payors, healthcare professionals, and patients in understanding, evaluating, and accepting the data.

One critical component of this collaborative effort is to expand and clarify the definitions of clinical endpoints. Traditional classifications, such as those in the DSM-5, focus on diagnostic criteria, but a broader perspective is needed to include relevant symptoms. Developing functional outcomes measures that can be tracked digitally is essential for this expanded scope. For example, in the context of SUD, measures could include craving reduction. In major depression, extent of social interaction, improvement in sleep measures, or engagement in activities, such as exercise, could be readily quantified. In other disorders, outcomes such as the reduction of tardive dyskinesia might be considered.

Expanding and prioritizing the list of acceptable clinical measures and encouraging innovation in measures that meet the existing criteria for clinically meaningful change has potential to improve evaluation of mental health treatments, including digital tools. Broadening this purview would support mental health researchers and clinicians in designing studies and interpreting results that will lead to improvements in mental health care. Additionally, developing standardized approaches to clinical trial design and specifically offering best practices for creating optimal control arm conditions to account for placebo and expectancy bias would be beneficial.

Creating a framework for defining and measuring clinical efficacy and safety in mental health research would enable more precise and reliable evaluations of new treatments and interventions, fostering innovation and improving patient outcomes across the spectrum of mental health care.

FDA should strengthen its proactive approach to educating digital health product developers

As previously mentioned, the FDA has been actively pursuing innovative communication strategies to enhance its engagement with stakeholders in the digital health space. This includes the development of numerous digital health guidance documents that provide critical information and direction for industry stakeholders. Additionally, the FDA has introduced interactive tools like the Digital Health Navigator, which allows developers to easily access relevant resources, and the Digital Health Inbox, which enables direct communication for questions and clarifications regarding regulatory processes. However, despite these advancements, challenges remain. Many developers still find it difficult to navigate the regulatory landscape due to varying interpretations of guidance and the complexity of regulatory requirements. This uncertainty can hinder innovation and delay the introduction of new digital health solutions into the market.

To better support the development of digital mental health products, the FDA could adopt an even more proactive approach to educating digital health product developers. Such an initiative would involve several strategies to enhance communication and provide clearer guidance on regulatory processes while also highlighting the many existing resources available to developers, such as the Total Product Lifecycle Advisory Program (TAP).

FDA should consider new ways to showcase existing tools, resources, and pathways to developers. This may include expanding attendance and presentations at large digital health developer conferences, where the FDA can directly engage with key stakeholders. Additionally, interacting with large venture capital firms and startup incubators would allow the FDA to reach a broader audience and provide valuable insights to companies in the early stages of development.

FDA could adjust its communication strategy by developing new educational materials in formats that resonate with a tech developer audience. Traditional regulatory documents may not be as effective for this group. Instead, the FDA could create infographics (building from current decision trees such as the Digital Health Policy Navigator) and journey maps that simplify and further visualize the regulatory pathways. These assets would make it easier for developers to understand the requirements and navigate the approval process.

Clarifying review requirements by purpose (e.g., diagnosis, monitoring, treatment) with specific examples would also be beneficial. By showcasing real examples and cases in the mental health space, the FDA can highlight the nuances and best practices for different types of digital health products. Additionally, drawing on best practices from other industries, such as radiology, could provide valuable models for developers to follow.

Facilitating direct communication and connections with the developer community is essential for fostering innovation. The FDA could host educational webinars with Q&A sessions and regular "Ask Me Anything" sessions, like those conducted by ARPA-H. These initiatives would provide developers with direct access to regulatory experts and offer opportunities to address specific concerns and challenges early in the development process.

By adopting a proactive approach to outreach and education, the FDA can better support digital health product developers. Through enhanced communication, targeted educational materials, and direct engagement, the FDA can clarify regulatory processes, reduce confusion, and facilitate the development of innovative digital health products that improve patient outcomes—none of which should decrease the regulatory standard and the protections that standard provides.

Non-government organizations could play a bigger role in supporting mental and behavioral health stakeholders

Existing organizations can play a crucial role in supporting the needs of developers, healthcare professionals, users, and regulators in the digital health space. These organizations can leverage their expertise and resources to address the unique challenges and foster innovation in digital health. The following section identifies potential roles for various organizations; these organizations are mentioned as examples—other organizations may also be appropriate.
The Meadows Mental Health Policy Institute, for example, can provide holistic support to healthcare professionals and health systems. Their comprehensive educational resources can help healthcare professionals integrate digital mental health tools into their practice effectively. This support includes explaining regulatory requirements, identifying suitable digital tools, and helping implement best practices for patient care.

As another example, the Peterson Health Technology Institute has expertise in assessing the effectiveness of digital health tools. Through rigorous evaluation and research, the Peterson Institute can provide valuable insights into which digital tools are most effective for specific mental health disorders. This information could form the basis for a centralized reference tool to help healthcare professionals, patients, and users make informed decisions about which mental and behavioral health to incorporate into their treatment plans, perhaps in tandem with the American Psychiatric Association's evaluation model.

The Digital Medicine Society (DIME), for example, can serve an important role in developer education and preparation. By creating educational programs and resources tailored to the needs of digital health developers, DIME can help ensure that developers understand regulatory requirements, best practices in clinical research, and the nuances of digital health innovation. This support can help developers create high-quality, effective digital health products that meet regulatory standards and address real-world clinical needs.

The Digital Therapeutics Alliance (the Alliance), or a similar group, can play a significant role in health application accreditation, evaluation, and recommendations. By establishing standards for digital health tools and providing a framework for their evaluation, the Alliance can help ensure that only high-quality, effective tools are recommended for clinical use. This accreditation process can build trust among healthcare professionals and patients, promoting the adoption of effective digital health solutions.

The American Health Insurance Plans (AHIP) can promote accountability and incentives based on outcomes, value, and the total cost of care. By generating guidelines for payors to evaluate digital health products, AHIP can help ensure that insurance coverage decisions are based on robust evidence of efficacy and cost-effectiveness. This approach can encourage the development and use of high-value digital health tools that improve patient outcomes while also managing healthcare costs.

Finally, the American Medical Association (AMA) can support the rapid coding of new digital therapeutic areas. By developing and updating medical coding systems to include new digital health interventions, the AMA can facilitate the integration of these interventions into clinical practice and reimbursement processes. This support can help ensure that healthcare professionals are appropriately compensated for using digital health tools and that these tools are recognized by the broader healthcare system.

By leveraging the expertise and resources of existing organizations the digital health ecosystem can benefit from greater support without overtaxing government resources. These organizations and their related training conferences can play key roles in providing holistic support, evaluating tool effectiveness, educating developers, accrediting health applications, promoting accountability, and facilitating reimbursement, ultimately advancing the adoption and impact of digital health innovations.

FDA should consider enabling greater flexibility in mental and behavioral health submissions

To improve the regulatory process for mental and behavioral health, many participants felt FDA should consider enabling greater flexibility in the study design and data requirements for regulatory submission.

While placebo requirements make sense in most randomized control trials, using sham applications as a comparison to mental and behavioral health is perceived by some participants as overly burdensome for developers and may fail to offer a believable substitute for trial participants. Unlike traditional pharmaceuticals, creating an effective placebo for digital interventions is complex and may be impractical. When appropriate, to address the risk of mental and behavioral health and its intended purpose, providing alternatives to sham apps, such as the absence of treatment through the app, may be an option to streamline the

evaluation processes while simultaneously making the research more consistent with typical digital tool engagement patterns. FDA has signaled its intention to issue a draft guidance on approaches to placebo controls and trial design in DMHT-T trials titled, "Clinical Evidence Considerations for Digital Mental Health Treatment Devices, including Computerized Behavioral Therapy Devices" in 2025.[m]

Additionally, the FDA should continue to work with stakeholders to incorporate real-world evidence (RWE) into its decision making, including for label expansion. RWE, which is derived from real-world data collected outside of traditional clinical trials, can provide valuable insights into the effectiveness and safety of digital health products in everyday use. Allowing post-market data to contribute to the evidence base for mental and behavioral health would not only expedite the regulatory process but also reflect the dynamic and iterative nature of digital health innovation.

These FDA-specific recommendations are provided as options for consideration to modernize and adapt the current regulatory framework to better accommodate the unique characteristics of digital mental health tools while still providing necessary controls to protect patients. By adapting placebo requirements, as appropriate, accepting real-world evidence, and regulating use cases, the FDA can facilitate the development and deployment of innovative digital health products—ultimately improving mental health care for patients. Also, as noted throughout this report, payor reimbursement is a separate process that may be influenced by flexibilities in FDA review.

Government agencies should enhance collaboration through continued interagency task force efforts for digital mental health tools

To streamline the development and implementation of mental and behavioral health, government agencies could establish an interagency task force dedicated to digital mental health. This task force would bring together relevant federal agencies to foster collaboration, clarify regulatory pathways, and accelerate product innovation and adoption of mental and behavioral health.

According to the Meadows Institute report, "Relevant federal agencies should partner to develop more precise definitions and categories of mental and behavioral health and clarify regulatory pathways to facilitate their safety, dissemination, and appropriate use."[11] This partnership would involve leaders from the FDA, CMS, NIMH, NIDA, ASTP/ONC, AHRQ, SAMHSA, HRSA, ARPA-H, Consumer Financial Protection Bureau (CFPB), and potentially

m https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cdrh-proposed-guidances-fiscal-year-2025-fy2025#under

other agencies like the CDC and IRS. For example, collaboration with ASTP/ONC to support interoperability could improve mental health RWD, and thus strengthen RWE for mental and behavioral health and other mental health interventions.

By working together, these agencies can ensure a coordinated approach to addressing the complexities of mental and behavioral health product research, regulation, and adoption. This includes evidence generation, recommendations, payment, privacy and security, implementation, and tax incentives. Such comprehensive coordination would drive clarity about processes across the industry, increase access to care, decrease confusion for healthcare professionals and patients, and inspire ongoing innovation among developers.

Additionally, enabling developers to interact with the task force or representatives from these agencies would support better coordination and access. Developers would have the additional tools needed to navigate across multiple government stakeholders, streamline interactions, and expedite the development and approval of mental and behavioral health.

In addition to addressing the aforementioned concerns regarding clinical measures, another key initiative for interagency collaboration would be revisiting the FDA/CMS parallel review process as a template for collaboration that could be applied to digital mental health products. A model for this type of interagency coordination around mental and behavioral health is the recently proposed CMS CY2025 rule that assigns billing codes for FDA-authorized mental and behavioral health, which is a potential path to faster reimbursement. However, it does not apply to all mental and behavioral health. Providing a dual evidence generation and joint submission pathway for FDA-CMS evaluation could potentially help streamline research and development efforts and increase speed to market.

Strengthening interagency task force efforts for mental and behavioral health would significantly enhance collaboration among government agencies. By aligning efforts across the full product lifecycle and engaging with developers, this task force could streamline regulatory pathways, increase access to care, reduce confusion, and foster innovation in the Mental and behavioral health space.

Conclusion

There is a high level of excitement for the potential of mental and behavioral health to improve patient access and care. However, regulating digital health products is inherently challenging, and the unique aspects of mental health disorders add an additional layer of complexity. Mental health disorders are diverse and multifaceted, which can complicate defining clear clinical endpoints and outcomes measurements. This complexity is compounded by the rapid pace of technological innovation in digital health, which often overtakes the existing regulatory frameworks designed for more traditional medical devices and pharmaceuticals.

Frustration exists among all stakeholders involved in the mental and behavioral health ecosystem. Government agencies are, in some situations, unable to enact change without congressional intervention. And these agencies may experience challenges in keeping up with the fast-evolving technology landscape and in providing clear, timely information to a developer audience that may lack regulatory experience. Developers, on the other hand, find it challenging to navigate the complex and often ambiguous regulatory pathways, leading to uncertainty and delays in bringing new products to market. Then, healthcare professionals and payors face difficulties in assessing the clinical relevance, effectiveness, efficacy and safety of digital mental health tools, which affects their ability to integrate these tools into clinical practice and reimbursement models. Researchers are hindered by the lack of standardized endpoints and robust evidence frameworks. Lastly, without clear clinical evidence, the users—patients and consumers—are left to navigate a confusing array of options with little guidance on efficacy and safety.

There is a pressing need to clarify and communicate existing regulatory pathways and resources more effectively. At the same time, it is essential for the FDA to evolve its interactions with industry, non-profits, and other government agencies. This evolution should aim to enhance collaboration, streamline processes, and improve access to effective digital mental health products. By fostering better communication and understanding among all stakeholders, the regulatory environment can become more conducive to innovation while simultaneously ensuring that safety and efficacy standards are upheld.

In summary, while the development and deployment of mental and behavioral health presents unique challenges, there are opportunities for improvement through better communication, collaboration, and an adaptive regulatory approach. All stakeholders—government, developers, healthcare professionals, payors, researchers, and patients— acknowledge the challenges and are willing to work together to improve access to new technologies. Addressing these challenges can lead to more efficient pathways for the development and implementation of mental and behavioral health, ultimately benefiting all stakeholders and improving mental health outcomes for patients.

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Appendicies

AGENDA

ADVANCING DIGITAL MENTAL HEALTH INNOVATION

Closed-Door Forum Agenda
May 21, 2024; 10AM – 2:30PM (EST)
1333 New Hampshire Avenue NW;
Rooftop Meeting Room
Washington, DC, 20036

Meeting Description:
A Foundation-convened closed-door forum to focus on accelerating innovation in spaces where mental health digital tools can be helpful (assessment, intervention, diagnostics)

10am **Welcome & Opening Remarks**

10:20am **Rules of Engagement**

10:30am **Discussion #1:** Themes That Will Make a Difference

- What are the themes the report should most emphasize?
  - Building from the pre-meeting survey responses
- For each theme:
  - Any revisions to current barriers/solutions/enablers?
  - Are any barriers missing?

12pm **Lunch Break**

12:30pm **Discussion #2:** Barriers for Additional Discussion

- Discuss up to 4 of the individual barriers identified in the pre-meeting survey

1:45pm **Discussion #3:** Potential Impact/Next Level of Effort

- If the priority themes are addressed, by how much might we accelerate innovation in digital mental health tools?
- What might the next-most-important barriers be?
- What additional information should be in the report?

2:25pm **Wrap Up & Next Steps**

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Thank you to these individuals and others who shared expertise and perspectives for this project

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