# Digital Therapeutics for Healthy Longevity: A Roadmap

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Abstract: Non-communicable diseases (NCDs), including common mental disorders, not only impose an enormous health burden on individuals but also lead to substantial economic burdens for healthcare systems. Especially individuals with lower socioeconomic status are affected by NCDs. Digital therapeutics (DTx) have the potential to offer low-cost personalized interventions easing the burden of NCDs and addressing inequalities in health. This position paper highlights the importance of preventive care and offers a roadmap toward DTx for healthy longevity.

## 1 INTRODUCTION

Non-communicable diseases (NCDs) such as cancer, cardiovascular diseases or diabetes, and common mental disorders (CMDs) such as depression or anxiety not only pose an enormous health burden on individuals but also lead to substantial health economic challenges for healthcare systems (Jacobson et al., 2023; Vandenberghe & Albrecht, 2020). In 2012 NCDs were the leading cause of death (WHO, 2014). Numbers increased to approximately 73% of all deaths by 2017 (Roth et al., 2018). NCDs also lead to a major economic burden for NCD households. Especially the population in lower-income countries and China is affected by costs associated with NCDs (Murphy et al., 2020). Also, in developed countries like Switzerland NCDs account for about 80% of the health costs (Wieser et al., 2014). Unmodifiable risk factors for the development of NCDs are age, genetics, and environmental factors. Modifiable factors primarily relate to aspects of lifestyle, for example, tobacco and excessive alcohol consumption, low daily activity, food choices, and lack of resilience. Especially individuals with low socioeconomic status are substantially affected by NCDs (Mackenbach et al., 2008), a highly relevant socioeconomic inequity (Federal Office of Public Health, 2016). At the same time, this group is underrepresented in clinical trials (Davis et al., 2019; Sharrocks et al., 2014). This fact leads to an important problem as clinical trials that aim at developing novel digital therapeutics (DTx), i.e., evidence-based software for the prevention, management, and treatment of disease (Digital Therapeutics Alliance, 2019), may not work for those individuals with a lower socioeconomic status. Thus, DTx may not at all lower the socioeconomic inequalities in health and thus, will also not reduce the health and economic burden of NCDs and CMDs (Carrilero et al., 2021; Kowatsch, 2023).

To this end, we recommend a paradigm shift where healthcare systems depart from curative care and incentivize primary, secondary, and tertiary prevention. We, therefore, highlight the importance of scalable DTx for healthy longevity and that these DTx are also effective in vulnerable individuals with lower socioeconomic status.

Next, we outline a roadmap toward DTx for healthy longevity. We provide a list of stakeholders that may be important in pushing forward innovation in this area with substantial societal impact. Then, the building blocks of DTx and potential business opportunities are discussed. Here, we provide two examples of corresponding initiatives in Switzerland

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and Singapore. We close this position paper with a discussion and outline of future work.

# 2 ROADMAP

The WHO defines healthy aging as "the process of developing and maintaining the functional ability that enables well-being in older age" (WHO, 2015, p. 228). Healthy longevity extends this definition to all stages of life: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 2006, p. 1). Therefore, a holistic approach to DTx is required, an approach that does not neglect social or psychological well-being. DTx for healthy longevity are defined as DTx for primary, secondary, and tertiary prevention. DTx for healthy longevity have, therefore, the overall goal to maximize the average quality of life and ensure that the increased lifespan is accompanied by an increased health span (Beard et al., 2016; Chen et al., 2018). For such DTx to be successfully deployed, healthcare systems must support innovative ecosystems, the development of novel DTx, and business models.

## 2.1 Innovative Ecosystem

Developing DTx for healthy longevity requires an innovative ecosystem of stakeholders that combine complementary expertise from various disciplines. We conducted expert interviews with medical doctors, DTx experts, payers (health insurers), as well as technology and innovation managers from both academia and the healthcare industry.

The following stakeholders were identified to be essential for such an innovative ecosystem: policymakers, regulatory and public health bodies, experts in biomedical ethics, public and private hospitals, healthy and patient populations, patient organizations, academic health institutions (e.g., medical and public health schools), digital health start-ups, biomedical laboratories, physiotherapists, nursing facilities, health and stress management coaches, diet and nutrition experts, hospitality facilities, and corporate health care units. These stakeholders together can establish new DTx with a holistic focus on mental, physical, and social health.

We also identified local initiatives and educational programs at universities, like executive education, to promote innovation in DTx for healthy longevity and dedicated DTx innovation and accelerator programs (e.g., the Dartmouth Innovation Accelerator for Digital Health). Moreover, DTx design and trial platforms are required, such as Ethicadata.com, Mahalo.health, or MobileCoach.eu.

## 2.2 Digital Therapeutics

DTx for healthy longevity can trigger personalized preventive care support at opportune moments (receptive states) in case a vulnerable state is detected or predicted (Nahum-Shani et al., 2023; Keller et al., 2023). To this end, the three building blocks of DTx cover *states of vulnerability*, *states of receptivity*, and *personalized support* as depicted in Fig. 1. Moreover, DTx also have the potential to improve themselves with every human-DTx interaction, for example, through reinforcement learning algorithms (Liao et al., 2020). Each of the three building blocks is discussed in the following sections, as well as a design and evaluation framework for DTx.

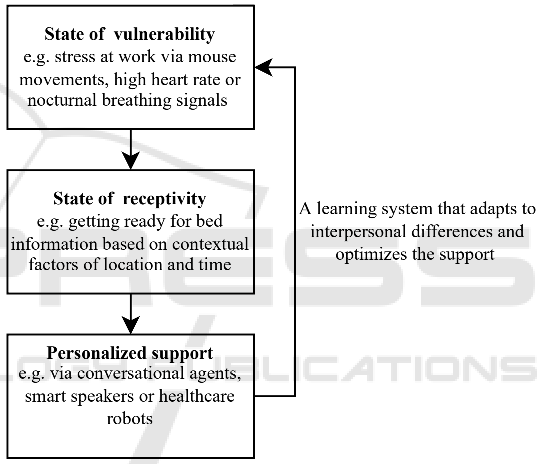


Figure 1: Building blocks of a DTx (adapted from Keller et al. 2023, Fig. 6.1, p. 67).

### 2.2.1 State of Vulnerability

First, for a DTx to decide on personalized support, a specific state of vulnerability must be measured or predicted. A vulnerable state is a "person's transient tendency to experience adverse health outcomes or to engage in maladaptive behaviors" (Nahum-Shani et al., 2015, p. 3). Therefore, the first step in developing an effective DTx is to measure or – if possible – even predict adverse health outcomes or maladaptive behaviors by using relevant sensor data streams or patient-reported outcome data. Examples are the measurement of nocturnal breathing signals for early detection of Parkinson's disease (Yang et al., 2022) or acoustic cough detection to assess asthma control or predict attacks (Tinschert et al., 2020). Digital biomarkers can also be used in primary prevention.

For example, it has been shown that stress at the workplace can be measured via computer mouse movements (Banholzer et al., 2021). More basic biomarkers include step count, heart rate, and average sleep duration and quality per night.

Recent improvements in consumer technology (e.g., wearables, smartphones, smart speakers, or smart TVs) further increase the quality of sensor data. Accordingly, “mobile health technologies are evolving from descriptive monitoring tools to digital diagnostics and therapeutics” (Sim, 2019, p. 965); this evolution of data streams requires more work before digital biomarkers can improve patient outcomes (Carovos et al., 2019).

#### 2.2.2 State of Receptivity

New technologies also enable more effective means of how and when to deliver support by DTx. Context-aware notification management systems on smartphones or smartwatches can increase the response rate to notifications (Künzler et al., 2017, 2019; Mishra et al., 2021). For example, support is better perceived when engaged in working, studying or when getting ready for bed (Choi et al., 2019). Contextual factors, such as geolocation or time, can therefore influence states of receptivity. To this end, effective DTx deliver personalized support at the right time, i.e., the target is in a state of receptivity, after a vulnerable state was measured or predicted. However, such context-aware DTx may also raise privacy and data security concerns which, in turn, can represent substantial adoption barriers. It is, therefore, of utmost importance to comply with any legal, ethical, and regulatory requirements.

#### 2.2.3 Personalized Support

Virtual or augmented reality, healthcare robots, or smart speakers allow for a new way of delivering personalized support with conversational agents (CAs) such as chatbots or virtual assistants like Amazon’s Alexa or Apple’s Siri (Kowatsch and Fleisch, 2021). CAs are computer programs that mimic human conversation via voice or text chat (Bickmore & O’Leary, 2023). Humans can perceive CAs as social actors (e.g., digital health assistants) and build a working alliance (Kaveladze & Schueller, 2023). The latter is an important relationship quality robustly linked to treatment outcomes (Del Re et al., 2021). DTx that use conversational agents can reach and engage individuals in a highly scalable manner (Kowatsch et al., 2021). Barriers of implementing CAs can be liability issues (Schlieter et al., 2022), for example, patient safety was often overlooked in prior work (Laranjo et al., 2018). Recent technological advances in large language models for healthcare promise safer and more accurate CAs in the future (Singhal et al., 2022).

#### 2.2.4 Design & Eval. Framework for DTx

As for the design of scalable and evidence-based DTx, digital health companies, researchers, and/or clinicians have the responsibility to validate and evaluate the effectiveness of the DTx’ individual building blocks (Kowatsch et al., 2019, Coravos et al., 2019). Therefore, a design and evaluation framework for DTx has been proposed (DEDHI) to support both researchers and practitioners (Kowatsch et al., 2019). DEDHI consists of four phases. Preparation, optimization, evaluation, and implementation. It was derived from the Multiphase Optimization Strategy (Collins, 2018) and several other frameworks, e.g., Campbell et al. (2007). DEDHI specifies the goals and tasks, technical maturity, evaluation criteria, and implementation barriers for each phase.

### 2.3 Novel Business Models

Digital health companies that focus on prevention and disease detection are underrepresented on the health continuum with most businesses focused on disease management (Cohen et al., 2020). And even though it is “far better to prevent disease than to treat people after they get sick” (Levine et al., 2019), only 3% of total US healthcare expenditures are spent on prevention (Pryor and Volpp, 2018). Against this background and the health and economic burden of NCDs and CMDs, there is a substantial need for successful business models for prevention and aging society (Coughlin, 2017). An exchange platform for DTx may be a viable business model in this regard (Wortmann et al., 2022). DTx for healthy longevity, blended with various other online or online preventive care services, can be offered and bought by different types of consumers. For example, there could be offerings like “Healthy Longevity Holidays” with a blended DTx approach, were a target person (or family) uses a DTx before and after the holidays while getting personalized on-site coaching sessions based on the data collected via the DTx during the holiday period. In another, secondary prevention example, national screening programs like Donna are offered. Donna is a program for early detection of breast cancer for women over 50. Women are automatically scheduled for a mammography and questionnaire every two years which significantly reduces mortality (Warner, 2011). Finally, Germany's DIGA concept represents an example for tertiary prevention with DTx (FIDMD, 2020). Doctors can prescribe this class of DTx while health insurance companies take over the reimbursement. The DTx *deprexis*, for example, can be prescribed as an adjunctive treatment for people with depression. It has been shown that this DTx results in better treatment outcomes than human-delivered psychotherapy alone (Berger et al., 2018). Another example is the DTx *zanadio* for individuals with obesity (Forkmann et al., 2022). The estimated revenue of DIGAs in Germany was around 55 million EUR in 2022 (McKinsey & Company, 2022). A search in the PitchBook database for privately held venture capital-backed companies in "longevity" shows a rising number of deals and total capital raised from 14 (€62.83 M) in 2017 to 49 (€333.57 M) in 2022 indicating the potential of DTx for healthy longevity.

# 3 EXAMPLES

With two specific initiatives in Switzerland and Singapore, we would like to illustrate the potential of DTx for healthy longevity according to the roadmap outlined above.

## 3.1 Switzerland

First, Switzerland was recently ranked as the most innovative country (WIPO, 2022). The key to innovation is university-industry collaboration and matching preconditions (Rajalo et al., 2017). The Switzerland Innovation initiative was invented to improve collaboration by opening innovation parks, a cluster for specific industries, e.g., in Basel for life sciences. In 2022, the Switzerland Innovation Park OST (SIP-OST) was founded in the canton of St.Gallen to focus on health, industrial engineering, and digitalization. This focus area enables opportunities for innovation in DTx. With respect to this position paper, SIP-OST is currently developing a strategy for a DTx ecosystem with a focus on healthy longevity. The region has access to clinical and non-clinical populations with the cantonal hospital of St.Gallen, the children's hospital, the geriatric clinic, the rehabilitation clinic in Gais, and the Hirslanden Clinic. For the development of minimally invasive biosensors, SIP-OST can foster the expertise of the Swiss Federal Laboratories for Material Science and Technology (EMPA). For example, EMPA developed textile-based ECG electrodes for long-term monitoring (Weder et. Al, 2015) which is now the spin-off Nahtlos. Also, this region is one of Switzerland's biggest IT hubs, and has the infrastructure to build and scale DTx for healthy longevity. The Center for Laboratory Medicine, Labor Dr. Riesch, Labor Team W, or Microsynth are some examples of laboratories focusing on biomedical analyses. Synergies with established organizations and competence centers (e.g., the cantonal hospital and the Centre for Digital Health Interventions) and the recently founded HSG School of Medicine and HSG Institute of Computer Science allow the development of scalable DTx. The HSG Chairs of Information, Technology, and Innovation Management, Entrepreneurship, Digital Health Interventions, International Business Law and Health Care Management enable the development of new business models to bring new DTx for healthy longevity to the market. A healthy start-up culture is built with initiatives like Startfeld, START Global, or Startup@HSG. In addition to the dovetailing of technological, medical, and health-economic expertise in Eastern Switzerland, it has a geographically unique location between Lake Constance and the Alps. This is particularly relevant for primary, secondary, and tertiary prevention of NCDs and CMDs, as a walk or a hike in nature promotes physical and mental health (Hansen et al., 2017). The rural areas also enable the development of DTx projects and services with a strong focus on remote monitoring and virtual clinics. The digital health company OnlineDoctor, for example, connects patients and dermatologists. Eastern Switzerland, therefore, harbors a promising ecosystem to develop innovative DTx for healthy longevity.

## 3.2 Singapore

Singapore will likely be the fifth oldest country worldwide by 2050 by median age (United Nations, 2015). The recent adaptation to their aging society will probably be an example for other nations on how to transform the healthcare system to meet the need of the global demographic shift. Healthier SG is a healthcare transformation program that addresses the aging of its population (Healthier SG, 2022). All relevant stakeholders were involved in the development of Healthier SG. At the center of Healthier SG lies the challenge of changing personal health-seeking behavior (Knittle et al., 2020) and greater emphasis on preventive care instead of curative care. Healthier SG designed a five-step process to reach the program's goals. First, everyone in Singapore will choose a family doctor, who can educate them on improving their health and who will build a relationship with them. Second, personal health plans will be developed depending on lifestyle and screening. Annual check-ins as primary prevention will be implemented. Third, local partners help people to stay on track with their health plans and, at the same time, promote social well-being. Fourth, a national family doctor health program will be implemented for over 60-year-olds in 2023. And finally, and most importantly, policies will incentivize preventive care, IT systems will be developed to ensure a seamless sharing of data, and healthcare manpower will be equipped with the corresponding skills. Additionally, DTx like H365 promote daily activity by rewarding health points which can be exchanged for vouchers.

# 4 DISCUSSION AND FUTURE WORK

It is of utmost importance to lower social inequalities in health. DTx for healthy longevity offer scalable means to reach and engage vulnerable individuals. To ensure the effectiveness of such DTx, principal investigators of clinical studies should, therefore, especially target and consider individuals with a lower socioeconomic status. This can be achieved, among other approaches, with the help of community partnerships (Bonevski et al., 2014). It is now time to give forethought to strong incentive structures and evaluation methods to promote high-quality and equitable DTx for healthy longevity. Clinicians, (business) organizations, public bodies, and regulators have the joint responsibility to design an ecosystem where innovative DTx for an aging society can strive. To come to these solutions, one must first conduct iterative, interdisciplinary, and user-centered healthy longevity studies. Feasibility, optimization, evaluation, and implementation studies must be conducted from a technical, medical, behavioral, and health economic perspective. The resources required depend strongly on which application scenario lies in focus (e.g., a healthy vs. patient population). Depending on that focus, appropriate partnerships and funding sources can be selected.

As a next step, we will work on a globally scalable DTx design and trial service based on MobileCoach.eu. The objective of this service is to accelerate the design of evidence-based DTx for healthy longevity and with it, to reduce the inequalities in health.

# 5 CONFLICT OF INTEREST

TK is affiliated with the Centre for Digital Health Interventions (CDHI), a joint initiative of the Institute for Implementation Science in Health Care, University of Zurich; the Department of Management, Technology, and Economics at Swiss Federal Institute of Technology in Zürich; and the Institute of Technology Management and School of Medicine at the University of St Gallen. CDHI is funded in part by the Swiss health insurer CSS. CSS was not involved in this research. TK is also a co-founder of Pathmate Technologies, a university spin-off company that creates and delivers digital clinical pathways. However, Pathmate Technologies was not involved in this research.

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