AMCP Partnership Forum: The evolving role of digital therapeutics

SUMMARY

Digital health tools, specifically digital therapeutics (DTx), which are primarily used to prevent, manage, and treat medical conditions, pose both challenges and opportunities to the health care system. To address needs related to coverage evaluation and access to DTx, AMCP held a virtual multistakeholder forum from August 31 to September 1, 2021. The group of 41 experts convened included representatives from payer, pharmacy benefit manager, integrated delivery system, patient advocacy, and DTx innovator organizations, along with individual health economists, academicians, and other key stakeholders. Participants were asked to (1) identify current marketplace challenges and areas of opportunity around coverage and use of DTx and (2) provide input to assist health care decision makers in making coverage decisions for DTx. Areas of opportunity identified by participants included standardizing product definitions and categorization across the DTx industry; emphasizing the value of regulatory approval in establishing standards of evidence for DTx; establishing evidence frameworks to guide coverage and reimbursement decisions for DTx; considering unique DTx product aspects such as data security, privacy, and product updates; advancing awareness and professional expertise in DTx among all health care stakeholders; and promoting DTx adoption and equitable access.

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Digital health tools, specifically digital therapeutics (DTx), which are primarily used to prevent, manage, and treat disease, offer new ways to deliver and receive health care and represent a growing range of potential products.[1] For instance, digital health-related mobile applications currently number more than 350,000, with more than 90,000 new applications added in 2020 alone. Additionally, digital biomarkers have been validated in feasibility studies and are increasingly used as endpoints in clinical trials. And while nearly two dozen DTx products worldwide have been granted market authorization through a regulatory process and are commercially available, another nearly 90 are in development.[1]

Within the DTx category, however, there is a high degree of variability in types of products (eg, mobile applications, wearable devices), as well as in their accompanying evidence of product quality or to support claims of safety and efficacy.[1] Additionally, most digital health applications do not undergo regulatory review, whereas other DTx products gain market authorization or clearance from a regulatory body like the US Food and Drug Administration (FDA), which is required to make efficacy claims. And some DTx require a prescription whereas others do not, adding further confusion for patients, providers, policymakers, and payers.[1]

Additionally, product coverage and reimbursement by health plans varies, and, therefore, patient access challenges persist. In 2019, AMCP held a Partnership Forum to examine the systems and processes that would support DTx adoption and use.[2] In that forum, participants identified characteristics that differentiate DTx from other digital health products, the evidence requirements for regulatory approval and payer evaluations, where coverage of these products might fit within health care benefits (eg, pharmacy, medical, or other), and the need for stakeholder education.[2] These findings were echoed in a recent viewpoint article that called for a harmonized approach for managed care decision makers to consider appropriate DTx product choice, assess product quality, evaluate the value of DTx in the context of overall care, and determine benefit coverage.[3]

Despite these calls for more defined approaches for DTx coverage and reimbursement, results from a recent survey of 70 managed care and industry representatives and other managed care stakeholders indicate significant differences in payer resources and capabilities related to the evaluation and coverage of DTx.[4] Payers appear to be moving toward more defined approaches to cover DTx but need meaningful evidence, including clinical trials and real-world evidence, to support evaluation and coverage decisions. For manufacturers, this ambiguity in payer requirements and variable coverage is the most significant factor in choosing not to pursue developing DTx products.[4]

To address these and other ongoing needs related to the evaluation and coverage of DTx, AMCP built upon prior learnings and held a virtual Partnership Forum from August 31 to September 1, 2021. The group of 41 experts convened included representatives from payer, pharmacy benefit manager, integrated delivery system, patient advocacy, and digital therapeutic innovator organizations, along with individual health economists, academicians, and other key stakeholders.

Forum participants were asked to (1) identify current marketplace challenges and areas of opportunity around coverage and use of DTx and (2) provide input to assist health care decision makers in making coverage decisions for DTx. To accomplish this, they reviewed survey findings, engaged in panel sessions, participated in breakout groups, and deliberated draft key considerations developed by AMCP staff with feedback from AMCP member committees prior to the forum. These proceedings synthesize discussion from the two days; however, the findings should not be construed as consensus or the perspective of individual participants' organizations.

Standardize Product Definitions and Categories

Participants acknowledged that challenges arise because of variation in definitions and categorization across the digital health industry, including those of regulatory bodies such as the FDA and Centers for Medicare & Medicaid Services (CMS). For instance, definitions of digital health, digital health technology, and DTx differ slightly across various sources (Table 1) and categories are generally broad, encompassing many types of products. These factors may cause confusion as individuals and organizations discuss needs related to DTx.

To reduce this confusion, participants considered how to standardize definitions and categorize products, for instance, by making distinctions based on factors like the product claim (eg, whether it diagnoses, actively monitors, prevents, or treats a condition) or whether it requires a prescription. In addition, participants recommended establishing a taxonomy or classification system of DTx products to help identify which treatments should be reviewed for coverage. Consistent industry standards like those of the National Institute for Health and Care Excellence, for example, to assist payment and reimbursement decisions, would streamline the determination of which products need to be reviewed, by whom, and how often.[5] Participants

TABLE 1 Definitions Related to DTx[4,5,9,10]

Term	Organization	Definition	Categories
Digital health	US Food and Drug Administration[9]	Technologies that use computing platforms, connectivity, software, and sensors for health care and related uses.	• Mobile health • Health information technology • Wearable devices • Telehealth/telemedicine • Personalized medicine
Digital health technologies	National Institute for Health and Care Excellence[5]	Apps, programs, and software used in the health and social care system. They may be stand-alone or combined with other products such as medical devices or diagnostic tests.	• Provide an intervention • Aid understanding/ communicating • Offer system services
DTx	AMCP[4]	Products designed to stand alone or work in combination with existing medications or treatments, helping patients prevent, treat, and/or manage their disease while ensuring optimal health outcomes from therapy. A key distinguishing feature of a prescription (or regulated) DTx product is that it makes a health claim that is validated by a third party (eg, a regulatory authority).	• Treat a disease • Manage a disease • Improve a health function (eg, prevent a disease)
	Digital Therapeutics Alliance[10]	Deliver evidence-based therapeutic interventions 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 = digital therapeutics.

indicated that, ideally, establishing these standards would be done as a collaboration among stakeholders including providers, information technology experts, and managed care experts.

Another standardization challenge identified by participants was that the appropriate benefit placement for coverage of these unique products might not fit precisely into the existing benefit category paradigm of medical, pharmacy, and durable medical equipment. As a potential solution, participants suggested developing a new stand-alone digital benefit category. However, this would necessitate a defined approach for making coverage decisions and updates to CMS regulations to enable such a change.

Emphasize the Value of Regulatory Approval

Participants cited the value of regulatory approval for making DTx coverage decisions (Table 2). Although some questioned whether regulatory approval of DTx is always needed or expressed concern that requiring regulatory approval for coverage may narrow patient access, most highlighted the importance of an independent review by a regulatory body for a baseline of scientific accuracy, safety, effectiveness, manufacturing quality, and appropriate use.

Additionally, participants debated the differences between FDA approvals for pharmaceuticals and FDA marketing applications for medical devices, under which many DTx are reviewed. Although labeling from regulatory authorities can establish a basic standard of evidence and inform coverage evaluation for pharmaceutical products, this may not be true for medical devices. Types of device designations and the evidence submission required for each are defined by the FDA; however, they vary in degree from clearance following a Premarket Notification (also called 510(k) clearance), to Premarketing Approval, which is the most stringent type, to less stringent types of exemptions.[6]

Participants also noted that registrational trials for DTx tend to be shorter and smaller than other clinical trials and that regulatory submission requirements may not provide all the information needed for coverage determinations such as the product scalability, usability, and accessibility. To address some of this uncertainty, participants proposed establishing an expectation for real-world evidence to provide additional information such as where DTx products fit in treatment paradigms and their expected use.

TABLE 2 DTx Coverage Decision Considerations

Consideration	Perspectives discussed
What is the role of approval and/or market authorization by a regulatory body, such as the FDA, in making coverage decisions?	• FDA approval may be a prerequisite for coverage, especially if a product makes a therapeutic claim ◦ Additional perspective: Requiring regulatory approval for coverage may inadvertently narrow patient access • FDA approval is only the first step of the coverage decision evaluation and does not guarantee payer coverage of a product ◦ Additional perspective: A product should be evaluated for coverage based on the strength of its evidence with or without approval • The intended benefit category (eg, medical, pharmacy, stand-alone DTx) for coverage of a product should be clear • Prescription and nonprescription products likely need to have separate guidelines for making coverage decisions
Which is the appropriate body to evaluate for coverage given their unique aspects (eg, data privacy and security)?	• A P&T Committee or equivalent body is needed to review the evidence for DTx products • Additional data, privacy, and security expertise may be needed to evaluate DTx products for coverage given their unique aspects
What evidence should stakeholders expect to accompany DTx products to make coverage decisions?	• Data demonstrating improvement compared with standard of care with rigorous clinical trial design are important with these products ◦ Additional perspective: The data generated will depend on the type of product and its anticipated benefit • A dossier approach is helpful to ensure adequate data are provided to payers to inform coverage determinations for DTx products ◦ Additional perspective: This may lead to these products being evaluated similarly to drugs despite important differences ◦ Additional perspective: Dossier adoption among decision makers will need to increase
What level of evidence, including real-world evidence, is required to make appropriate DTx product coverage decisions?	• Existing evidence standards, with clear definitions based on DTx type, should be leveraged ◦ Additional perspective: Even with strong evidence, awareness and educational gaps must be overcome to consider DTx coverage within payer organizations ◦ Additional perspective: Innovators should consider conducting supplemental studies to provide information beyond what is submitted to regulatory bodies • The level of evidence required for coverage decisions should be consistent across product types and product claim • The appropriate comparator in terms of the product's place in the treatment paradigm should be considered • Budgetary impact and cost-effectiveness models for DTx products are ideal • Value-based payment models may be useful to justify value and address uncertainty
What should stakeholders expect regarding collection, storage, and processing of user information?	• Data security and privacy should be demonstrated and maintained by DTx developers • The product information should include specifics of how and what data will be used • Prescribers need clear expectations of data delivery parameters, including frequency, and how the data are to be used once received • Standards and definitions to enable data interoperability, incorporation of data from individual product portals, EHRs, and claims need to be defined
What are the standards by which DTx product updates should be communicated?	• At minimum, DTx developers need to communicate changes that impact patient care or reimbursement • Special attention should be placed on updates that may impact safe use • A dossier format could define communication requirements • Communication standards should differ for product approval vs ongoing product updates • Payers need standards for what updates should trigger coverage reevaluation for DTx products

DTx = digital therapeutics; EHR = electronic health record; FDA = US Food and Drug Administration; P&T = Pharmacy and Therapeutics.

Establish Evidence Frameworks and Review Processes

Other evidence challenges discussed by participants arise from lack of an established evidence framework. Currently, there are gaps related to the evidence requirements for market entry, the levels of evidence stakeholders can expect to accompany a DTx product (eg, sham- or active-comparator-controlled clinical trial, real-world data pilot), and the information needed for DTx products to be evaluated for coverage (Table 2). Participants advocated bridging these gaps using a DTx dossier approach, such as the AMCP Format for Formulary Decisions, to create a framework that would standardize communication of the evidence and supplemental information for evaluation of multiple types of products based on their benefit/risk profile, alternative options, and claim.

Participants also examined the role of Pharmacy & Therapeutics (P&T) committees or equivalent bodies to review and evaluate DTx products for coverage (Table 2). Most saw the P&T committee as the appropriate body to evaluate DTx from a clinical perspective as it currently does for pharmaceuticals and some other medical devices. However, it was acknowledged that the P&T committee may lack the expertise needed to evaluate DTx products in terms of privacy and data security, for instance. As potential solutions, participants suggested adding a data security expert to the committee, having a DTx subcommittee, or having a separate group, such as an innovation center, assist with DTx evaluation.

Consider Unique Product Aspects

Participants recognized that there are special considerations in the evaluation and coverage of DTx products owing to their unique aspects. Examples of specific issues regarding DTx include interoperability between products and existing data systems, and ownership and security of the data they generate (Table 2). Interoperability, for instance, may affect downstream provider workflow and, thus, adoption and access if the data are not easily incorporated into the clinical decision-making process. These challenges remain even in an integrated system as many DTx must be accessed through product-specific web portals. Additionally, data generation raises concerns regarding patient accessibility and usability of those data, as well as concerns regarding patient privacy.

Participants also raised important considerations related to product lifecycle management. As developers improve products and release updated versions, for example, how will product version or discontinuation be managed, as it could create harm if unsupported products providing potentially outdated treatment remain available? Manufacturers need clear guidelines on which product updates require communication and how and to whom (eg, patients, providers, payers) these communications will be provided.

Participants suggested that communications should be triggered based on the type of updates (Table 2). For example, manufacturers should communicate updates that directly impact patient care such as changes to a care algorithm or patient usability, or updates that impact how patient data will be stored, shared, or used. Further, participants proposed that manufacturer communications should focus on any effect the update may have on the safety and efficacy of the product and should provide actionable insights to understand if and how to adjust patient treatment.

Lastly, participants discussed when or if an update should lead to reevaluation by a P&T committee or like body. They concluded that it was important that payers have standards for what magnitude of change should trigger a revaluation of the product, for instance, if there are changes in the safety or efficacy, or substantial changes in the way the product is delivered.

Advance Product Awareness and Professional Expertise

Participants highlighted the need for improved DTx product awareness and development of professional expertise through education across all health care stakeholders. Product awareness challenges may result, for instance, from the inconsistency of DTx product inclusion in horizon scanning databases and compendia. Many payers use pipeline references and drug database updates (eg, First Databank, Medi-Span) to track and respond to new product availability, and clinicians often use drug indexing databases (eg, Micromedex), evidence synthesizers (eg, UpToDate, DynaMed), and clinical treatment guidelines to stay abreast of current treatment options. Given the volume of DTx products coming to market, if they are not added to these standard resources, awareness, and, thus, the ability to systematically evaluate DTx for coverage or to incorporate them into a treatment regimen, may be hindered.

Lack of awareness may also affect coverage as it may lead to the perception that employers do not want to pay for these products or that patients will not use them given all the other technology competing for their attention, despite indications that demand for innovative health solutions like DTx is growing.[7] Therefore, participants underscored the

significance of ensuring DTx products be included in commonly used reference materials to foster product awareness, which may, in turn, drive greater coverage.

Additionally, given the novelty of many DTx products, participants saw advanced education as key to aid understanding of the place and potential benefit of DTx in patient care and increase the ability to critically evaluate and manage DTx products. They considered educating pharmacists to be especially important, as many DTx products are intended to supplement drug therapy and may require a pharmacist for dispensing. Education opportunities include embedding DTx training into pharmacy and other health science curriculums, developing advanced training and continuing education for practitioners, and publishing DTx-related best practices.

Promote Adoption and Equitable Access

An additional area of opportunity identified by participants was the promotion of adoption of and equitable access to DTx. Participants called on industry leaders to focus on general digital health literacy among both health care stakeholders and patients and, specifically, to educate patients regarding the benefits and risks of DTx being incorporated into their care.[8] They also recognized that addressing provider needs such as ease of integration into their workflow is important to improving adoption of DTx. And as an increase in adoption occurs, participants emphasized that it will be critical to consider that many factors, including but not limited to Internet availability, technological literacy, and demographics such as age and culture, play a role in ensuring equitable access among various patient groups.

Future Directions

The considerations and perspectives highlighted in these proceedings may guide digital health innovators in the standards of evidence expected to accompany DTx, assist health care decision makers in making coverage decisions for DTx, and improve the understanding of DTx benefits, risks, and value, thereby achieving greater patient access. Following the completion of the forum, these should be considered when developing guiding principles for making DTx coverage decisions. Participants also encouraged other efforts such as including DTx in the AMCP Format for Formulary Submissions, developing stakeholder education on DTx, and advocating for responsible policy to govern DTx and further improve patient access.

Limitations

One limitation of these proceedings is that a different mix of stakeholders or individuals might have resulted in a different set of challenges or opportunities identified. Additionally, had participants not been provided draft definitions and considerations on standards of evidence for DTx products, the group might have generated a different set of conditions. Finally, although the definitions and considerations were voted on and debated, a large portion of the discussion centered on specific wording, and consensus was not sought or achieved.

Conclusions

As the role of DTx in health care continues to grow and evolve, DTx developers and health care decision makers need to have a shared understanding of the requirements for their coverage and reimbursement to optimize patient access. Areas of opportunity identified by participants included standardizing product definitions and categorization across the DTx industry; emphasizing the value of regulatory approval in establishing standards of evidence for DTx; establishing evidence frameworks to guide coverage and reimbursement decisions for DTx; considering unique DTx product aspects such as data security, privacy, and product updates; advancing awareness and professional expertise in DTx among all health care stakeholders; and promoting DTx adoption and equitable access. Addressing these areas will be critical not only for current, commercially available products but also for DTx products in development now and in the future.

DISCLOSURES

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