Exploring digital therapeutics: The next paradigm of modern health-care industry

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Abstract
In this era of 21st century, the most valuable resource is data. Digital technology can generate terabytes of data which has a tremendous potential in the modern-day world. Pharmaceuticals play an essential role in improving and maintaining the health of patients. However, their cost in health-care budget is a major issue. Due to high prevalence and unfavorable consequences, managing chronic and lifestyle disorders has now become areas of major clinical concern globally. Harnessing this digital technology in our overburdened health-care industry can improve the treatment outcome and even replace the existing treatment. Health authorities such as U.S. Food and Drug Administration (USFDA) are also acknowledging their potential. FDA’s Center for Devices and Radiological Health has established the “Digital Health Program” which seeks to promote public health and provide continued regulatory clarity by enhancing outreach to digital health customers and developing and implementing regulatory strategies and policies for digital health technologies. The main focus of this article is to give an overview of digital therapeutics (DT), its clinical applications, role of regulators, and challenges ahead along with potential areas for developers and to present an update on major developments and initiatives taken in this field. The most important advantages of DT are that it has direct access to patients, decreases cost of treatment, encourages healthy lifestyle modifications, and can substitute or complement conventional treatments. Many of these models are still in infancy stage, and further research and development is needed to demonstrate their enormous potential in near future. If used judiciously, they can modernize our health-care industry.

Keywords: Digiceuticals, digital technology, mobile applications, U.S. food and drug administration

OVERVIEW
The convergence of conventional pharmaceutical industry with the modern digital technologies is set to open a whole new set of opportunities. Modern pharmacotherapeutic significantly improvises on existing approaches for improving and maintaining the health of the patients. However, controlling the cost of health care poses a major challenge for the governments across the globe. Digital health-care technologies can contribute to reducing the health-care costs and improve the treatment outcome, especially for lifestyle and chronic diseases. The burden of chronic diseases in terms of morbidity and finances, more so for the developing world, is enormous. A testimony to this is the fact that the U.S. spends 86% of all the health care on chronic diseases every year, and approximately half of the American population are suffering from diseases such...
as diabetes, heart diseases, obesity, hypertension, smoking, and chronic respiratory disorders. Developing countries such as India and China also have the highest incidence of Type 2 diabetes in the world. Therefore, embarking on digital technologies in the health-care industry can prove to be a shot in the arm for further improving the health of the community.

INTRODUCTION

Sean Duffy, CEO of Omada Health, first used “Digital Therapeutics” (DT) in 2013 to describe its online coaching software to help prediabetics avoid getting sick by exercising more and losing weight. DT is defined as “a health discipline and treatment option that utilizes digital and online health technologies to treat a medical or psychological condition.” They are technology-based solutions in the form of tools such as smartphone applications (app), wearable devices (tracking sensors), web-based studies, social networks, behavioral science, and telemedicine platforms to monitor patient activity and social interaction to detect and intervene when required. Table 1 highlights the difference between digicelicals and wellness tracking applications.

DT can claim clinical benefits in three ways:

Digital services
They modify patient behavior and help in driving a clinical outcome, for example, Omada health’s digital behavior platform for weight loss.

Adjunctive digital therapeutics
This tier complements traditional therapeutics, indirectly improving the clinical outcome, for example, Proteus Digital Health’s Discover medication.

Digital drug replacement
They substitute conventional medicine. This requires stringent criteria in terms of clinical trials and the Food and Drug Administration (FDA) review, for example, reSET application for treating substance abuse disorder.

Table 1: Difference between digital therapeutics and wellness tracking applications

| Category               | DTs                                      | Wellness tracking applications                     |
|------------------------|------------------------------------------|----------------------------------------------------|
| Indication             | Focused on one condition mostly          | Focused on various condition                      |
| Prerequisite           | Regulatory requirement like multicenteric RCTs among target population | Minimal technical requirement for downloading from application store |
| Therapeutic claim      | Safe and proven therapeutic value by collection and analysis of real-world evidence | Unsubstantiated claims about clinical benefits |
| Mode of access         | B2B2C                                    | B2C                                               |
| Key performance indicators | Compliance | Number of users                                  |
|                        | Prevention of readmission or             | Usage                                             |
|                        | Repeat intervention in a given amount of time | Direct turnover                                  |
| Reimbursement claim    | It can be reimbursed by payers depending on DT compliance | It can only be subscribed by consumers.             |

Table 1: Difference between digital therapeutics and wellness tracking applications

B2C = Business-to-consumer, B2B2C = Business to B2C, RCTs = Randomized controlled trials, DTs = Digital therapeutics

A host of companies are collaborating with health-care providers to shape up various DT programs in different diseases. Most of these initiatives are currently US based, but emerging trends from countries such as Japan, UK, and India are a positive development [Table 2].

KEY MILESTONES IN DIGITAL THERAPEUTICS

Digital prescription program (June 2013)
It was launched by WellDoc with an aim to help diabetic patients manage their condition using a mobile app. Blue Star was the first digital phone app approved by the FDA to manage diabetes.

Diabetes prevention program
It is a lifestyle modification program for diabetes prevention clinically proven to be more efficacious than lifestyle modifications launched by Omada Health, Canary Health, and Blue Mesa Health. It includes close monitoring of patients in terms of diet, weight, and physical activity and associates them with health coaches, clinicians, or peer groups. This helps to intervene at the time of exacerbations and reduce the frequency of symptoms.

Program aimed to curb substance abuse disorder
ReSET application developed by Pear therapeutics. It is a prescription DT used in conjugation with the standard treatment. It claims to improve clinical outcome by increasing patient’s adherence to treatment.

Various DT initiatives are currently underway for a host of diseases:

Asthma
Asthma was launched by propeller health partnered with GlaxoSmithKline. It consists of a sensor attached with an inhaler to monitor usage and provide feedback. It is used along with medicines and claims that medication needed by the patients is less.

Schizophrenia
Thrive digital app launched by Pear therapeutics. It

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is used along with antipsychotic medication and targets positive symptoms of schizophrenia.

**Insomnia**
An online therapy program called Sleepio was launched by Big Health which involves visual exercises to induce sleep. It claims to replace sleeping pills, being more efficacious and cost-effective.

**Heart disease**
A physician approved nutritional and lifestyle plan that guides patients to improve their health states launched by Suggestive therapeutics. It monitors physical activity, heart rate, and rhythm.[12]

**Stress incontinence**
“INNOVO” is the first transcutaneous electrical stimulator launched by Atlantic therapeutics in women to treat stress urinary incontinence. It offers a safe, clinically effective, and noninvasive choice.[13]

Various stakeholders involved in the development of DT are depicted in Figure 1.

**THERAPEUTIC BENEFICIARIES OF DIGITAL THERAPEUTICS**
Chronic debilitating diseases related to behavior can be immediate beneficiaries for DT. Usually, cognitive behavior therapy is a significant component of their treatment. DTs can offer a solution in terms of a mixture of prevention and therapeutic value. For example, in patients of Alzheimer disease which are expected to rise due to aging population and increased diagnostic awareness, DTs can be very fruitful.[14] Round the clock, monitoring of bipolar and depression patients can improve their quality of life, as psychiatrists cannot monitor a patient 24 h a day. Such technologies can be helpful in bringing a behavioral change among smokers and alcoholics.[15] These tools have shown a positive impact in patients of HIV and sexually transmitted infections in terms of acceptance.[16] Various applications have been made for efficient and timely management of perioperative patients.[17] Feasibility of these technologies in modern clinical practice clinics, for example, clinical surgery and rehabilitation, is also upcoming.[18] Table 3 highlights advantages and disadvantages of DT.[9]

### Table 2: List of various digital therapeutic programs running across the world

| Program name | Company | Origin | Domain |
|--------------|---------|--------|--------|
| DCP          | Omada   | US     | Prediabetes, type-2 DM, hypertension, high cholesterol |
| Blue Star    | Welldoc | US     | Type-2 DM |
| Virta        | Virta Health | US | Type-2 DM |
| Discover Ablify Mycete | Proteus | US | Ingestible sensors |
| reSET        | Pear Therapeutics | US | Substance abuse |
| reSET-O      | Pear Therapeutics | US | Opioid disorders |
| Thrive       | Better Therapeutics | US | Type-2 DM, CHD/CAD, chronic conditions |
| Big Health   | US     | Mental health |
| Headspace    | US     | Stress, insomnia |
| IQVIA        | US     | Health-care technology and clinical research collaboration |
| Kaja Heath   | US     | Chronic back pain |
| Livongo      | US     | Prediabetes, type-2 DM, HTN |
| Merck innovation fund | US | Venture capital fund |
| Mount Sinai  | US     | Health-care system |
| NHS          | UK     | Checkup for stroke, kidney disease, type-2 DM, CAD |
| Otsuka       | Japan  | Digital pill aripiprazole with Proteus |
| Propeller Health | US | Digital management of asthma/COPD |
| Roche        | US     | Type-2 DM, mental health program |
| mySugr       | Roche  | US     | Digital analysis platform |
| Solera       | US     | Type-2 DM/chronic diseases |
| Xealth       | US     | Rehabilitation and care |
| ALKTO1       | AKLTO1 | US     | Food intake and calories |
| PT PAL       | PT PAL | US     | Cannabis addiction |
| My fitness   | US     | Asthma  |
| Stop cannabis| US     | Addictions |
| Asthma MD    | US     | Be safe |
| Workit Health| US     | Preventing suicide |
| Be safe      | US     | |

DCP = Dynamic control programme, DM = Diabetes mellitus, HTN = Hypertension, CHD = Coronary heart disease, CAD = Coronary artery disease, COPD = Chronic obstructive pulmonary disease

**OPPORTUNITIES FOR DEVELOPERS CAN BE LEVERAGED INTO TWO PRIMARY WAYS**

**Explicit:** Revenue from product/digital therapeutics
Some DTs such as WellDoc’s Blue Star and Pear Therapeutics’ reSET can be reimbursed through insurance depending on the medical benefit they offer. DT manufacturers can give license to other interested
manufacturers and also there is opportunity of selling data to the same therapeutic field manufacturers for their future development of products.\cite{8}

**Implicit: Nonrevenue benefits from digital therapeutics**

Through the collection of proprietary data source and its use in training, input and feedback through artificial intelligence offers unique competitive advantage. Collection of data through DT helps in executing innovative contracts and presentations of clinical effectiveness data to payers. It can be used as a pilot-runs offering before fully covering it by payers. Manufacturers also can claim real-world evidence value of their DTs to payers. The life cycle of the DT can be updated rapidly through regular software updates and this can be utilized effectively during their sales pitches.\cite{8}

**STEPS TAKEN BY US FOOD AND DRUG ADMINISTRATION**

- Approval of the reSET application (1st mobile App) for substance abuse disorder through the de novo premarket review pathway. Furthermore, reSET-O application for opioid use, schizophrenia, and anxiety disorder
- The FDA is running a Pre-Cert Pilot Program for developing digital health-care technologies
- In 2018, 12 health-care algorithms using Artificial Intelligence software received FDA clearance.\cite{19}
- FDA’s Center for Devices and Radiological Health has established the Digital Health Program which fosters collaboration, enhances outreach to digital health customers, and develops and implements regulatory strategies.\cite{20}
- The “Digital Health Innovation Action Plan” has been issued which ensures all Americans to have timely access to high-quality, safe, and effective digital health products.\cite{20}

**SCOPE OF DIGITAL THERAPEUTICS IN INDIA**

DT can play a vital role in India where universal health care is a challenge, but the use of digital tools is increasing at the same time. Rather than focusing on treatment of chronic diseases, there is a growing need to monitor unhealthy lifestyle behavior. Furthermore, in a country where an unmanageable doctor-to-patient ratio is a big hurdle, adopting technology to collect data will help prescribers to get more time in discussing solutions to patient problems. Regulatory obstacles should be addressed by the Central Drugs Standard Control Organization (CDSCO) to implement DT in India.

**ROADBLOCKS IN DIGITAL THERAPEUTICS**

1. Distinguishing DT from health and well-being market is needed when thousands of health applications are running worldwide
2. Regulatory preparedness as only DT initiatives entail regulatory approval
3. Incentivization and Affordability: DT companies need to find ways of working in health-care ecosystem to align incentives between pharmaceutical companies, beneficiaries, and health-care providers
4. Education and technology adjustment for the patients to DT when issues of adherence and compliance are widespread in conventional therapies
5. To promote the development of research program for DT, it is necessary to offer incentives to researchers for addressing unmet medical needs.

**Table 3: Advantages and disadvantages of digital therapeutics**

| Advantages                                                                 | Disadvantages                                                                 |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| No toxicity and other associated side effects                             | Compromised patient privacy                                                   |
| Direct access to patients                                                 | Legal liability for injuries                                                  |
| Minimizes costs associated with attending hospital or doctor’s clinic     | Cross-jurisdictional practice of medicine                                      |
| Minimizes time in administrative tasks and routine communication and more | Serious mistake while using DT might affect thousands of patients at a time    |
| more time spent on treating patients                                       | without ready mechanisms for detection and correction                        |
| More efficacious as ensures continuous monitoring of patient vitals       | Some applications cannot guarantee the accuracy of the diagnosis               |
| Encourages adherence to healthy lifestyle behavior and prescribed         | Some applications might give false claims which are designed without           |
| medications                                                              | scientific input of medical professionals                                      |
| Opportunity to pair them with proven medications                          | Cybersecurity of patient’s data is a big responsibility for the DT companies   |
| Increases ways to interact with and empower patients                      |                                                                               |

DT = Digital therapeutic
CONCLUSION

DT is an emerging field of medicine in the overburdened health systems. Clinical trials are a must to prove their credibility. If used judiciously, they can even improve the treatment outcome. DT can provide safer and less expensive options than traditional treatment, which, in turn, can save billions of dollars in health care, especially in chronic and behavioral disorders. Regulatory authorities are also acknowledging their potential. Policy-makers need to make DT more readily available to the patients by ensuring adequate verification and reproducibility and educating health-care providers and patients regarding the advantages of DT. From mobile medical apps and fitness trackers to software that supports the clinical decisions which doctors make everyday, digital technology can turn out to be a revolution toward affordable health care worldwide.

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