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Possible Application of Digital Solutions in Oncology Drug Development

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ABSTRACT

Digital Therapeutics is a novel digital health segment involving software to provide new insights into human biology and oncology. Digital health offers solutions that apprehend patient-reported outcomes (PROs) and permits monitoring of symptoms and management of patient. Digital Therapeutics facilitates therapeutic interventions based on the evidence by way of applications supported by software while aiming at the prevention, surveillance, control, as well as medicaments of symptoms. Advanced developments in cancer treatment through Digital Therapeutics suggest routine supportive care in oncology to provide improved patient-centred care. Digital Solutions proffer an innovative strategy for optimal drug development in oncology.

Keywords: Digital Therapeutics, Digital Health, Patient-Centered Care, Patient-Reported Outcomes (PROs), Software Applications, Oncology, and Drug Development.

INTRODUCTION

Recent Digital Technology advancements have brought an innovative evolution in the field of Medical Sciences. Digital Health has become crucial to daily patient-centred care and drug development. Consequently, a novel subsection of Digital Technology has recently emerged called Digital Therapeutics. FDA approved the first prescription digital therapeutic in 2017 for treating substance use disorder (SUD) across a de novo submission for classification as a Class II medical equipment. Since then, the latent use of Digital Therapeutics has acquired incredible attention (Collins et al., 2017). The development of Digital Therapeutics in the form of new start-ups has been progressively functioning worldwide. Digital Therapeutics is purely a therapeutic intervention based on software. This novel subsection of therapeutics has gained the attention of all clinical pharmacologists familiar with biological and chemical medicines involving specific targets in physiological processes. Seeking its intense benefits and needs for supportive care in oncology, the current research is focused on the latest trends in Digital Therapeutics for optimal drug development and patient care in oncology.

With an increase in new cancer cases, various therapies have evolved worldwide. Generally, the latest treatments are pretty costly. Moreover, multiple drugs are obtainable in oral formulas for administration at home, with minimal face-to-face physician monitoring. Proper Patient management with minimal costs is required on priority. Every new approach should be centred on patient care involving tumour-directed treatment and patient-oriented care through the entire journey of disease (Head et al., 2011). Management goals are not just to acquire improvements in overall survival rather over and above patient-reported outcomes about life quality, minimal emergency, and advancements in symptoms are necessary. Therapies

targeted on molecules, immune-oncology, and oncology on precision radiation have metamorphosed the treatment of oncology infrastructure (Collins et al., 2017). These advancements have enhanced convolutions in treatment as an amalgamation of therapies necessitates utmost attention and modifications in the pathways of patients. Enhanced obtainability of oral treatments administered at home leads to reduced healthcare surveillance compared to hospitals.

Moreover, oral therapies take a long time and cause new toxicities. Thus, careful surveillance of adverse events during self-administration of medicines at home has become essential to enable immediate intervention and reduce the disease severity. In recent times, minimal services in oncology treatment have led to enhanced cancer complexity and incidence. It has spotlighted the requirement for novel techniques and strategies so that all patients get optimal treatment throughout the disease cycle.

Advancements in digitalized conversations and clinical healthcare technology have resulted in digitalization in the healthcare sector. Enhanced access and technological uptake amongst the clinicians and patients have resulted in enormous quantities of usable data in digitalized records of health that yield a crucial part of clinicians' decision-making processes. The healthcare sector enormously utilizes self-reported data (Lee et al., 2018). Data at the patient level offers medical data in real-world, involving scope for enhanced clinical decision-making, empowerment of patient, improvised health results, and cost reduction. At the same time, the confidentiality of patient and data compliance in terms of privacy regulations is crucial.

Digital Therapeutics- Definitions

Digital Therapeutics is a sub-division of Digital Health that involves health discipline and treatment choice while utilizing online health technologies in treating medical or psychological conditions. Digital Health explains all technologies that affect patients in terms of health. It includes various products used for wellness purposes and the healthcare sector. Digital Therapeutics is differentiated from Digital Health in terms of its primary feature of offering software-oriented therapeutics delivered to patients to manage or prevent severe disorders and health complications.

Various terminologies like Digitalized Healthcare, Telephonic health, as well as e-Health can be interchanged and are expounded as the purpose for healthcare services reinforced by digitalized technological strategies to improvise services pertaining to healthcare. eHealth services could be facet of every step of the involved procedures of healthcare, such as treatment, diagnosis, symptoms, decision-making, and monitoring, et al. Telemedicine describes clinical solutions offered flexibly at home by physicians using telecommunication provisions. Healthcare operations like patient evaluation, treatment, and monitoring are performed without the requirement of inpatient consultation. However, the legalities of these operations range as per jurisdiction. Tele-monitoring is using digital technology that consistently monitors the critical signs of patients.

Digital Therapeutics set algorithms on the basis of clinical regulations and practices, which change data collected into applicable comprehensions with an aim to bring usefulness to clinical results based on evidence. They can be used in concurrence with drugs, medicated products, medicinal devices, along with rest of therapies to increase and aid medical treatment. As per the danger level of set algorithms, Digital Therapeutics are characterized as medicinal equipment. Based on regulatory status, these are utilized as per prescription.

Additionally, Artificial Intelligence (AI) has emerged as a different advanced technology with more comprehensive concepts of digitalization in healthcare. It contains the potential and capacities pertaining to ML, comprising algorithms pf computer to build successful drug interventions and predictions about disastrous health diseases like cancer. From the healthcare perspective, Digital Health can be categorized into solutions associated with sensors or not and which apprehend ePROs allowing patient monitoring only or enable monitoring of patients and management of symptoms by physicians.

Evolution of Digital Therapeutics

Though the term 'Digital Therapeutics' evolved in 2012, the notion of applying digital technology to the healthcare sector is old. In Psychological Sciences, Artificial Intelligence (AI) was first applied in model interactions with a therapist, dating back to the 1970s. Technological advances and individuals' participatory attitudes have accelerated technology use. US Food and Drug Administration (FDA) 2010 approved its prescription for the Bluestar Diabetes Management System platform in the US. FDA approved market authorization in the US in 2015 after seeking its effectiveness amongst 4000 patients in the cases of multilingual depression treatment in the US and Europe through various randomized control trials.

FDA approved its first prescription for Substance Use Disorder (SUD) in 2017. FDA first approved Digital Therapeutics as the first 'smart pill' system in 2017 that involves drug tablets with an ingestible sensor to analyze the effectiveness of treatment while assisting clinicians in improving clinical results for schizophrenia, bipolar disease and depression. The evidence-driven advancement of digital therapeutics evolved in 2017 as a non-profit association. The Digital Healthcare Act was further passed by the German Parliament in 2019, permitting the physicians of Germany to prescribe Digital Therapeutics.

Digital Therapeutics for Cancer Care

Global estimates depict that more than 10 million deaths are attributable to cancer every year in 2020; World Health Organisation (WHO) estimated about 2.26 million cases of breast cancer, 2.21 million cases of lung cancer, 1.93 million cases of colon and rectum, 1.41 million cases of prostate, 1.20 million cases of skin, and 1.09 million cases of stomach cancer. It was estimated that lung cancer resulted in 1.80 million deaths, colon and rectum cancer led to 916000 deaths, liver cancer resulted in 830 000 deaths, breast cancer to 685000 deaths and stomach cancer to 769000 deaths in 2020 (WHO, 2020). Various therapies, drugs, and interventions have been developed to cure the disease. The cancer journey of every patient is divided into three phases:

- Active treatment phase;
- The recovery phase involves the restoration of depleted nutrients;
- The maintenance phase involves maintenance of health in preventing recurrence.

It is an estimation that the disease affects multiple fronts, including physical, psychological, and nutritional, varying from one individual to the other, wholly depending on the type of cancer and biological make-up of the patient.

Digital Therapeutics for cancer care is a novel segment involving innovative digitalization involving merging technology and health to build a transformational module that delivers clinical outcomes relevant to disease improvement while sustaining the patient's quality of life affected by cancer globally. Digital Therapeutics offers a personalized evidence-based therapeutic intervention through intelligent programming that helps prevent, manage, or treat any medical disorder. It can further amplify traditional therapy and improve patients' health worldwide.

The physicians organize various scientifically validated nutritional programs involving treatment and managing the patient health. Digital Therapeutics offers end-to-end support to cancer experts and patients in multiple ways. Besides collecting, monitoring, and diagnosing patient data, these programs help capture patient-reported outcomes (PROs) while allowing the physicians to monitor the symptoms and overall patient management. A variety of patient-oriented care aspects, including reassurance, adherence to treatment and efficiency, and minimal hospitalizations, are valuable prospects leading to enhanced overall results.

Digital Tools involved in Improving the Health of Cancer Patients

Evidence supports the power of symptom-monitoring tools during chemotherapy that helps improve cancer patients' quality of life while enhancing survival (Velikova et al., 2004). Various studies have reported data depicting web-based platforms reporting cancer symptoms (Collins et al., 2017). The patient-reported information is collected by the nurses and managed by calling patients at home. It helps in managing chemotherapy-related conflicts amongst the patients and physicians. Also, it has been reported that patients who receive this assistance can tolerate their chemotherapy better (Luderer et al., 2018). Various digital health companies are working on establishing applications at cancer centres located worldwide.

These software applications permit patients to monitor their symptoms while analyzing the data collected from intelligent symptom tracking and management support. That helps establish an existing care management regime for the patients and clinicians. Furthermore, more complex therapy combinations have emerged in the market that offers a source of real-time data providing insights into the experience and patients' side effects. These insights are not attained from clinical trials.

Various studies have suggested that digital health solutions assist in addressing most of the overlooked conflicts and issues that patients face during their cancer treatment (Velikova et al., 2004). These issues involve nutrition, fatigue, depression, et al. Digital Therapeutics make it possible for the patients to track their symptoms while analyzing and sending data to physicians who can easily follow up with patients. For instance, Voluntis's Theraxium is an application that makes cancer patients record, diagnose, identify, qualify, and report their associated symptoms to manage them better during cancer treatment.

Recent Trends in the Digital Therapeutics

Digital Therapeutic Solutions, Engagement, and Improved Outcomes

Digital Therapeutic programs are devised to assist the patients in becoming more engaged in the care of their cancer that can help reduce daily complications. The improved outcomes are attained by applying behavioural science based on evidence and a telehealth remote care system, enabling the patients and physicians to achieve their goals (Denis et al., 2017). Digital Health and Telehealth have been extensively expanded in the last decade but are devoid of necessary inputs from patients and sustenance of their psychological status or lifestyle attributes. The most worthwhile goal in attaining better results is for the patients to remain active with instructions provided by the clinicians regarding their daily activities. It can, however, be achieved by fabricating a patient-partnered care plan, which helps dynamically adjust to the patient's psychology and physical status.

The integrated approach provides various benefits to the providers, involving minimal clinician fatigue, enhanced enjoyment in practice, and enhanced care delivery to served populations.

Behavior Modifications to Improvise Health Outcomes

Shared decision-making is an essential outcome that concerns improved patient-centred care. When patients estimate that they directly impact their care plan- that it involves particular lifestyle attributes and that they can attain the tasks in the project- it is pretty evident to achieve sustainable lifestyle behaviour modifications (Denis et al., 2018). Attaining behavioural and cognitive modification levels that result in meaningful, improvised quality metrics and health benefits necessitates dynamically constantly driven individualized resources and content.

Digital Therapeutics applications in outpatient oncology involve catering to digital messages to patients' particular clinical and lifestyle conflicts, like disease and medication-related, emotional support, quality of life, and social health determinants. These kinds of resources deliver optimal assistance to the patients without making them contact with their team of caregivers. It enables the practitioners to have free time and concentrate on other core issues effectively (Lee et al., 2018). These approaches enhance confidence in self-

management that influences a positive outlook while minimizing the stress and burden of adherence to the care plan. Digital Therapeutics programs enable patients to receive messages and valuable hints that make them alert about their health and confident that somebody is taking care of them. Various studies suggest that patients feel connected with such applications as a cancer diagnosis is an isolated process.

Digital Health Solutions in Oncology

1. **AsyMS** is a mobile phone based remote system monitoring solution that determines the rate of severity of cancer and each associated symptom (CTCAE based) through 10 particular chemotherapy related symptoms questionnaires like nausea, vomiting, diarrhea, constipation, hand-foot syndrome, mucositis, flu, fatigue, and pain. Patients will receive immediately automated evidence-based self-care advice based on their symptom reports.
2. **Aware** is a phone wearable sensor based remote system monitoring, Fitbit based passive data collecetion and PROs and determines through symptoms like pain, fatigue, concentration problems, feeling sad, anxious or worried, irritation, shortness of breadth, numbness, nausea and loss of appetite.
3. **Automated Voice Response (AVR) system** is a phone based symptom management toolkit that involves symptoms questionnaires about fatigue, pain, insomnia, constipation, poor appetite, vomiting, anxiety, neuropathy, cough, peripheral, mouth sores, depression, and weakness. Patients can receive immediate paper based information for symptom management; phone based calls for adherence management.
4. **Bioconnect** is a web-based application system that involves weekly self-scoring of 13 common symptoms of patients involving fever, shivers, asthenia, pain, decrease in the volume of urine, shortage of breadth, pain while swallowing, bleeding in mouth, and prolonged febrile neutropenia.
5. **BREATH (Breast Cancer e-Health System)** is a web based distress reporting with cognitive behavioural therapy involving information, assignment and assessment automated by video. It does not involve any therapist. It is a self-management intervention assigned to assist psychological adjustments.
6. **Cankado** is a web based application involving self-reporting symptoms and alert functions to the patients.
7. **Care Expert** is web based application with three supportive functions including continuous communications, reinforcement of self-driven agency, and cooperative agency with a sense of being looked after. It involves high patient usefulness and usability related to system reliability and real time reporting amongst breast receiving outpatient chemotherapy.
8. **CHOICE** is also a web based application involving global symptom distress reporting while providing information which is personalized tailored to the requirements of patients. Patients can share their own knowledge and experience to manage their own care in a better way. It is tailored to individual's personalized information and self-management support, e-communication with experts and cancer nurses.
9. **eCO (eCediranib/Olaparib)** is a smart phone based application that monitors the blood pressure linked to the application through Bluetooth. It also seeks diarrhea symptom management.
10. **HRQOL in routine oncology practice** are touchscreen computers that monitors depression scale, and HRQOL symptoms.
11. **Interactive Voice Response System (UVR)** is a phone based system with patients rates symptoms twice weekly for 4 weeks through automated calls. Email alerts are sent to the staff for monitoring.
12. **OASIS (ONCOLOGY ASSOCIATED SYMPTOMS AND INDIVIDUALIZED STRATEGIES)** is a web-based application designed to monitor and track symptoms distress with educational information regarding symptoms of cancer. It provides self-management strategies for symptoms.

Clinical Benefits and Limitations of Digital Solutions

The benefits and limitations of Digital Therapeutics implementation in patient management in oncology have been summarized in the table (Timmermann et al., 2017). The benefits and limitations have been published in various publications and researchers. Digital therapeutics influences stakeholders, practitioners, caregivers, nurses, patients, healthcare systems, and pharmaceutical companies in multiple ways, along with limitations concerning their technology advancements, costs, regulatory issues, and changes in strategies (Yount et al., 2014).

STAKEHOLDERS	BENEFITS	LIMITATIONS
PATIENTS	Direct communication with practitioners	Difficulty programing technology
	Maximum involvement in decision-making	Require specific training and education
	Information available 24/7	Time-consuming
	Symptoms and disease related treatment	Depersonalization
	Enhance patient centricity	
	Influences treatment adherence	
PRACTITIONERS	Enhanced interaction with patients	Specific training required
	Involving patients in decision making	Extra Time dedication for consultation
	Real world collection of data in real time	Changes in Practices
	Enhanced motivation	
	Optimal management	
	Effectual time management	
NURSES	Effectual Time Management	Specific Training required
	Time saving in patient analysis	Extra Time for consultation
	Enhanced quality services	
	Better communication system	
CAREGIVERS	Reduced Burden	Extra technical knowledge required
	Enhanced Satisfaction	

Discussion

Digital Therapeutics and health solutions must be implemented into the patient care pathway for utmost care in oncology while adopting authentic guidelines. Integration and implementation of these technologies are pretty debatable, with contemplation provided as if digital tools collaborate with current healthcare practices in a disruptive or gradual manner. The European Society for Medical Oncology(ESMO) has formulated a Magnitude of Clinical Benefit Scale (ESMO-MCBS) to assess the magnitude of the clinical advantages and effectual anticancer therapies improvement analysis. That could enhance the integration of digital tools in healthcare and oncology treatment processes.

Numerous evidence-based supportive care guidelines suggest that implementing Digital Therapeutics in daily routine is suboptimal (Ruland et al., 2013). That spotlights the necessity for more appropriate use of procedures, patient care and personalized care offered promptly. Digital solutions provide opportunities to address various unmet needs in preventing and managing cancer-related adverse events. It involves increased communication amongst cancer patients, educating patients and care providers, standard clinical assessment integration with PROs during daily clinical practice, assisting patients in surveillance of their conditions, improvised empowerment of patients, self-management, and enhanced evidence for clinical trials based on PRO endpoints in researches analyzing anticancer treatments and evaluations of supportive care interventions.

CONCLUSION

Digital Therapeutics involves software-based treatments and interventions that are delivered with the interface of digitalization. Advancements in Digital Technology offer various opportunities for healthcare professionals leading to innovation in medicine, patient care, devices, and healthcare software. At the same time, multiple challenges are involved in integrating digital tools in oncology. Fabricating clinical trials to assess digital tools is considered a long process as digital solutions require immediate availability for assessment in real-world settings. It is vital to discover common ground with solutions delivered to combat critical issues, limitations, and challenges in setting and integrating Digital Therapeutics, Digital Tools, and Software Systems in oncology patients' supportive care.

REFERENCES:

1. Collins A, Burns CL, Ward EC, Comans T, Blake C, Kenny L, Greenup P, Best D.(2017). Home-based telehealth service for swallowing and nutritional management following head and neck cancer treatment. *J Telemed Telecare.*;23:866–872.
2. Denis F, Yossi S, Septans AL, Charron A, Voog E, Dupuis O, Ganem G, Pointreau Y, Letellier C. (2017). Improving survival in patients treated for a lung cancer using self-evaluated symptoms reported through a web application. *Am J Clin Oncol.*;40:464–469.
3. Denis F, Basch EM, Lethrosne C, et al. (2018) Randomized trial comparing a web-mediated follow-up via patient-reported outcomes (PRO) vs. routine surveillance in lung cancer patients: final results. *J Clin Oncol.*;36:abstract 6500.
4. Head BA, Keeney C, Studts JL, Khayat M, Bumpous J, Pfeifer M. (2011).Feasibility and acceptance of a telehealth intervention to promote symptom management during treatment for head and neck cancer. *J Support Oncol.*;9:e1–e11.
5. Lee TT, Kesselheim AS. (2018).U.S. Food and Drug Administration Precertification Pilot Program for Digital Health Software: Weighing the Benefits and Risks. *Ann Intern Med.*;168:730–732. doi: 10.7326/M17-2715.
6. Luderer HF, Coolidge K, Campbell AN, Nunes EV, Maricich YA. (2018). Digital Therapeutic for SUD Demonstrates Dose-Dependent Improvement in Outcomes. *J Pharmacokinet Pharmacodyn.*;45:S84–S85
7. Ruland CM, Andersen T, Jeneson A, Moore S, Grimsbø GH, Børøsund E, Ellison MC. (2013). Effects of an internet support system to assist cancer patients in reducing symptom distress: a randomized controlled trial. *Cancer Nurs.*;36:6–17.
8. Timmerman JG, Dekker-van Weering MGH, Stuiver MM, et al. (2017). Ambulant monitoring and web-accessible home-based exercise program during outpatient follow-up for resected lung cancer survivors: actual use and feasibility in clinical practice. *J Cancer Surviv.*;11:720–731.

9. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. (2004). Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. *J Clin Oncol.* ;22:714–724.
10. World Health Organization (Health Report), WHO, 2020.
11. Yount SE, Rothrock N, Bass M, Beaumont JL, Pach D, Lad T, Patel J, Corona M, Weiland R, del Ciello K, Cella D. (2014). A randomized trial of weekly symptom telemonitoring in advanced lung cancer. *J Pain Symptom Manag.*;47:973–989.