Article

Developing Digital Therapeutics: The University Health Network Experience

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ABSTRACT

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FOUNDATION

The COVID-19 pandemic has been particularly revealing of the state of "eHealth", "digital health", and "virtual care" in addressing the needs of healthcare systems under the strain of demand and the restrictions brought on by public health concerns of the spread of the virus. The vast majority of what was deployed to address the needs of patients and providers were video conferencing platforms, which were quickly eschewed due to poor usability and increased scrutiny over privacy and security concerns and replaced with the simple telephone. Even this modest use of technology was short-lived, as most returned to in-office visits when public health directives allowed for it or when virtual care billing codes expired[1].

This oversimplification of digital health is motivation to differentiate its more advanced form: the validated digital *therapeutic*. These innovations can come in the form of novel "digital-first" models of care that break with the status quo from the perspective of policy, reimbursement, or jurisdiction[2]. They have explicit intent to enforce and produce better health outcomes through consistent guideline-directed, evidence-based protocols to provide patients and their families with more timely, accessible, and appropriate care. There is also the intent to eliminate low-value care, at a time where the pandemic has strained the supply side of the healthcare system. Many specialists will admit that they are looking for the opportunity to eliminate routine follow up care for patients that are stable and thriving[3,4].

We believe there is a need to distinguish between common and increasingly generic terms used to describe the current landscape of interventions, and the now emergent *digital therapeutic*. The reality is that digital technologies are so pervasive in healthcare that it is difficult to have a single category for such innovations. Certainly, technologies that are used for logistics, workflow management, and for simple communication between patient and providers should not all be considered equally innovative. The notion of the digital therapeutic is perhaps where the promise of eHealth and digital health has always been; that interventions would be *evidence-based* expert systems, technologically *advanced* in providing *decision support* to both provider *and patient*, and capable of *significantly improving health outcomes*[5–7]. Over the last twenty years, since the founding of the Centre for Global eHealth Innovation at the University Health Network (UHN), these tenets continue to be our focus, even as the terms to describe our work continue to be defined and redefined.

ORIGIN

UHN's "Program in eHealth Innovation" was founded in 1999 by Dr. Alex Jadad, who envisioned that a team tasked with imagining hospitals of the future should be embedded within the hospital system itself. The Centre would eventually be placed a mere few floors above the bustling urban downtown emergency department of the Toronto General Hospital, part of a quaternary care academic health sciences organization. It would eventually bring together an interdisciplinary team of scientists, engineers, clinicians, informaticians, and administrators to create an environment where so-called "misfits" could dream up new ideas and conduct the research and development needed to have a meaningful impact for invested patients and providers. The byline for the newly constituted Centre for Global eHealth Innovation would become "Creative, Collaborative, Centered on People".

A significant catalyst for the creation of the Centre was obtaining a major infrastructure grant from the Canadian Foundations for Innovation. This funding enabled an entire floor of the new Fraser Elliott Building at Toronto General Hospital to be dedicated to our efforts, with more than 15,000 square feet space for 70 staff and students, which included a 6000 square foot lab which would be developed for experimentation and evaluation of new health technologies. The Centre is home to staff scientists, software engineers, product subject matter experts, informaticians, quality assurance staff, and graduate students. It shares physical space with Healthcare Human Factors, a globally recognized team of human factors engineers, user interface and user experience designers, service designers, cognitive psychologists and other professionals who deal with the complexity of the psychosocial aspects of people working with health systems. Both groups work together in a unique embedded environment three floors above the emergency department, with access to facilities that allow us to recreate clinical environments to test the workflow around a particular device or the usability of the system itself. In particular situations where the simulation or the technology or the workflows are too complex, we perform in situ testing from within the hospital itself during off hours, or as necessary. Since 2004, the teams have had great success in working with industry to develop not only the safest products based on human factors engineering methods, but also those that have a good user experience. In fact, the goal is often to design and develop the technology that may even seemingly "disappear" from the workflow because of how well they integrate and how simple they are to use.

The Centre's ability to be able to recruit both patients and providers from within our setting for studies, as well as to be able to observe clinicians and patients interacting with one another within our healthcare system, is a unique and necessary attribute in developing advanced, safe and usable technologies. The ability to look beyond the device, beyond the touchscreen, beyond the mouse and keyboard, to encompass all aspects of the workflow, the team dynamics, and the organizational design is at the heart of our design philosophy.

Another aspect of the development of technologies is the necessity to develop them under a recognized quality management system standard such as ISO 13485 and other de facto standards such as the US FDA's 21 CFR Part 820. In 2014, UHN made the decision to abide by and be certified under these standards, so that we follow the same standards that we expect from our vendors, as well as recognizing the inevitability of our work being advanced that it would warrant regulatory scrutiny. Since that time our software process follows this rigorous quality management program which allows for the eventual clearance and approvals through regulatory bodies like Health Canada and the FDA[7–9].

PIPELINE

Digital therapeutics are increasingly being regulated as software as a medical device (SaMD)[8,10,11]. They are also prescribed to patients rather than marketed and accessed through an app store platform. At the Centre, we developed a pipeline of targeted therapeutics that support the management of chronic conditions. Our collaborative approach often begins with pairing our knowledge in health informatics and human factors with the expertise of our constituent clinical centers within UHN, such as the Princess Margaret Cancer Centre, the Peter Munk Cardiac Center, and the Banting and Best Diabetes Centre.

Our clinical champions provide exemplary care but are limited by the number of specialists and supporting staff available. Digital therapeutics have the ability to encapsulate that knowledge — the clinical expertise, know-how, and experience — into a system that can be deployed at scale and provide decision making that a specialist and their support staff would normally perform. As described, these systems would be considered SaMD because of their advanced decision support and could be prescribed to patients. They are better suited to deliver care into new spaces where people live, work, and play, as well as new healthcare environments like pharmacies that can deal more directly in the care of patients living with chronic disease. Finally, they can address care where care does not exist. Equity gaps exist both in urban areas where the cost of living is high and the ability to pay for services is an issue, and in the vast distances where remote communities cannot access timely and

appropriate care. The pandemic surfaced the stark reality that the quality of care patients receive is dependent on where they live. We have an opportunity now with digital therapeutics to close the three levels of the digital divide; our work continues to break down barriers of *access* while advancing greater *use* and better *outcomes* as a result of our well-designed expert systems.

At the Centre, we have maintained our original mandate to develop digital solutions for chronic disease management. From *Ned* for prostate cancer survivorship[12], to *breathe* for respiratory conditions such as asthma and COPD[13], to *iCanCope* for youth living with pain[14], our products are designed to deliver a targeted therapeutic effect. Although it is tempting to develop these types of interventions as a monolithic platform to broadly manage chronic disease, we have found that patients want and need a bespoke interface that aligns with their lived experience of health and illness. Our applications may share common software components (eg, data management, chatbot, alerting) but the experience of engaging with them is designed to feel personal, thoughtful, and compassionate. We know that the engagement with digital therapeutics directly elicits positive outcomes[15], and a lack thereof may result in poor or neutral outcomes.

Most traditional telehealth, remote patient monitoring, and digital health interventions tend to be built for ease of implementation for the provider and simplifying their workflows, rather than the utility or engagement of the patient and their families. We see the dependency on users to administer their own "digital dose" as a unique challenge to the efficacy of digital therapeutics. In response, we have found it critical to meet the patient and their needs on their own terms. Our deep involvement in the user centered design process in the development of our applications serves to determine the optimum frequency and nature of touchpoints, along with how they relate to the severity of the condition and the role of the patient in their own care[16]. We make very deliberate design decisions for our patients rather than attempting a single interface for all their interactions with the health system that does little to ensure effective engagement.

Within our pipeline of digital therapeutics, our most mature platform is *Medly* for the management of heart failure (HF). HF is the most complex, costly chronic condition to manage in healthcare. HF occurs when the heart is unable to pump enough blood to meet the body's needs. It is the most rapidly rising cardiovascular disease in Canada, with more than 50,000 new diagnoses each year, and affects over one million Canadians[17,18]. With recurring exacerbations, HF is the single most common reason for hospital admission and readmissions in Canada[19]. Due to advancements in the clinical management of HF, more Canadians are living with HF and other comorbid conditions, further adding to the HF burden on the Canadian health system. To address these growing demands, we conceived Medly in 2009 with a mandate to improve HF patient outcomes and decrease the cost of delivering care[20,21]. The Medly program is a digital translation of the specialized clinical knowledge and operational processes at the Peter Munk Cardiac Centre at UHN. Central to the program are two key components: (1) the Medly *System*: the core technology that supports the active monitoring of patients to support clinical management and patient self-care; and (2) the Medly *Service*: the key people and processes required to operationalize the Medly System.

The Medly *App* prompts patients to capture their daily readings, including weight, blood pressure, heart rate and HF-related symptoms. Patients can use a Bluetooth weight scale and blood pressure monitor to send readings automatically or manually enter the values on the app. The Medly *Algorithm*, a rules-based expert system validated by HF specialists, immediately analyzes entered readings against set personalized thresholds and provides the patient with instant feedback and instructions. The algorithm also alerts the patient's care team for further assessment and triage as needed. The Medly *Dashboard* provides Medly clinicians with real-time contextualized data on their patients' clinical status and recent symptoms consistent with acute exacerbations. Clinicians can rapidly identify and respond to patients who trigger an alert via the Medly algorithm, navigate into a specific patient's profile to get a comprehensive overview of their daily readings over time, alert history, lab results, and medications. Clinicians can also use secure email and messaging to review and respond to patient alerts. Medly was developed following ISO 13485 Medical Device Quality Management standards, a certification it maintains today, and has clearance by Health Canada as a Class II Medical Device for its advanced decision support capabilities and alerting. Due to Medly's advanced alerting system and streamlined clinical workflow, one Medly *Coordinator* is able to provide comprehensive care for up to 300 complex chronic patients. As a single point of contact for patients, the Medly Coordinator is able to build trust with patients and caregivers, understand their comprehensive needs and medical history, and support them with care navigation. A coordinated network of healthcare providers within the hospital enables the coordinator to collaborate with all providers in the patients' circle of care through a shared digital record. This allows for more cohesive care management and smoother transitions between clinical services. Together, the Medly System and Service help foster communication between patients and providers and create efficiencies in clinical workflows.

The utility of *Medly* has been demonstrated over the course of the last decade, with dozens of studies and peer reviewed publications documenting the evidence that initially informed, then validated, the design and implementation of the platform[21,22]. The evidence supporting its use has been demonstrated across the Quadruple Aim[23], encompassing improved patient outcomes, optimized population health, improved patient and provider experience, and cost effective care. Specifically, the platform has been able to demonstrate a 50% reduction in heart failure related hospitalization and a 24% reduction in all-cause related hospitalizations, improved quality of life, and improvements in prognosticators of heart failure, including BNP and ejection fraction[24].

The primary mechanism in which *Medly* is able achieve these outcomes is the level of engagement patients have in their own care on a daily basis. Patients have made it a routine to systematically assess their own health every morning. The *Medly* algorithm will instantly provide them with feedback on self care tactics, diuretics adjustments, or seeking additional care from the clinic. Although we've designed the system such that octogenarians and older could use the platform, we did not expect the level of engagement from this group that we experienced. We have shown that those 70 years of age or older, adherence rates with the platform were more than 80% over the course of one year, dispelling the myth that older adults cannot engage with such technologies[25,26].

LEGACY

With an original $6M investment in 2002, the Center for Global eHealth Innovation has attracted more than $160M in external funding. Through its staff scientists, students, and associates, the Centre has published more than 500 peer-reviewed academic articles, and has been entirely self-sustaining for the last fifteen years, with products and services that are being used in more than 100 countries and impacting the care of patients globally. The next 20 years will show a greater maturity in the academic discipline of digital health and certainly greater promise in clinical practice, with the true emergence of digital therapeutics as an effective form of treatment for chronic disease.

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