The Emerging Role of Digital Therapeutics in Medical, Surgical and Radiation Oncology

Description

Recent studies have shown the emergence of digital therapeutics (DTx) as potential solutions in the cancer care continuum to improve medication adherence, chemotherapy tolerance, and overall survival, while potentially reducing financial toxicity. In this review, the authors examine these new modalities and possible future benefits for cancer patients.

Learning Objectives

Upon completing this activity, the readers should be able to:

- be familiar with the regulatory process for digital therapeutics, recognize the specific flaws and burdens associated with the current system, especially as it pertains to the practice of radiation oncology; and
- be comfortable discussing the general utility of digital therapeutics with oncology patients; and
- understand the infrastructure required to implement digital therapeutic solutions.

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Disclosures

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- Radiation Oncologists
- Related Oncology Professionals

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Abstract

Digital therapeutics (DTx) are software interventions of therapeutic value supported by scientific evidence to prevent, manage, and treat a broad spectrum of physical, mental and behavioral conditions. Current data supports integration in the setting of chronic medical conditions such as diabetes, hypertension, opioid dependence, and insomnia. Recent clinical studies have shown emergence of DTx as potential solutions in the cancer care continuum to improve medication adherence, chemotherapy tolerance, and even overall survival. In addition, evidence suggests that these digital interventions may have a significant impact on lowering the cost of health care for current patients and cancer survivors. Given the potential financial toxicity for oncology patients, these modalities, such as digital patient-reported outcomes (PROs), are being actively investigated to determine the economic benefits as well. As DTx emerge in medical, surgical and radiation oncology, further studies are needed to ensure the needs of patients are met with respect to digital literacy and equity. In this review, we will explore these new modalities and the spectrum of possible future benefits.

Keywords: Digital therapeutics, digital health, patient-reported outcomes, quality of life, overall survival, software as a medical device, virtual reality

Digital therapeutics (DTx) are defined by the Digital Therapeutics Alliance as "evidence-based therapeutic interventions driven by high-quality software programs to prevent, manage, or treat a medical disorder or disease" (DTxalliance.org). In short, there are 2 requirements to be considered a DTx. First, it must be software – often categorized as software as a medical device (SaMD). Briefly, hardware refers to physical devices such as phones, computers, tablets or sensors, whereas software refers to a collection of instructions telling hardware what to do. Second, since DTx are designed to offer therapeutic value, they must be approved for use by recognized regulatory agencies such as the Food and Drug Administration (FDA). Digital sensors, wearable devices, virtual reality (VR) systems with therapeutic intent, and artificial intelligence (AI) devices are all examples of DTx.[2]

For SaMD to enter the public markets, it must either obtain de novo premarket approval (PMA) or qualify for 510(k) clearance. Devices with 510(k) clearance can forgo clinical trials and testing if the device is "substantially equivalent" to something already on the market. For de novo PMA, clinical trials must show adequate safety, efficacy, and be either equivalent or superior to the standard of care. Even after FDA approval, postmarket surveillance must be performed to identify long-term side effects; these roughly

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Table 1. Results From Oncology Clinical Studies Incorporating Digital Tools

PRODUCT	COMPANY	THERAPEUTIC AREA	MECHANISM	STUDY POPULATION	TRIAL DESIGN	OUTCOMES
Oleena, Moovcare, Kaiku Health[16,17]	Voluntis, Sivan Innovation, Elekta	Remote care monitoring	Patient reports symptom, DTx evaluates symptom severity, DTx provides a personalized recommendation to manage the symptom	Advanced solid cancer patients, n = 766	RCT of DTx vs conventional symptom monitoring; survival endpoint	Median OS improved 31.2 mos vs 26 mos, *P* = 0.03. Significantly better HRQL and lower ER admission. Oleena patients remained on CTX longer.
Oleena, Moovcare, Kaiku Health[18]	Voluntis, Sivan Innovation, Elekta	Remote care monitoring	Patient reports symptom, DTx evaluates symptom severity, DTx provides a personalized recommendation to manage the symptom	Lung cancer patients, n = 98	Prospective f/u with DTx vs retrospective conventional	Median OS improved, 22.4 mos vs 16.7 mos, *P* = 0.0014
Oleena, Moovcare, Kaiku Health[73]	Voluntis, Sivan Innovation, Elekta	Remote care monitoring	Patient reports symptom, DTx evaluates symptom severity, DTx provides a personalized recommendation to manage the symptom	Lung cancer patients, n = 121	RCT of DTx vs routine f/u	Median OS improved 22.4 mos vs 16.7 mos, *P* = 0.0014
Oleena[27]	Voluntis	Remote care monitoring	Patient reports symptom, DTx evaluates symptom severity, DTx provides a personalized recommendation to manage the symptom	Ovarian cancer patients, n = 16	Pilot study to assist managing hypertension and diarrhea	87% of diarrhea events limited to grade 1
Attune[28]	Blue Note	Symptoms of anxiety and depression related to cancer	DTx that incorporates principles of CBSM and CBT	Breast cancer patients, n = 123	RCT evaluating DTx CBT vs relaxation training vs control	Greater increases in stress management skills in CBT/ relaxation groups, *P* < 0.001
Attune[74]	Blue Note	Symptoms of anxiety and depression related to cancer	DTx that incorporates principles of CBSM and CBT	Advanced prostate cancer patients, n = 192	RCT of 10 weeks Attune CBSM vs health promotion	Men in DTx CBSM group reported greater improvement in ability to relax
Untire[29]	Tired of Cancer	Cancer-related fatigue	Step-by-step program incorporating stress reduction exercises, physical activity, educational topics and daily tips	Patients with cancer-related fatigue, n = 799	RCT evaluating DTx vs control	DTx group showed greater improvements in fatigue severity, interference and QOL, *P* < 0.01

translate to phase I, II, III and IV clinical trials, respectively.

In contrast to hardware-based medical devices, SaMD regulation places larger emphasis on the phase IV component, since software is regularly updated. There are enough differences between hardware-based medical devices and SaMD to warrant independent regulatory processes. Appropriately, the FDA started a Software Precertification Pilot Program to "help inform the development of a future regulatory model that will provide more streamlined and efficient regulatory oversight of SaMD developed by manufacturers who have demonstrated a robust culture of quality and organizational excellence, and are committed to monitoring real-world performance of their products once they reach the US market."[3] The 9 companies selected to participate in the Pre-Cert Pilot Program are Apple, Fitbit (Google subsidiary), Verily (Google subsidiary), Johnson & Johnson, Pear Therapeutics, Phosphorus, Roche, Samsung, and Tidepool. This program will attempt to define the regulatory infrastructure for future SaMD approvals, emphasizing the developer's track record for good manufacturing practices in the setting of software development. This way, instead of trying to anticipate the relative safety and efficacy of eventual software updates to an approved DTx, the due diligence is centered on the developer's credibility to produce ethical products.

Table 1. continued

PRODUCT	COMPANY	THERAPEUTIC AREA	MECHANISM	STUDY POPULATION	TRIAL DESIGN	OUTCOMES
Kaiku Health[48]	Elekta	Remote care monitoring	Tool to report symptoms	Patients with advanced cancer treated with anti PD-LI, n = 37	Prospective single-arm study	Study showed feasibility
Kaiku Health[75]	Elekta	Remote care monitoring	Tool to report symptoms and educational material on management	Advanced lung cancer patients, n = 21 and providers n = 48	Single-arm study with DTx	Tool improved communication with provider, saved time by decreasing phone consultations
Optimune[76]	Gaia	Remote care monitoring	Internet-based intervention based on CBT techniques to treat depression, anxiety and fatigue	Breast cancer patients, n = 363	RCT of standard care + DTx vs standard care	DTx group showed greater improvements in QOL and dietary habits
Bliss[30]	N/A	Symptoms of care-induced pain	Immersive intervention based around pictures and videos in VR	Bone Marrow Biopsy patients, n = 126	Randomized phase III study	Showed feasibility in use of DTx to aid pain and anxiety caused by procedures
Sidekick Health[15]	Sidekick Health	Remote care monitoring	Tools to log food, track activity, report symptoms and receive educational material	Breast Cancer patients, n = 18	4-week, single-arm study	High level of retention and engagement showed feasibility of wide-scale use in treatment of breast cancer
Zemedy[63]	Bold Health	GI symptoms of abdominal pain, altered bowel habits and defecation-related anxiety	DTx offering GI and IBS-specific CBT	Patients with IBS, n = 121	Crossover RCT	Showed benefit and reduction of symptoms for patients suffering from IBS and similar symptoms
SHUTi[23]	N/A	General insomnia/ cancer-related insomnia	DTx using CBT for insomnia	Patients who downloaded the app, n = 7216	Real-world data	Showed high levels of engagement and clinically meaningful improvements in sleep
University of Pennsylvania[33]	N/A	Symptoms of anxiety experienced in the waiting room before oncology appointments	VR-guided meditation using pictures and videos, followed by surveys	Patients, family and staff in a radiation oncology setting, n = 119	Random population study	Showed positive responses and reported decreases in pre-appointment anxiety
Ieva Pelvic Digital Health System[61]	Renovia, Inc.	Symptoms of fecal incontinence	Use of a motion-based VBF device and adjacent app	Women with fecal incontinence, n = 27	Single-arm study	Showed a significant improvement in symptom severity and showed an improvement in QOL

Abbreviations: CBT, cognitive behavioral therapy; CBSM, cognitive behavioral stress management; CTX, chemotherapy; DTx. digital therapeutics; ER, emergency room; f/u, followup; GI, Gastrointestinal; HRQL, health-related quality of life; IBS, irritable bowel syndrome; mos, months; OS, overall survival; PD-L1, programmed death ligand 1; QOL, quality of life; RCT, randomized controlled trial; VBF, vaginal biofeedback; VR, virtual reality.

With these definitions, it is important to differentiate DTx from other digital wellness apps that exist in the consumer marketplace. To be considered a DTx, it is essential that high-quality clinical studies support efficacy and the intervention be of a therapeutic nature available either over the counter or prescribed by a physician.[4,5] DTx can work alone or in combination with other drugs and active treatment measures.[6]

Applications in Oncology

In 2016, a Blue Ribbon Panel was established as part of the Cancer Moonshot program to design a roadmap toward exploiting new advances in cancer diagnosis, prevention, and treatment.[7] As part of this initiative, attention was focused on the importance of patient-centered care and prioritizing prevention strategies, acknowledging that although therapeutic interventions have improved, many patients will live with their cancers like a chronic disease. In addition, the key lifestyle changes affecting cancer development were highlighted, citing the need for behavioral approaches to control smoking, obesity, and sedentary behavior.

If diet, nutrition, obesity, sedentary behavior, and lack of emotional and social support are contributing to the increasing global rise in cancer,

strategies are urgently needed to address these health issues at scale.[8] This challenge may provide DTx a potentially transformative role in supporting self-management of chronic conditions that complements conventional cancer screening, monitoring and treatment with the promise of increasing efficiency, improving outcomes and decreasing costs.[9] In the US, the population is aging and has been increasingly affected by chronic conditions; indeed, nearly two-thirds of Medicare beneficiaries have 2 or more medical conditions and nearly one-quarter have 4 or more chronic condititions.[10,11] In a recent study of over 230,000 Medicare beneficiaries, a third of newly diagnosed cancer patients had concomitant anxiety or depression with higher monthly health care costs ranging from $735 to $1931, depending on when the condition was diagnosed and the tumor type.[12] Patients with significant comorbidities during cancer treatment face increases in all-cause mortality as well as treatment-related toxicity.[13] During cancer treatment, symptoms are common, potentially leading to functional decline as well as the need for unscheduled visits to the clinic or ER. Conventional systems may not detect clinical changes in advance of acute deterioration, limiting the chances for provider intervention and thus paving the way for potential DTx to bridge the gap.

Currently, the main indications for DTx in oncology have been associated with managing treatment-related symptoms, with significant interest in optimizing digital transfer of patient-reported outcomes (PROs), as well as cognitive behavioral stress management.[1] The goals of incorporating DTx into oncology care, explored in recent clinical studies, are improved overall survival and quality of life, less acute intervention visits in urgent care centers or hospitalizations, improved adherence to the treatment plan, and more effective ways for patients to manage symptom distress and report their medical symptoms to their care teams (**Table 1**).[1,14] Although current evidence-based studies supporting the integration of DTx into cancer care are limited, the ones that have been completed show potential to improve outcomes. The first step to incorporating a DTx is ensuring that there is adequate patient engagement. Using a 4-week DTx that consisted of food logging, activity tracking, surveys, and receiving educational content to improve quality of life for breast cancer patients through mindfulness, sleep, stress management, and nutrition, data showed that there was high retention, engagement, and acceptability.[15] These results were especially encouraging given that most of the patients were actively receiving chemotherapy, radiation therapy or both. In this study, the app collected information such as engagement, retention, step goal attainment, and PROs about energy, stress and quality of sleep. A randomized study is being planned to continue this work.

Another recent study evaluated 766 patients with advanced solid cancers, randomizing them to a DTx intervention for digital symptom monitoring vs conventional symptom monitoring. In the experimental arm, patients self-reported 12 common symptoms from the National Cancer Institute's Common Terminology Criteria for Adverse Events.[16,17] Results showed improved overall survival in the intervention group (31.2 months vs 26.0 months, $P = 0.03$), significantly less emergency room (ER) visits (34% vs 41%, $P = 0.02$) as well as improved Health Related Quality of Life (HRQL) (34% vs 18%, $P < 0.001$). In addition, the DTx intervention group patients were able to remain on chemotherapy longer (8.2 months vs 6.3 months, $P = 0.002$). Similar improvements in overall survival (OS) have been reported for patients with lung cancer, with those randomized to a DTx intervention having a median OS of 22.4 months vs 16.7 months in the control arm.[18]

Digital PROs have also been evaluated in the cancer surgery setting, with data showing improved postoperative symptom control;[19] in this study, patients underwent thoracotomy for primary or metastatic cancer involving the lung. Following hospital discharge, all patients reported symptoms via automated telephone calls for 4 weeks. The 100 patients included were randomized to a control group or intervention group, with the intervention consisting of an email alert generated to the clinical team if a subset of symptoms exceeded the threshold for severity. The intervention group experienced a greater reduction in symptom threshold events than controls (19% vs 8%) and a more rapid decline in events. Similar findings have also been reported in the setting of gynecologic cancer, esophageal cancer, colorectal cancer, and liver cancer surgery.[20]Although the assessment of ePROs is feasible in surgical oncology patients with the opportunity for triggered intervention, there have not yet been any large-scale randomized controlled trials, thus slowing adoption.

Recent data suggest that digital PROs can be applied in large, real-world, population-based studies with similar findings.[21] Barbera reported the Canadian experience of inviting cancer patients to report 9 PRO symptoms at kiosks in clinic waiting rooms prior to visits with care teams reviewing the results.[22] The patients were matched with a comparison group who did not use PROs, finding an 8% reduction in ER visits and a 14% reduction in hospitalizations. Real-world data also support the integration of DTx into the setting of patients with chronic insomnia, with results from 7216 patients using the intervention outside of a clinical trial reporting 61.4% had a meaningful response.[23] Thus, available data suggest significant potential for DTx to improve outcomes both in

Table 2. Examples of Prescription DTx Designed to Improve Quality of Life in Oncology Patients With Comorbid Conditions

PRODUCT	COMPANY	THERAPEUTIC AREA	MECHANISM	IMPACT	REVENUE MODEL	FDA APPROVAL TYPE
BlueStar RX[42]	WellDoc	T1DM, T2DM	Mobile app providing personalized digital coaching	1.7-2.0 average decrease in HbA1c in first 3-6 months of use	Employers or health plans	510(k)
Insulia[43]	Voluntis	T2DM	Mobile app to assist with insulin titration	Higher rates of HgA1c < 7% at 4 months	Commercial insurance	510(k)
dNav[44]	Hygieia	T2DM	Mobile app leverages AI to make insulin dosing adjustments	Lower HgA1c within 3 months	Medicare and commercial insurance	510(k)
reSET[45]	Pear Therapeutics	Substance use disorder	Mobile app that delivers therapy based on community reinforcement approach	Doubled abstinence rates (40% vs 18%) and retention rate (76% vs 63%)	Commercial insurance	de novo
reSET-O[46]	Pear Therapeutics	Opioid use disorder	Mobile app to assist transmucosal buprenorphine therapy	Increased retention by almost 15%	Commercial insurance	510(k)
Somryst[47]	Pear therapeutics	Chronic insomnia	Mobile app delivers 9 weeks of CBT	45% quicker time to fall asleep, 52% reduction in time spent awake at night, 45% reduction in severity of insomnia	Employers	510(k)

Abbreviations: AI, artificial intelligence; CBT, cognitive behavioral therapy; FDA, Food and Drug Administration; HgA1c, hemoglobin A1C; T1DM, type I diabetes mellitus; T2DM, type 2 diabetes mellitus.

the prospective clinical trial as well as the real-world setting, suggesting scalability across large cancer patient populations.

Other studies have focused on additional clinically relevant digital measures.[24-26] Liu et al reported a positive overall patient experience in those randomized with a digital intervention to manage the acute treatment-related effects of diarrhea and hypertension associated with systemic therapy for ovarian cancer.[27] In breast cancer patients, greater increases in stress management skills were reported in the randomized digital intervention group compared with the control group ($P < 0.001$).[28] Finally, investigators have also reported the potential of DTx to decrease fatigue, with Spahrkäs et al reporting greater improvements in fatigue severity and overall quality of life ($P < 0.01$).[29]

Pain associated with cancer and its treatment is another promising area of DTx investigation. One recent study of 126 patients evaluated whether a DTx incorporating VR could improve the experience of patients undergoing a bone marrow biopsy.[30] The study was a multicenter randomized phase III trial evaluating the VR intervention named Bliss before and during the procedure, exploring this VR DTx for its potential as a distraction therapy. Although the intensity of the pain did not improve in the VR intervention arm, the Bliss relaxation method was well tolerated with high satisfaction of both patients and providers. Early data in the pediatric/adolescent populations also shows hope for improving outcomes, with a pilot randomized trial comparing VR to iPad distraction therapy in 20 patients favoring the VR arm with trends toward less pain and distress.[31]

Review of VR DTx suggests a range of possible uses, including distraction from painful procedures, chemotherapy, and hospitalization itself.[32] In their assessment, Chirico et al reviewed 19 studies that evaluated the efficacy of a VR intervention during chemotherapy, finding that all reported a reduction of patient distress with less anxiety and fatigue as well. In the 3 studies they reviewed where patients were tested during painful procedures, there was significant pain reduction. Finally, the authors evaluated 4 studies that evaluated the effects of a VR intervention on hospitalized patients, finding all studies demonstrated positive effects. Recent data also support integration of VR strategies to improve relaxation in a radiation therapy department for patients, family/friends, and staff.[33] At the University of Pennsylvania, 119 subjects were selected to participate in a VR relaxation experience in the waiting room and participate in a follow-up survey. The experience consisted of a natural scenario on a lake with a guided meditation. The satisfaction of this group was positive; 96% enjoyed the experience and 97% would recommend to others, with the majority (80%) noting more relaxation and (65%) less anxiety.

Additional radiation oncology studies incorporating DTx are beginning to emerge, suggesting significant potential to improve patient outcomes.[34-36] Indeed, applications in the setting of protracted multiweek

courses of therapy would align well to determine if such interventions could improve well-being during treatment and avoid interval unscheduled medical care such as ER visits and hospitalizations. Data from the SHIELD-RT trial, which incorporated machine learning to identify patients at high risk of unplanned acute care and then randomized to usual care vs twice weekly MD visits, support this approach and reported a significant decrease in acute-care visits during radiation therapy from 22% to 12%.[37] With data suggesting that DTx can retain patients receiving chemotherapy on schedule, future studies can also evaluate whether such benefits can be seen in patients receiving radiation therapy to result in fewer treatment interruptions. DTx that address symptom management may be particularly relevant to improve outcomes in patients receiving combined modality therapy. Moreover, with many patients experiencing financial toxicity during treatment,[38] DTx may hold promise in improving overall function by decreasing fatigue and stress, thus mitigating the economic cost of time away from work.

In addition, cancer patients may benefit from DTx that can be prescribed to help them manage comorbidities, which can frequently increase the cost of care. This is especially important since nearly 50% of the US population has a chronic disease such as diabetes, heart disease, obesity, hypertension, and chronic respiratory conditions.[39] DTx solutions currently exist to improve management of type 2 diabetes, substance use disorder, major depressive disorder and insomnia,[4] all of which can complicate the course of cancer care. In addition to comorbidities, medication adherence is a significant issue with estimates that globally, up to 50% of patients do not take their medication as recommended; in the US, the cost of this is estimated to be $289 billion annually.[40] DTx solutions being tested range from AI systems using psychological modeling to personalize conversations to foster medication adherence, to digital pills that have sensors that send a record of the ingestion to a mobile app shared with the health care team.[41]

Some prescription DTx may improve quality of life in oncology patients with comorbid conditions (**Table 2**). BlueStar RX, Insulia, and dNav are marketed for patients with type 2 diabetes.[42-44] These mobile apps are primarily designed to assist patients with insulin titration using AI. Pear Therapeutics produced 2 FDA-approved products directed toward patients with substance use disorder, opioid use disorder, and chronic insomnia.[45-47] They function through the ability to deliver cognitive behavioral therapy (CBT) as adjuncts to pharmaceutical therapy. In addition to on-demand therapy delivery, CBT, biofeedback training and medication adjustment AI, remote patient monitoring (RPM) is being heavily explored in oncology. Many of these apps are readily available "over-the-counter" and do not need a prescription. While high-level evidence is lacking, initial feasibility studies have shown promise for RPM solutions such as those designed by Kaiku Health,[48] Navigating Cancer,[49] and Noona.[50]

The studies incorporating Noona into the clinical workflow have shown promising results with implications for radiation oncology outpatient clinical workflow. Peltola et al evaluated its integration with 44 cancer patients and 17 health care professionals; 93% of the patients and 88% of the medical professionals reported that the program was easy to use.[50] A study of 765 patients with breast cancer randomized to follow up with Noona vs traditional phone calls, changing to the opposite group after 6 months, and then evaluating preferences at 1 year, reporting that 30% of patients favored Noona, 30% traditional phone calls, and an additional 30% noted that both were equally good.[51] Takala et al recently described integrating Noona into the clinical workflow of Tays Cancer Centre in Finland with 253 patients with early stage breast cancer.[52] More than 82% of patients regularly engaged with the app and 89% of patients were still responding 3 months after radiation therapy treatment concluded. During treatment, 39.3% of patients engaged with the app to report symptoms while 60.7% engaged with treatment-related questions or to ask advice about treatment. Interestingly, anxiety as well as tiredness and pain were reported via Noona far more often than during the in-person visits, suggesting that Noona may transcend some barriers patients face in traditional reporting. In an additional study of 1420 patients, the Noona cancer follow-up application (CFUA) was evaluated along with a traditional callback feature triaged by a digital tool.[53] Noona's CFUA in this study improved the accessibility rate of telephone services such that the same number of nurses was able to manage more contacts in less time and became an accepted part of the workflow so that all nurses used this feature daily or at least weekly. Importantly, the investigators surveyed the nurses and noted that they favored the integration of the digital tools. These findings suggest that future studies are needed to determine the full impact of incorporating these digital tools into routine practice.

As the effectiveness of cancer treatments has improved, there are more global survivors, and more patients dealing with cancer as a chronic disease. Estimates suggest that by 2030, 22.1 million cancer survivors will be living in the US.[54] Up to half of all cancer patients at some point in their course will experience anxiety, depression or psychosocial distress[55] with evidence that this can especially lower the quality of life of survivors and adversely impact

long-term survival.[56] As treatments improve and are associated with higher rates of long-term survival, the need for patient compliance and adoption of healthy lifestyle behaviors is especially important given the risks of recurrence and late effects. Indeed, there can be a wide range of side effects with the more complex treatment modalities, such as immunotherapies, which are being increasingly combined with radiation therapy. Whether these combinations may affect patients' long-term quality of life is not well studied at this time but digital monitoring systems may be useful to track not only acute but also late sequelae.[57,58]

With respect to chronic pain, DTx hold promise to address the interpretation of pain via a neural systems approach.[59] DTx may also soon play a role in management of late effects of cancer therapy, with potential to integrate solutions to treat incontinence.[60] No data yet exist on outcomes in cancer patients, but data so far have been encouraging. Weinstein et al reported the results of a single-arm, 10-week prospective pilot trial in women with fecal incontinence, finding there was significant improvement in symptom-specific severity and quality of life using the DTx.[61] Karaman et al reported that patients who received treatment with a transcutaneous electrical stimulator had less urinary incontinence than patients who just performed Kegel's exercises, suggesting that there may be a role in the oncology setting for patients as well.[62]

In addition to incontinence, patients can also experience effects of bowel dysfunction after pelvic radiation therapy. Data in the setting of patients with irritable bowel syndrome (IBS) have shown how effective a mobile DTx can be to self-manage symptoms.[63] Additional DTx are being piloted that integrate a patient's genetic and baseline gut microbiome data with results showing effective symptom severity reduction including IBS, diarrhea, and constipation.[64]

Key Considerations: Practice Incorporation, Access to DTx, Digital Literacy, Digital Equity

Given the changing health care landscape since the adoption of the Affordable Care Act, DTx may emerge to fill gaps to improve quality and patient experience. As noted above, some systems such as Noona are already showing that the clinical experience can be improved while accommodating more patients and the same level of staff. With the Radiation Oncology Alternative Payment Model (RO-APM) in effect as of January 2022, 4 quality measures are being evaluated, some of which could be impacted by DTx: the plan of care for pain, the treatment summary communication, screening for depression and follow-up plan, as well as an advance care plan.[65] Since the model looks at a 90-day episode of care, DTx may help evaluate patients during and after treatment. RCM of pain and VR interventions may hold future promise in relieving pain while additional CBT DTx may help manage depression. With the digital callback features and interactions of many DTx, the patient experience may be improved. More studies are needed to quantify the return on DTx investment in terms of enhancing the patient and staff experience as well as decreasing staffing, increasing efficiency, and even intervening earlier to address disease recurrence or late effects.

Even after identifying a DTx that may benefit a patient, significant barriers must be overcome before implementing the device in mainstream practice. Software developed by for-profit companies have a goal, expectedly, to generate revenue. Ultimately, the most secure revenue line comes from universal commercial insurance coverage. However, many DTx are not universally covered and products such as leva and Nerivio are paid out of pocket, restricting the DTx to patients with resources and potentially exacerbating health inequities. Future methods of reimbursement for DTx may include some form of managed care such as employers, accountable care organizations, and Medicare Advantage health plans.

In addition to financial incentives to the health care system, the end user and provider must be accepting of digital technology. Digital health literacy has been defined as the "capabilities and resources required for individuals to use and benefit from digital health resources."[66] Self-report instruments to measure such competence, such as the Digital Health Literacy Instrument (DHLI), which includes evaluation of operational skills, navigation skills, information searching, reliability, and relevance, have shown significant correlation with age, education, internet use, health-related internet use, health status and health literacy.[67]

In 2021, 85% of US patients own a smartphone, a number expected to increase with no known saturation point. This statistic does not change by race/ethnicity but does decrease with lower socioeconomic means.[68] A disproportionate number of older "baby boomer" patients (born in 1946 to 1964) are digitally illiterate. However, if the user experience is well designed, seamless and automated, the barriers to overcome digital illiteracy may be avoided entirely.[66]

Another benefit of SaMD is patient-generated health data, but providers must be wary. Although using DTx to passively collect data can generate novel digital biomarkers and insights, as well as improve overall patient care efficiently and effectively, data ownership and stewardship do not yet have the robust regulatory oversight needed.[69]

While 85% of the US population has a smartphone, the 15% who do not are most likely to benefit

from DTx. In the setting of a global pandemic, remote access became increasingly important, yet digital inclusion may be lacking and must be factored in when developing and incorporating DTx solutions since digital access can be considered a new social determinant of health.[70,71] In this age of all things digital and data-driven, thoughtful management and oversight of data is critical to producing meaningful yet relevant results.

One potential area to expand digital inclusion may be with the opportunities within the decentralized clinical trial (DCT) landscape.[72] Since only 5% of eligible patients participate in clinical trials, there may be significant improvement with DCTs such that a wider range of patients can enroll secondary to the reduced costs and commitments. Mitigation of economic, geographic, and job disparities may be possible with DCTs and DTx with ePROs may have a prominent role. With this system, it may be possible to recruit digitally from communities that have been historically marginalized from clinical trials. Current infrastructure to foster the widespread adoption of DCTs is lacking but with the continued emerging spectrum of DTx, such support may soon arise.

At one of the author's institutions, incorporating DTx into the clinic workflow required a few "readiness checks." DTx utility is demographic dependent. Prior to an attempt at introducing DTx into the clinic, each institution's patient and staff constituency should be evaluated for digital literacy, DTx acceptability, electronic medical record interoperability, and avenues for financial support in the anticipated absence of insurance reimbursements.

Conclusion

DTx is a subdivision of digital health defined by evidence-based software interventions to prevent, manage, or treat a medical disorder or disease. Although formal use of the term dates back to 2012,[2] only more recently have studies reported improved outcomes with the integration of DTx into clinical practice. Given the potential for DTx to improve outcomes across the spectrum of cancer care, further data in the oncology setting is eagerly awaited.

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