# PROF TAKASAKI YOHSUKE, PROF MAK VINCENT AND PROF ICHIRO KAWACHI - WRITTEN EVIDENCE (FDO0023)

Title**: Digital health and therapeutics (DH/DTx) for behavior change: An introduction for policy makers**

## Contents

## Reasons for submitting evidence

This paper serves to address the following questions presented by the Committee:

9. Lessons learned from international policy and practice, and from the devolved administrations, on diet-related obesity prevention.

10. The effectiveness of Government planning and policymaking processes in relation to food and drink policy and tackling obesity.

11. The impact of recent policy tools and legislative measures intended to prevent obesity.

12. Policy tools that could prove effective in preventing obesity amongst the general population, including those focussed on the role of the food and drink industry in tackling obesity.

https://committees.parliament.uk/call-for-evidence/3344/

## Foreword

Population aging is linked to an increase in non-communicable diseases or NCDs (e.g., diabetes, hypertension, cancer), which has significant associated financial burdens for patients and the healthcare system. For this reason it is imperative that we shift our conventional, market-centric health services and products – which rely heavily on expensive medicine and surgery – to deep-tech-driven, people-centric health promotion, disease prevention, and curative treatment through digital solutions. The latter, known as digital health and therapeutics (DH/DTx), are both necessary and effective in finding a solution to a root cause of NCDs – unhealthy behavior – and is now attracting attention. This trend is accelerated by advancement in artificial intelligence, which has tremendous potential in generating deep insights from health-related big data and real-world data – and in personalizing clinical interventions in order to steer people's behavior in healthier directions.

To unleash this potential, it is essential, especially for policy makers, to grasp the market situation, the cost-effectiveness of DH/DTx , the challenges that need to be overcome, and the opportunities to embrace. The aim of this paper is to respond to such needs by reporting: (1) a systematic literature review of scientific articles on DH/DTx; (2) a qualitative analysis of the current market situation, with a mapping exercise; and (3) a quantitative case study that aims to understand the clinical and market impacts of DH/DTx and introduce an analysis approach. The paper focuses on Japan as a case. Japan, a rapidly aging society with escalating healthcare costs related to Non-Communicable Diseases (NCDs), is actively implementing various preventive healthcare policies. These includes first setting a policy and regulatory foundation of DH/DTx utilizing digital technology and then implementing it. Japan's efforts in tackling these issues by promoting DH/DTx could thus serve as a model for other countries, including LMICs, offering a blueprint for addressing these challenges more swiftly and efficiently.

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Vincent's pedagogical experience ranges from undergraduate to MBA, executive, and PhD-level teaching. He was previously an award-winning case writer at the University of Hong Kong's Centre for Asian Business Cases (now the Asia Case Research Centre), producing over 20 business cases which have been used worldwide. His consulting work includes a study of online/offline retail prices and price comparison websites, as well as a consumer survey study on the functioning of the market for Internet access, both commissioned by the European Commission.

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## Executive summary

Population aging is linked to an increase in non-communicable diseases or NCDs (e.g., diabetes, hypertension, cancer), which is associated with significant financial burdens for patients and the healthcare system. In the search for a solution to a root cause of the rise in NCDs – viz., unhealthy behavior – "digital health (DH)" and "digital therapeutics (DTx)," i.e., evidence-based therapeutic interventions driven by high-quality software programs to prevent, manage, or treat a medical disorder or disease, have been proposed.

In this paper we report: (1) a systematic literature review of scientific articles on DH/DTx; (2) a qualitative analysis on the current market situation, with a mapping exercise; and (3) a quantitative case study on the clinical and market impacts of DH/DTx. This paper attempts to carry out far more comprehensive work than has been done so far in the analysis of DH/DTx so that the stakeholders, especially policy makers, can grasp the market situation and be introduced to an approach to calculate how cost-effective DH/DTx could be. –

The systematic literature review reveals the significant potential of DH/DTx, particularly through the application of behavioral economics and information and communication technology (ICT) in managing chronic diseases like Type 2 Diabetes (T2D) and obesity. Studies indicate that financial incentives, when thoughtfully designed to align with human psychological tendencies, can effectively motivate health-related behaviors. Moreover, ICT, including text messaging, wearable devices, and smartphone applications, have shown promise in enhancing disease self-management and facilitating weight loss, despite some limitations related to their preliminary nature and operational challenges. The effectiveness of integrating behavioral economic principles into health promotion strategies, such as using deposit contracts and lottery-based incentives, highlights the importance of incentive design. Additionally, the emergence of ICT and gamification offers new methods for implementing these strategies, broadening their applicability and impact. However, the field is in its early stages, indicating a vast "blue ocean" of opportunity for further research and application in healthcare. This domain holds promise for improving health outcomes and achieving cost-effectiveness, especially in areas with limited resources.

Our qualitative analysis through market research sheds light on the burgeoning landscape of DH/DTx, underscoring their reliance on ICT and

Artificial Intelligence (AI) technologies. This investigation reveals a dynamic yet nascent market characterized by a preponderance of early-stage startups, primarily concentrated in the United States and, to a lesser extent, the United Kingdom, with the Asian region's potential still emerging. These entities predominantly focus on health promotion and behavioral modification prior to and following clinical intervention, employing methods such as gamification, lifelogging, and remote monitoring, often supplemented with online consultation and coaching. However, a notable gap in the utilization of scientific and clinical evidence, alongside a deficiency in medical expertise among company leadership, raises questions about the liability and capacity of these ventures. Additionally, technological sophistication, particularly in AI and behavioral economics applications like nudging and choice architecture, remains in its infancy, indicating significant room for advancement. Regulatory barriers further complicate market entry, highlighting the need for global harmonization of regulatory frameworks to foster innovation and growth in the DH/DTx sector.

Our cost-effectiveness analysis on DH/DTx in Japan demonstrates their potential as cost-effective solutions. Utilizing conservative assumptions and following international guidelines, we found DH/DTx interventions to be financially viable. This suggests that DH/DTx not only offers a competitive alternative to traditional interventions but also significantly reduces the financial burden of diabetes on the healthcare system.

Finally, the paper concludes by proposing that an interdisciplinary and sectoral approach among the government, business and academia needs to be promoted in the area of DH/DTx with a strong initiative taken by the government. The proposed approach includes interdisciplinary research and development environment, a mechanism of applying behavioral economics in DH/DTx-related policies and business, further creation and use of evidence for applications, and the building of regulatory frameworks and a venture ecosystem. The paper also highlights the importance of facilitating multi-industrial competition and collaboration, such as among pharmaceutical companies, medical-device manufactures, DH/DTx-specialized ventures, and others.

# 1. Background to the study

## 1.1. Pressing needs to address NCDs globally: Obesity and Japan as an example

The increase in NCDs in recent decades, as a result of an aging population and obesity, is creating significant financial burdens globally. Since 1975, global obesity rates have nearly tripled. By 2016, over 1.9 billion adults aged 18 and older were classified as overweight, with more than 650 million suffering from obesity. This statistic indicates that approximately 39% of the adult population is overweight, while 13% are obese (WHO, 2021) (The Lancet Gastroenterology & Hepatology, 2021). The World Obesity Atlas 2023 indicates that if current trends continue without significant improvements in prevention, treatment, and support, over half of the global population will be living with overweight or obesity within the next 12 years (*World Obesity Atlas*, 2023).

Obesity is not a single-cause illness. Rather, multiple factors, including food intake, metabolism, energy expenditure, and physical activity, among others, affect weight gain, eventually resulting in obesity (Blüher, 2019). While the increase in calorie intake is related to the energy density of foods, especially fats and sugars, the decrease in metabolism is due to physical inactivity, resulting from, for example, a sedentary work style and transportation development with increasing urbanization and mobility (WHO, 2021).

As mentioned in the beginning of this paper, overweight and obesity are major risk factors for NCDs, which have been the leading cause of death, diabetes, and certain types of cancer, for instance, endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon (WHO, 2021). In 2017, obesity accounted for 8% of global mortality, an increase from 4.5% in 1990 (Ritchie and Roser, 2023).

If obesity were to remain at 2010 levels, at a prevalence of 5%, the estimated medical expenditure over the next 2 decades would be $549.5 billion, while a 1 percentage point reduction from the trend would reduce obesity-attributable medical expenditure by $84.9 billion. Furthermore, if obesity prevalence were kept as high as 15% constantly, obesity-attributable medical savings would total $1.9 trillion (Finkelstein *et al.*, 2012). These statistics underscore the urgent need for global initiatives to address the spread of obesity through improvements in medical policies, awareness campaigns, and interventions in lifestyle (Ritchie and Roser, 2023).

Obesity and diabetes are highly related. According to the results of multi-ethnic cohort studies, there is a strong relationship between body mass index (BMI, which is used as a rule of thumb to suggest obesity if it is too high) and diabetes in all ethnic groups (Maskarinec *et al.*, 2009). The BMI cut-off for disease onset was found to be substantially lower in Asian ethnic groups than among Westerners (Chiu *et al.*, 2011). For example, even though Japan's obesity rate is quite low compared to international standards, Japan ranked fourth in the world in terms of the number of diabetes patients in 2014, which is 10.8 million and represents 2.6% of global diabetic patients (Zhou *et al.*, 2016). The racial disparities in the incidence of obesity and diabetes are attributed to differences in dietary habits and genetic backgrounds. In Asian diets, carbohydrates serve as the primary source of energy, and foods with a high glycemic index can lead to elevated blood sugar and insulin responses, promoting insulin resistance and type 2 diabetes (T2D) (Mohan *et al.*, 2018). Regarding genetic backgrounds, East Asians have a higher frequency of genetic variants related to insulin secretion compared to Western populations, increasing the risk of developing T2D (Spracklen *et al.*, 2020). Thus, Japanese individuals have lower insulin secretion capabilities compared to Westerners, making them more susceptible to developing T2D even with mild obesity (Kodama *et al.*, 2013). At the same time, improvements in obesity are suggested to be particularly effective in managing T2D among Asian populations, including Japanese (Yang *et al.*, 2023).

Given these genetic factors, countries like Japan, despite having a lower obesity rate in international comparisons, still suffer from the impact of obesity on the development of diabetes, and improvement in obesity is effective in preventing diabetes. Consequently, in the Asian region, the prevention of diabetes underscores the importance of behavioral changes, including improvements in dietary habits (high carbohydrate consumption) and physical activity, addressing obesity and its upstream causes.

Moreover, the incidence of T2D was estimated to be at 8.8 (95% confidence interval, 7.4–10.4) per 1,000 person-years in a systematic review (Goto *et al.*, 2013). If Japanese people can lose around 2 kg by improving their lifestyle, they can delay the progression to diabetes (Kosaka, Noda and Kuzuya, 2005) (Kawahara *et al.*, 2008) (Saito *et al.*, 2011). A recent study in the US also showed that half of the cases of T2D could be prevented by reducing obesity (Cameron *et al.*, 2021).

The substantial economic costs for patients, households, health systems, and entire national economies resulting from diabetes and its complications,

including the direct costs of treatment and loss of work and wages, are significant. As an example, the annual financial burden of diabetes in Japan is $37 billion, based on the estimation in 2014 (Seuring, Archangelidi and Suhrcke, 2015). Among them, national medical expenditure for diabetes in Japan was 1.2trillion JPY (= 10.6 billion USD) in 2019 (Ministry of Health, Labour and Welfare Japan, 2021).

As observed from the example of diabetes above, Japan has no choice but seriously addressing the rapidly aging society and the continually increasing healthcare costs related to NCDs (Saito, 2014; Nomura *et al.*, 2017). Actually, various policies for preventive healthcare have been implemented. Japan achieved Universal Health Coverage through a national health insurance system, making the role of insurers particularly crucial in policy terms for preventive healthcare. Since 2015, Japan has mandated all insurers to create, publish, and implement a "Data Health Plan" to analyze health-related data such as medical check-ups and health records (Ministry of Health, Labour and Welfare, Japan, 2015). Based on this analysis, the Plan includes proposing customized health management plans tailored to the health status and lifestyle of individual subscribers, promoting early detection and treatment of diseases, reducing medical costs, and extending healthy lifespan.

Furthermore, in 2022, the Japanese government launched the "Medical DX Reiwa Vision 2030" policy to strengthen and promote comprehensive reforms in the economic and fiscal management of the social security sector (Ministry of Health, Labour and Welfare, Japan, 2022). This policy entails building a national platform for health and medical information using the public personal identification and data infrastructure (“the My Number system”). It is expected to facilitate easy access for citizens to their health and medical information (including care), enabling them to use this information for maintaining and enhancing their health.

Having laid a policy and regulatory foundation for utilizing digital technology in DH/DTx, Japan has earnestly commenced efforts toward the social implementation of DH/DTx (details to be discussed in the following section). The Japanese government aims to resolve medical challenges associated with changes in Japan's demographic dynamics and the consequent alterations in disease structure, specifically the increase in NCDs, such as lifestyle-related diseases including obesity. Such challenges are universal to the modern world where those with middle and low incomes will also sooner or later face.

Japan's efforts to tackle these challenges and promote DH/DTx serve as a role model for many other countries to enable them address these issues more swiftly and efficiently. This paper discusses Japan as a case study of a country at the forefront of addressing these challenges, taking obesity, a lifestyle-related NCD, as an example.

## 1.2 DH/DTx as a new solution for health

Under the universal trend of demographic shift and disease shift alterations as seen in the previous section, it is imperative that we upgrade from conventional, market-centric health services and products, which rely heavily on expensive non-curative medicine and surgery (the "downstream approach"), to deep-tech-driven, people-centric health promotion, disease prevention, and curative treatment through digital solutions, such as smartphones and apps (the "upstream approach").

The latter is known as DH/DTx. The advancement of artificial intelligence (AI), one of the main components of the Fourth Industrial Revolution, allows deep insights to be generated from big data and real-world data, in addition to the personalization of clinical interventions to steer people's behavior in a healthier direction which will be looked into more in details below. Thanks to both technological advancement and its more enabling environment, we are entering the next generation of healthcare as such, which will make our health systems and society more sustainable.

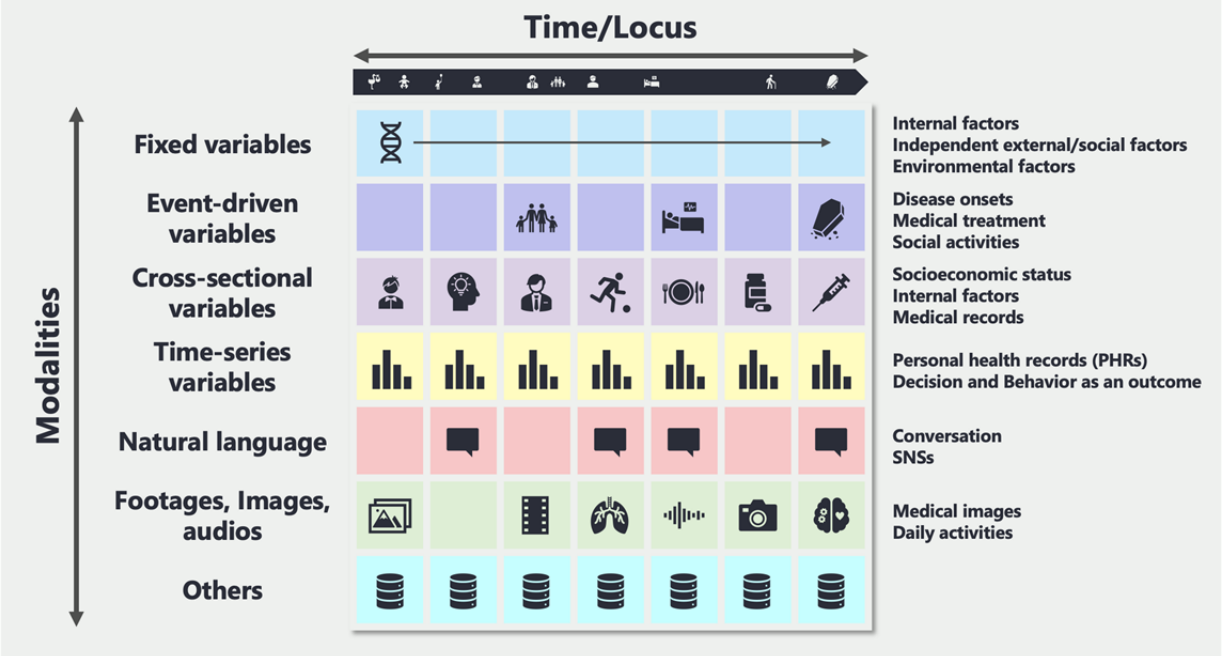
DH/DTx, unlike traditional medical treatments such as surgeries that physically remove tumors or drugs that have chemical and pharmacological effects, influence higher brain functions such as cognition and behavior. They have the potential to prevent and treat almost all diseases, including obesity, caused by individual cognition and behavior by encouraging behavioral change towards healthier diets, drinking habits, increased physical activity, and smoking cessation. This represents an area that was difficult to approach with traditional medical treatments, such as drugs or surgical procedures. For example, it is difficult to imagine becoming able to quit smoking through surgery or increasing vegetable intake by taking a pill.

Specifically, since apps or websites can aggregate users' historical time-series data, companies in IT-related industries (eCommerce, SNS, sharing economy, etc.) will be able to personalize their services with sophisticated AI technology to maximize customer engagement and enhance profit. As smartphones and wearable devices have become able to sense many

health-related parameters, the data can also be utilized more in medical research now.

Most recently, precision medicine, a data-driven approach, tailors treatments to individual genetic profiles, medical histories, and lifestyles, diverging from traditional "one-size-fits-all" methods (Ministry of Health, Labour and Welfare, Japan, no date). Therefore, it is reshaping healthcare by focusing on personalized data to create customized treatment plans. Figure 1 illustrates the lifespan data utilized in this approach. Due to the limitations of hypothesis-driven research in complex diseases, it has been advocated recently to promote the data-driven approach that is able to intricately analyze interrelated factors and enhance the understanding of complex disease mechanisms (Chiba University, 2020). This approach not only aims for more effective care with fewer side effects but also adapts to a broad range of diseases, including cancer, heart disease, and diabetes, through continuous patient monitoring and treatment adjustments. To fully exploit these benefits in a clinical setting, and thereby to bring medical science to the next level, the medical industry must import methodologies that other industries have been using to handle personal time-series data generated by mobile devices.

**Figure 1.** Diversity of health and medical information throughout the lifespan



## 2. Behavioral economics for health including DH/DTx

Behavioral economics, an economic discipline that emerged in the past 50 years, has revealed that human behavior is not perfectly rational and is often influenced by behavioral regularities such as decision framing and other psychological biases. As such, human behavior has been also deemed to be potentially modifiable with interventions through choice architecture with features such as the strategic use of default options. In recent years, behavioral interventions utilizing behavioral economics, called "nudge strategies," have gained popularity globally. The fruits of such behavioral economics have since been applied to the real world to modify individual behavior in a wide range of fields, ranging from marketing to management. Here, we briefly review a number of major concepts of behavioral economics including default options, loss aversion, framing effects, anchoring effects, and time discounting behavior (such as hyperbolic discounting and present bias), all of which could be useful to refer to in making relevant policies and business strategies. Our discussion builds on a work of by one of the authors, "Behavioral Economics and Public Health," that provides a pioneering exploration of applying insights from behavioral economics to address serious public health challenges, such as obesity, smoking, and excessive drinking (Kawachi, 2015). We will also discuss some examples of their utilization and their potential application in DH/DTx.

### 2.1 Default option

To begin with, a notable concept is the study by Johnson and Goldstein in 2003, which highlighted the default option effect in the context of organ donation (Johnson and Goldstein, 2003). Their research showed how default settings can dramatically alter participation rates and decision outcomes, emphasizing the power of pre-selected choices in critical decision-making scenarios. However, recent evidence presents a more complex picture of the effectiveness of default settings. Studies suggest that the impact of an opt-out organ donation system is more nuanced than previously thought, with some effects being limited and accompanied by indirect consequences and negative reactions (Molina-Pérez, Rodríguez-Arias and Delgado, 2022). This evolving understanding indicates that a single solution, like the opt-out system, may not suffice to significantly

affect behavioral changes related to health, such as enhancing organ donation rates. Instead, a broader, multi-faceted approach that acknowledges the complexity of human behavior and incorporates various societal, ethical, and psychological considerations is necessary to effectively influence individual behavior across different domains.

## 2.2 Loss aversion

Moreover, in terms of the psychological factors underpinning consumer purchase decisions, crucial role of behavioral economics had been noted from as early as in the 1970s. One of the central concepts of behavioral economics is loss aversion (Kahneman and Tversky, 1979). This understanding is pivotal in formulating effective product marketing strategies. Loss aversion posits that the distress associated with losses is perceived to be greater than the satisfaction derived from equivalent gains. The neurological mechanisms underpinning loss aversion are built upon the premise that specific brain regions process losses and rewards differently under risk (Tom *et al.*, 2007). By understanding these neuroeconomic underpinnings of human decision-making, interventions can be designed to frame health behavior choices from the perspective of avoiding losses (e.g., deterioration of health), rather than achieving gains (e.g., improvement in physical fitness). Moreover, experiments on loss aversion have demonstrated that framing academic achievement in terms of potential losses (point deductions for underperformance) rather than gains (point rewards for achievement) significantly improves effort and success (Bećirović, Zahirović Suhonjić and Stanić, 2022). When applied to DH/DTx, this framing effect suggests that presenting options with an emphasis on avoiding negative outcomes (e.g., forfeiting monetary deposits for failing to achieve behavioral targets) can more effectively motivate behavior change than awarding positive rewards.

## 2.3 Anchoring effects

As further concept that is related to marketing, more specifically to pricing strategies, is the anchoring effect. The effect has been shown to significantly sway consumers' valuation of products, in the case of initial price points serving as psychological anchors. These anchors, whether derived from external influences or internal benchmarks, fundamentally alter the perception and allure of subsequent price adjustments, such as

discounts. The persistence of this effect across various sectors underscores its robust influence on consumer psyche and decision-making in the realm of pricing. (Ariely, Loewenstein and Prelec, 2003; Simonson and Drolet, 2004) (Briesch *et al.*, 1997; Zong and Guo, 2022) An example of the anchoring effect applied in the design of interventions through DH/ DTx could be a weight management app. It calculates a recommended daily caloric intake based on the user's health and medical information, presenting this figure as an "anchor," and subsequently, a more lenient caloric intake goal is set (for instance, a target 20 to 30 percent higher in calories higher than the anchor). Due to the anchoring effect, users might perceive the lower goal as more achievable in comparison to the initially seen higher intake, thus promoting behavior adjustment (Paek, Yoon and Hove, 2011). In this manner, leveraging the anchoring effect aids users in gradually adjusting their perception of their caloric intake, supporting healthy weight management.

## 2.4 Time discounting behavior

Also, behavioral economics provides a plethora of insightful implications for understanding how individuals evaluate and compare present and future rewards or outcomes in their decision-making processes over time. The characteristics of time discounting behavior, wherein future rewards are prioritized less than immediate ones, lead people to value immediate benefits over future gains, often opting for short-term gratification over long-term health outcomes (Thaler, 1981). Particularly, the phenomenon of hyperbolic discounting, which implies a disproportionate valuation of nearer future rewards over those further in the future, suggests that a strong preference for immediate rewards poses a challenge in health behavior change (Laibson, 1997). This inclination to overly value present rewards and undervalue future ones, known as present bias, stands as a significant obstacle for health promotion programs and interventions, illustrating a tendency among individuals to choose short-term pleasures over long-term health goals (Thaler and Shefrin, 1981). This becomes crucial, for example, when considering how an individual makes choices (Inter-temporal choices) between immediate pleasures (O’Donoghue and Rabin, 1999), such as consuming junk food, and long-term health benefits, like reducing the risk of heart disease. Applying these concepts to DH/DTx could entail the following: To counteract time discounting and present bias, and enhance user engagement, features that reward health behaviors immediately could be integrated into apps and platforms. For instance,

providing a sense of small achievements instantly, such as earning virtual badges after exercising, is a feature already implemented in many smartphone applications. Furthermore, to mitigate the effects of hyperbolic discounting, functionalities that allow for the setting of short-term, achievable health goals and the visualization of progress could be effective. By accumulating small successes, users can maintain motivation towards long-term health objectives. Additionally, analyzing user behavior patterns to predict tendencies towards time discounting and present bias allows for the suggestion of more personalized treatment programs and interventions. Providing appropriate information and encouragement when users are making choices between short-term satisfaction and long-term health benefits would be able to promote healthier decisions. An example includes dietary tracking apps suggesting healthier alternatives when junk food is chosen, thereby enabling the execution of health promotion strategies tailored to each user's needs.

## 2.5 Paternalistic Libertarianism and Nudge Strategies: Behavioral Economics in Policy Application

The above examples of major behavioral economic concepts all find application potential with policy makers who seek to change health-related behaviors. This approach is underpinned by the philosophy of paternalistic-libertarianism, which is closely affiliated with nudge strategies and championed by Richard Thaler and Cass Sunstein (Thaler and Sunstein, 2003, 2009). The philosophy posits a framework wherein governmental and institutional bodies subtly guide individuals towards more beneficial choices in various spheres, including health, financial savings, and environmental stewardship. This paradigm operates under the auspices of maintaining individual autonomy while subtly orchestrating choice architecture to favor more advantageous decisions. Illustrative of this are strategies such as the strategic placement of healthier food options in more prominent locations to simplify healthier food choices, or the implementation of default enrolment in pension schemes with the provision for voluntary opt-out. Such methodologies are acclaimed for their efficacy in fostering socially beneficial behaviors while simultaneously preserving the essence of personal freedom.

## 3. Ethical consideration in promoting DH/DTx with behavioral economics

In promoting DH/DTx with the aforementioned concepts of behavioral economics, the principle of "Informed Consent", a cornerstone of contemporary medical practice, should be taken into consideration. This principle necessitates that prior to the administration of any medical procedure or treatment, the patient is required to provide voluntary consent, which is contingent upon a comprehensive briefing and subsequent understanding of various critical facets. These facets include the nature of the procedure or treatment, its potential benefits and risks, available alternative treatments, and the implications of opting against the proposed medical intervention. The ethos underlying the concept of informed consent is fundamentally rooted in the reverence for patient autonomy, ensuring the patient's right to self-determination. Additionally, it serves as a safeguard for maintaining transparency and upholding patient rights within the medical practice.

In contrast to the relatively direct correlation between informed consent and the observed pharmacological effects or side effects of conventional medications, the dynamics of behavior change for disease prevention and health promotion are more intricate. Behavioral change, utilizing the findings of behavioral economics, operates by appealing to individuals' instinctual aspects, and often remains largely unrecognized by the individuals it targets in terms of both existence and intent. Consequently, as illustrated in the case of default settings significantly influencing choices for organ donation (Johnson and Goldstein, 2003), interventions such as default options effectively intrude upon the realm of personal choice. This intrusion extends to informed consent, a crucial element of autonomous decision-making. Such interventions, while effective in guiding behavior, raise ethical concerns about the extent to which they alter personal agency without explicit acknowledgment or consent from the individuals affected.

These interventions often entail a complex interplay between immediate desires and long-term health objectives. Within this context and as seen in the previous section, DH/DTx, grounded in the principles of behavioral economics, are posited to play a pivotal role. DH/DTx, as a modality, operates under the principal-agent paradigm, where it assumes the role of an agent tasked with prioritizing the long-term health interests of the patient, the principal. This approach involves navigating and often contradicting the patient's short-term needs or desires, with the ultimate goal of ameliorating healthcare outcomes over the medium to long term.

More concretely, it encompasses balancing long-term objectives, like the goal of weight loss and its resultant health benefits, against short-term desires for immediate gratification, such as the impulse to consume a piece of cake. The latter represents not only a momentary craving but also the potential pleasure (or opportunity cost) foregone in favor of longer-term health benefits. The ultimate mission of DH/DTx is to maximize the total utility over an individual's lifetime. This requires a sophisticated understanding of the interplay between immediate sensory desires and long-term health goals, and the ability to navigate these often conflicting motivations in a way that optimally promotes overall well-being.

In the realm of behavioral modification, it is imperative to adhere to principles of ethical caution and transparency. This approach is essential to maintain the integrity of such practices, balancing their effectiveness with a respect for individual autonomy and informed choice. Ethical transparency, in particular, is crucial to ensure that individuals understand how their behavior is being influenced and for what purpose, thus preserving their rights and the legitimacy of the behavioral modification methodologies employed.

Given this scenario, there emerges a need for a novel and comprehensive medical agreement framework, specifically tailored for DH/DTx interventions. This framework should ideally embody a paternalistic approach, reflecting the necessity to guide patients towards beneficial health behaviors while considering their immediate preferences and inclinations. Concurrently, appropriate regulatory measures are essential to ensure that such interventions are executed ethically, respecting patient autonomy and the overarching goals of healthcare.

To achieve behavior change that adheres to medical ethics while respecting patient autonomy, Richard Thaler's "rules" for when it is appropriate to nudge serve as a valuable reference. His rules for ethical nudging emphasize transparency, simplicity, freedom of choice, welfare improvement, evidence-based strategies, cost-effectiveness, and ethical considerations. They advocate for nudges that are open, non-coercive, beneficial according to individuals' own preferences, grounded in empirical research, economically efficient, and respectful of autonomy and ethical standards. The goal is to help individuals make better decisions without limiting their options or manipulating their choices (Thaler and Sunstein, 2009).

For example, applying the principles of nudging in public health and medical contexts could involve placing healthier food options in prominent

places in cafeterias or making calorie information clear to encourage healthier eating choices, as well as designing urban environments that encourage regular physical activity through walkable spaces. These interventions facilitate healthier choices among individuals without restricting their freedom or manipulating their choices. Thus, the application of nudging in public health and healthcare interventions should focus on assisting individuals in making better health decisions based on their own preferences and needs, aiming to improve the overall health and wellbeing of society.

On the other hand, interventions that should not be applied are those that substantially limit freedom of choice through inadequate provision of information. For example, mandating the use of specific health services such as colorectal cancer screening, or deliberately hiding alternative options. These interventions could infringe upon individual autonomy and the ability to make informed choices.

Furthermore, research on public health nudging by Theresa Marteau and colleagues highlights that while nudging is widely recognized as a means to change human behavior and improve public health, its effectiveness requires scientific scrutiny. They emphasize the importance of evidence demonstrating the actual benefits of nudging for individual and collective health improvement (Marteau *et al.*, 2011).

## 4. Recent development of AI to facilitate health-related applications of behavioral economics

When visiting the App Store or Google Play and searching for apps using keywords, numerous apps offer services related to health promotion, disease prevention, and treatment adherence. However, the capability and liability of their services, including whether or not they are based on scientific evidence, are unclear. If an app could demonstrate solid scientific evidence about its clinical effectiveness or the methods of behavioral economics that it uses, it could become an innovative solution to the challenges that we face, especially regarding NCDs such as diabetes and hypertension.

Moreover, the emergence of ChatGPT, an AI chatbot released by OpenAI in November 2022 and built on a large language model (LLM) called the generative pre-trained transformer (GPT), has attracted a great deal of

attention. ChatGPT has shown an intelligence level equivalent to that of experts in some areas, and further social implementation and industrial use of such LLMs are expected in the future. The Center for Research on Foundation Models (CRFM) of the Stanford Institute for Human-Centered Artificial Intelligence proposed the term "foundation model" in August 2021, defining it as "any model that is trained on broad data (generally using self-supervision at scale) that can be adapted (e.g., fine-tuned) to a wide range of downstream tasks" (Bommasani *et al.*, 2022).

The CRFM report also mentions the medical applications of foundation models (Bommasani *et al.*, 2022). Just as LLMs learn from multimodal information such as text, images, video, and audio, in the medical field diagnosis and treatment are based on a vast amount of multimodal data such as doctors' records, diagnostic imaging such as CT and MRI, video such as four-dimensional ultrasound scans, and numerical data such as blood tests, and treatment is conducted based on a vast amount of multimodal data.

For example, the first author of this paper combines knowledge of behavioral economics with a foundation model based on such health and medical data to develop algorithms to promote behavior change that is optimized for each individual. In the future, DH/DTx is expected to be able to diagnose and predict diseases and generate optimal treatments for individuals by utilizing the foundation models built using health and medical data. As for the societal implementation of DH/DTx as behavioral change through the integration of foundation models and behavioral economics, it is conceivable, for example, to predict moments when consumers are likely to be tempted by smoking, drinking, skipping the gym, or visiting fast food outlets, and to provide nudges through smartphone apps in real-time to overcome these temptations. Of course, this technology is a double-edged sword, possibly being utilized to tempt consumers into taking precisely opposite actions for commercial purposes.

## 5. Literature review, with a focus on obesity

Unlike business services, the health and medical products and services are highly regulated around the world. They are designed to prevent or cure specific diseases and to promote health in general. If they are not based on firm scientific evidence, these products and services can harm – or even

kill – patients or users. Such scientific evidence should be produced in accordance with strict clinical-trial protocols and published in peer-reviewed scientific journals. Thus, searching scientific articles helps us to predict next-generation health and medical solutions that are not only innovative but also viable and reliable. We report a literature review in this section, focusing on obesity and interventional studies that can prove causality in higher-quality (rather than observational) studies.

In a comprehensive systematic review conducted in 2017, Kullgren *et al*. found 15 studies on T2D that used a variety of study designs and outcomes to test behavioral economic interventions in clinical, workplace, or health-plan settings (Kullgren *et al.*, 2017). They reported the following:

- ✓ 2 studies found that financial incentives increased weight loss;
- ✓ 2 studies used choice architecture modifications, and they had mixed effects in encouraging the completion of tests to screen for diabetes; and
- ✓ 11 studies focused on improving the self-management of diabetes.

Moreover, Wang *et al.* (2017) reviewed the application and effectiveness of Health interventions using mobile technologies (mHealth) for obesity and diabetes treatment and self-management. They found that 24 studies met the inclusion criteria, which were categorized into 3 types: mobile-phone text messaging, wearable or portable monitoring devices, and applications running on smartphones. While most are pilot studies or face certain constraints, some studies suggest that mHealth interventions are effective (Wang *et al.*, 2017).

Regarding financial incentives, Jeffery conducted a systematic review of studies on financial incentives and weight control between 1972 and 2010, finding that earlier studies had focused on operant learning concepts from psychology, while more recent studies relied on economic theory. The findings vary widely because of differences in incentive size and schedule, as well as contextual factors; for this reason, the question about the use of incentives had not been clearly answered (Jeffery, 2012). Then, Hoskins *et al.* (2019) also reviewed 81 studies about financial incentives for health-related behavioral change. Generally, rewards were preferred over penalties or lotteries, vouchers over cash, and smaller values over large (Brockmeyer *et al.*, 2017) (Finkelstein *et al.*, 2017) (Glanz *et al.*, 2019) (Jay *et al.*, 2019) (Kranker, 2018) (LaRose *et al.*, 2020) (Lesser, Thompson and Luft, 2018) (Michaud *et al.*, 2020) (Miranda *et al.*, 2018) (Shaw *et al.*, 2017) (Yancy *et al.*, 2019).

The traditional application of financial incentives for health-related behavior change had largely depended on principles of standard economic theory as mentioned above. However, contributions from behavioral economics lie not just in supporting monetary incentives but in the strategic design based on an understanding of human cognition to maximize their effects.

For example, as previously mentioned, insights from behavioral economics suggest that employing strategic penalties leveraging loss aversion, a negative economic incentive, could result in more effective behavioral change. The concept of hyperbolic discounting demonstrates a tendency for individuals to value immediate rewards over future greater ones. In health promotion strategies, leveraging this understanding can encourage participation in long-term health behaviors through immediate small benefits. Moreover, the impact of the same monetary incentive can significantly vary depending on the method of payment in behavioral economics. For instance, deposit contracts, which involve depositing money that is returned upon goal achievement, use loss aversion psychology to enhance motivation (Paxton, 1981). Conversely, prospective payments reward specific actions or outcomes upon achievement. A recent study systematically reviewed and conducted a network meta-analysis to assess the effectiveness of behavioral economic incentive programs in promoting healthy diets, weight control, and physical activity. The research meticulously analyzed data from 35 eligible randomized controlled trials, focusing on the impact of standard financial incentives and those enhanced with behavioral-economic insights on achieving health-related goals. The findings revealed that deposit contracts significantly outperform no incentive in promoting diet-weight control and physical activity, with lottery-based incentives also showing effectiveness but primarily in the short term. The study underscoreed the potential of integrating behavioral-economic principles into incentive programs to enhance their effectiveness in motivating healthy behaviors (Boonmanunt *et al.*, 2023).

Along with the advancement of information and communication technology (ICT), research on gamification (Cotton and Patel, 2019) (Fortunato *et al.*, 2019) (Patel *et al.*, 2021) and Internet-based interventions has also started to be reported relatively recently. Specifically, Internet-based interventions seem to be expanding the possibility of using behavioral

economics – and their capability – for intervention (Brandt *et al.*, 2020) (Hu *et al.*, 2020) (LaRose *et al.*, 2021) (Leahey *et al.*, 2014).

It has been found that the target disease (Ismail *et al.*, 2019) (Janssen *et al.*, 2017) and settings such as primary settings, the workplace, communities, and households, among others (John *et al.*, 2018) (Navathe *et al.*, 2019) (Saelens *et al.*, 2017) (Saxon *et al.*, 2019), have diversified. Some studies also demonstrated high cost-effectiveness, particularly in rural and remote settings, where limited resources and alternatives are available (Estabrooks *et al.*, 2017) (Horstman *et al.*, 2021) (Krishnan *et al.*, 2019) (Krukowski *et al.*, 2011) (Radcliff *et al.*, 2020).

Despite some positive findings, the systematic review revealed that behavioral modification based on major behavioral economics concepts, has not been fully promoted in healthcare through effective use of data and a deep understanding of behavioral economics. Both scientific studies and actual projects are at the early stages, making this area a "blue ocean." Further synergies of ICT technologies and behavioral modification, based on the principles of major behavioral economics that can be used for medical and health products and services, should be materialized in healthcare, as in other fields.

## 6. Qualitative analysis on the market situation of DH/DTx

As discussed, new and innovative products for DH/DTx rely on ICT and AI technologies. Therefore, many start-ups are emerging that have sufficient expertise in ICT and AI to take tremendous risks. In this section we briefly and qualitatively look at the market situation of DH/DTx.

As far as regulatory registration and schemes that affect market situation are concerned, global efforts to harmonize regulatory systems among countries are needed, as such systems are still barriers to entry for innovators and start-ups when it comes to recent situations in countries such as Japan, the UK, and the US, up to 2022 (Pharmaceuticals and Medical Devices Agency Japan, 2021) (Medicines and Healthcare products Regulatory Agency the UK, 2014) (US-FDA, 2022).

The first author conducted a mapping exercise on companies that are active in the area of apps related to diabetes as of early 2022. While the mapping exercise sheds light on obesity in general, the features of apps

dealing with obesity are varied, including whether or not they are based on scientific evidence; therefore, a further focus was necessary. While the details of this mapping are too vast to be included in this paper, we report the following key findings on the relevant market situation:

1) **Scale of the market:** In terms of the entire global market of DH/DTx, it is forecast that it will reach a $56 billion global opportunity by 2025 (Insider Intelligence, 2021).
2) **Development stage of companies:** Since DH/DTx are new concepts and trends, there is a limited number of later-stage start-ups, with the early-stage start-ups still dominant. No giant platformer exists to date.
3) **Regional gap:** The US, especially Silicon Valley, is a center of DH/DTx, while the UK also has a few promising start-ups. Some potential start-ups have their origins in the Asian region, but their activities are still under-represented in the global market.
4) **Phases of service**: Most start-ups focus on the phases of health promotion before visiting hospitals or on behavioral changes such as diet and exercise and follow-up treatment post-visit (please refer to Figure 6, which clearly shows the service phase).
5) **Methods of intervention:** Gamification, lifelogging, and remote monitoring, often combined with online consultation and coaching, are popular features.
6) **Use of evidence:** It seems that many of these start-ups neither utilize scientific and clinical evidence, nor have executives with a medical background, suggesting that their liability and capacity are questionable.

7) **Technological level:** The levels of AI technologies are not yet advanced, with further improvement expected. Few start-ups seem to have introduced nudge, default option, choice architecture, or other behavioral modification methods.

## 7. Financial impact of DH/DTx with a focus on Japan – A cost-effective analysis case study

Having learnt through the mapping exercise that an untapped market opportunity and business viability do exist, it is useful to analyze these issues quantitatively. In this section, we report a cost-effective analysis (CEA) focusing on the relationship between obesity, diabetes, and its

complications, using epidemiology and statistics for these three elements and with a focus on Japan as a case study.

To analyze the clinical and market impacts of DH/DTx from a government's perspective (as a purchaser or provider), CEA is one of the most effective methodologies for health economics to compare the costs and clinical effects of alternative health interventions. Policy-makers can use CEA results to achieve a specific health objective by selecting the most effective measure under a budget constraint. The cumulative costs and effects of a target product should be combined into a single metric, that is, cost per health outcome.

Here, we report a simplified CEA with some empirical assumptions and without time discount, detailed costs, and so on, following the guidance of the UK Health Security Agency (UK Health Security Agency, 2020) and WHO Guide To Cost-Effectiveness Analysis (Edejer and World Health Organization, 2003). The data used for the estimation, such as the incidence and prevalence of diseases, are aggregated from academic journals, with realistic assumptions.

We use the UK approach because the UK's National Health Service (NHS) and its affiliated National Institute for Health and Care Excellence (NICE), whose role is "to improve outcomes for people using the NHS and other public health and social care services," are world leaders in health economics analysis, including CEA in the public health sector (National Institute for Health and Care Excellence, no date). Since the NHS is financed through public funding (tax revenue), the UK government is keen to ensure the cost-effectiveness of its services, expecting NICE to take a leading role in this regard.

It is also important to consider which perspective (e.g., the patient's or the whole society's) is chosen, since, depending on the perspective chosen, the benefits and effectiveness vary, in addition to choice (GOV.UK, 2020). For the patient, the concern is whether a solution is directly beneficial to them: collective benefit is not of interest. For society as a whole, not only health expenditure but also wider social costs and benefits should be considered and included. Of course, healthcare providers, including hospitals, welcome profitability when introducing a solution.

The UK government also publishes guidelines to evaluate digital health products (UK Health Security Agency, 2020). Throughout the CEA in this chapter, this paper follows theses step-by-step guidelines; the six steps are shown below:

## ***STEP1: GET STARTED***

The evaluation approach at the very first stage of conducting CEA is as follows:

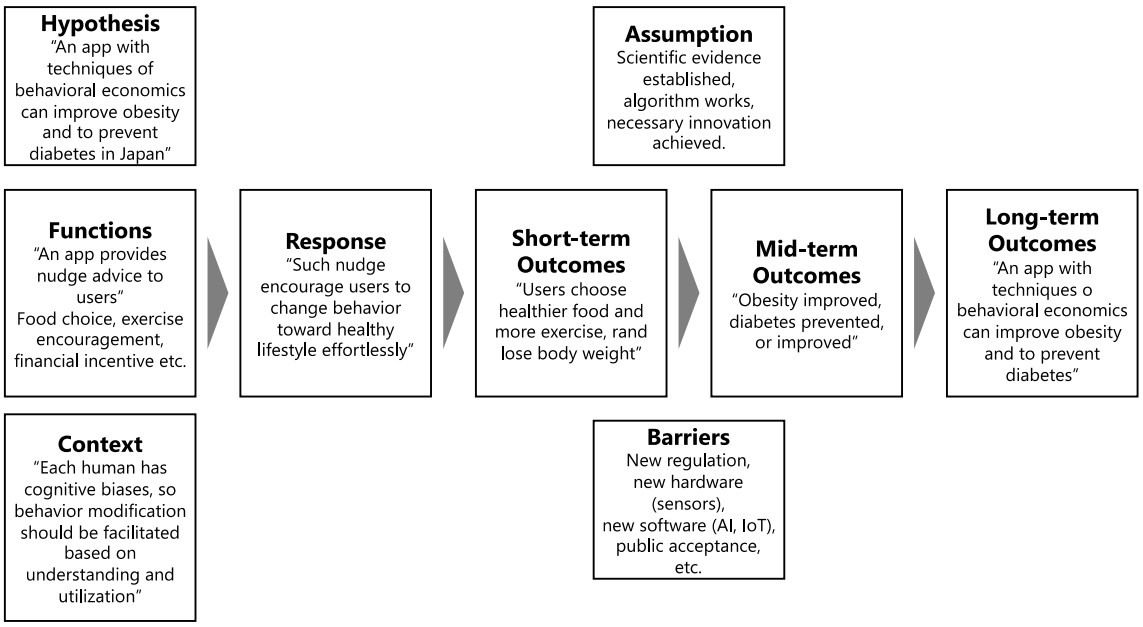
1) The purpose is "to improve obesity and to prevent diabetes in Japan."
2) The perspective is from the "Ministry of Health, Labour, and Welfare Japan" as a health-service policy-maker.

To proceed, we make use of the necessary data for CEA from the research and discussion briefly presented in the sections above.

## ***STEP2: DEFINE HOW A PRODUCT WORKS***

In order to clarify what the product does, and how it is expected to create the desired change, the following sample model for a digital health product provided by the guidelines is applied to a product designed to improve obesity and prevent diabetes through behavioral modification, specifically, nudge:

**Figure 2.** Model for a DH/DTx product using the behavioral economics technique



## ***STEP3: DESIGN YOUR EVALUATION***

Cost-effective analysis ultimately consists of two elements: costs and effectiveness. To be fair and safe, strict and conservative assumptions are made about both elements, particularly setting the estimation of effectiveness very low. Besides, it is obvious that obesity improvement can contribute to mitigating hypertension, liver disease, insomnia, even esthetics, all of which increase quality of life (QOL); therefore, it can easily motivate both an individual's and a society's willingness to pay. For the sake of simplicity, these benefits are eliminated, as they obviously cause underestimation.

Although costs should be divided into non-recurring and recurring costs and then summed for accuracy, for the sake of simplicity the monthly subscription fee of the ordinal smartphone app (10 USD/month) as a DH/DTx subscription fee is used. This is because the monthly subscription fee should cover the initial and fixed costs, for instance, R&D and data servers.

Although quality-adjusted life years (QALY) is commonly used as the measure of health effect, estimation of the QALY of health intervention requires clinical research. Instead of QALY, we report the use of disability-adjusted life years (=1-QALY, DALY), which is provided by the World Health Organization (World Health Organization, 2020).

## ***STEP4: CHOOSE YOUR EVALUATION METHODS***

First, we calculate how much DH/DTx would reduce the total financial burden imposed by diabetes in Japan, including the national medical expenditure for diabetes. In CEA for clinical effectiveness, an incremental cost-effectiveness ratio, or ICER, is frequently used as the main economic value of an intervention, compared with alternatives. An ICER is calculated as below (York Health Economics Consortium, 2016):

$$\text{ICER} = \frac{\text{Added costs}}{\text{QALYs}(1 - \text{DALYs})} = \frac{\text{Net Cost}_{\text{Option A}} - \text{Net Cost}_{\text{Option B}}}{\text{QALYs}_{\text{Option A}} - \text{QALYs}_{\text{Option B}}}$$

As a matter of convenience, some conditions are as follows:

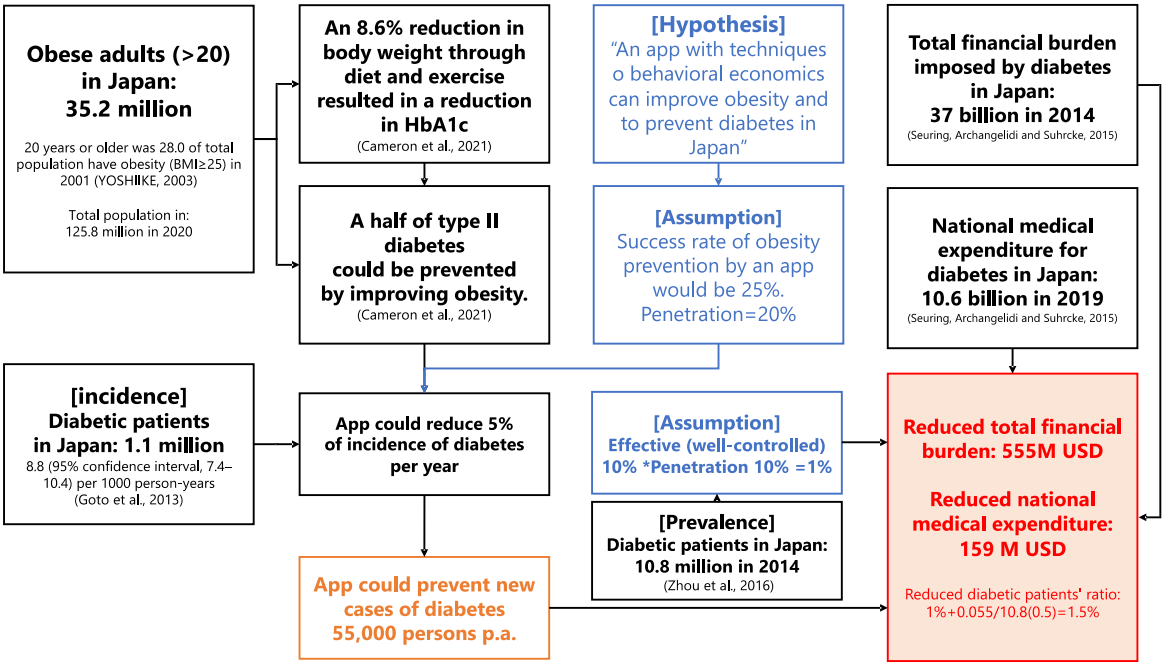
1) Instead of QALY, cumulative DALY (=1-QALY) is used, as explained above.

2) DTx is compared with a "non-action option," whose net cost is zero.

## ***STEP5: CARRY OUT YOUR EVALUATION, USING THE DATA***

As a result, the following evaluation diagram shows how much DH/DTx would reduce the total financial burden imposed by diabetes in Japan and the national medical expenditure for diabetes there (YOSHIIKE, 2003):

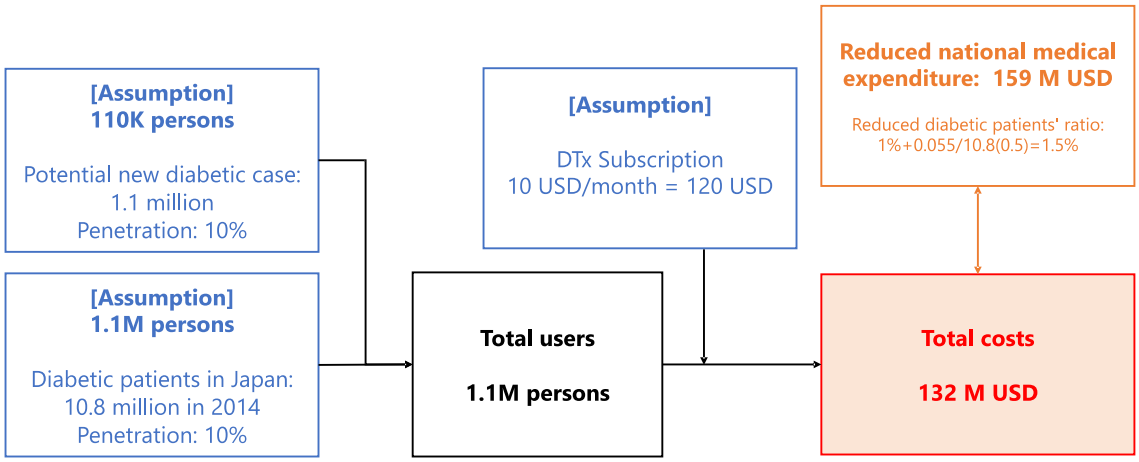
**Figure 3.** Financial impacts of DH/DTx for obesity (and diabetes) in Japan




To calculate "costs per DALY," first, the overall costs of DH/DTx should be estimated; they are calculated based on certain assumptions (see below):

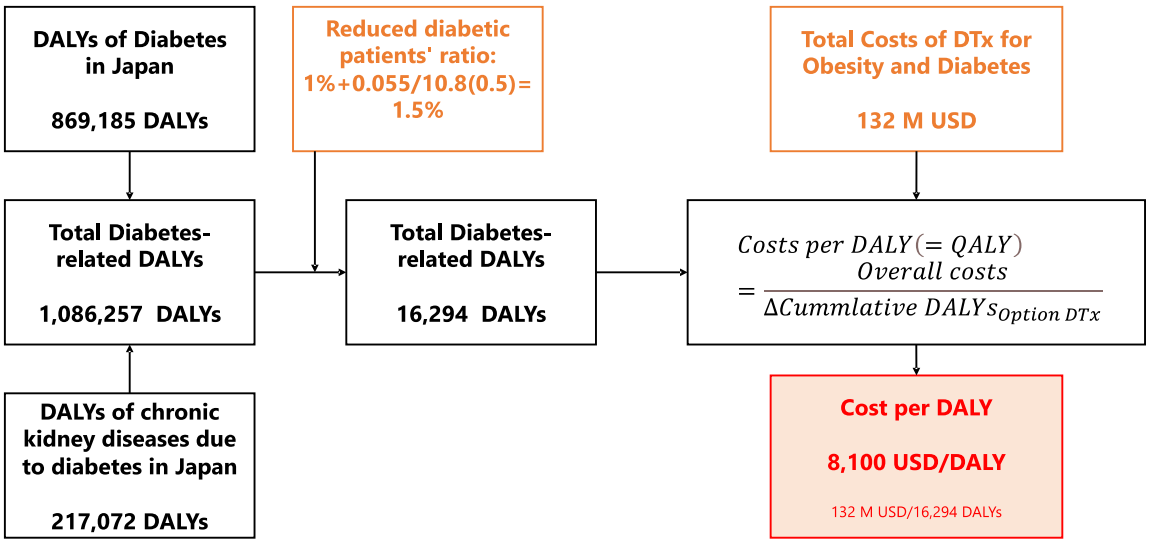
$$\text{Costs per DALY}( = \text{QALY}) = \frac{\text{Overall costs}}{\Delta\text{Cummlative DALYs}_{\text{Option DTx}}}$$

**Figure 4.** Total costs of DH/DTx for obesity (and diabetes) in Japan




Finally, "cost per DALY" is calculated, as below. The DALYs of diabetes in Japan and of chronic kidney disease resulting from diabetes in Japan are cited from "Global health estimates: Leading causes of DALYs" by the World Health Organization (World Health Organization, 2020).

**Figure 5.** The cost per DALY of DH/DTx for obesity (and diabetes) in Japan




## ***STEP6: USE YOUR RESULTS***

A recent systematic review showed that, among lifestyle interventions, those that followed a diabetes prevention program (DPP) curriculum had a median ICER of $6,212/QALY, while those that did not follow a DPP curriculum had a median ICER of $13,228/QALY (Zhou *et al.*, 2020).

Based on the above calculation, the "cost per DALY" of DH/DTx for obesity has been estimated at 8,100 USD/DALY. As mentioned earlier, despite the fact that obesity improvement can also contribute to mitigating hypertension, liver disease, insomnia, and esthetics, among others, the CEA in this chapter focuses on improving diabetes only. Hence, the "cost per DALY" resulting from the CEA here is largely underestimated. Even though strict and conservative assumptions are employed, the cost per DALY for DH/DTx is fairly competitive when compared to the current alternatives (vs ICER of $6,212/QALY of with-DPP, and ICER of $13,228/QALY of without-DPP).

To summarize, this CEA was conducted from the perspective of the Ministry of Health, Labour, and Welfare of Japan as a health-service policy-maker as mentioned in STEP 1. Therefore, if the impact were judged in relation to society as a whole, the result of the stepwise analysis from STEP 2 to 6 shows that the overall reduced total financial burden would be 555 million USD, which is 3.5 times higher than the reduced national

medical expenditure alone (159 million USD). Thus, the Japanese government's promotion of DH/DTx is justified from a financial perspective. Each country has its own demographics, epidemiological disease structures such as prevalence and incidence, disease burden, healthcare systems and systems that affect access to healthcare, and IT environments. Therefore, departments involved in health policies in each country are required to evaluate policies based on appropriate data and assumptions.

## 8. Policy implication

### 8.1. Importance of interdisciplinary and sectoral approach

As mentioned earlier, our systematic review focuses on the application of behavioral economics and also considers economic incentives in achieving behavioral change in relation to obesity. Our approach is motivated by the observation that there has been little collaboration between economists and medical researchers. In general, as economics and medicine are academically distant from each other, opportunities for collaboration may have been scarce. Second, most of the existing research was conducted in the public policy field, such as public administration, while there were few cases in which the private sector was the main researcher.

On the other hand, the quantitative analysis in this paper has demonstrated that DH/DTx has the potential to reduce the economic burden on society as a whole. However, society’s needs and the possible solutions to these needs are unmet, and therefore the deadweight exists. The reason for this is the lack of regulatory frameworks, mechanisms to fund risk money, and insufficient interdisciplinary research and development efforts.

The following are possible solutions to the above issues:

1) Create an interdisciplinary research and development environment. According to Schumpeter, innovation occurs when an unexpected “new combination” of existing things creates new value (Schumpeter, 1926). It is necessary to create an environment where things that are far away can be connected.
2) Establish a mechanism to promote the application of behavioral economics to policy and business, such as the Behavioral Insight Team

in the UK (Behavioural Insights Team, no date). And the further creation and use of evidence for applications should be accelerated in the health and medical fields by building a system of collaboration between the public and private sectors.

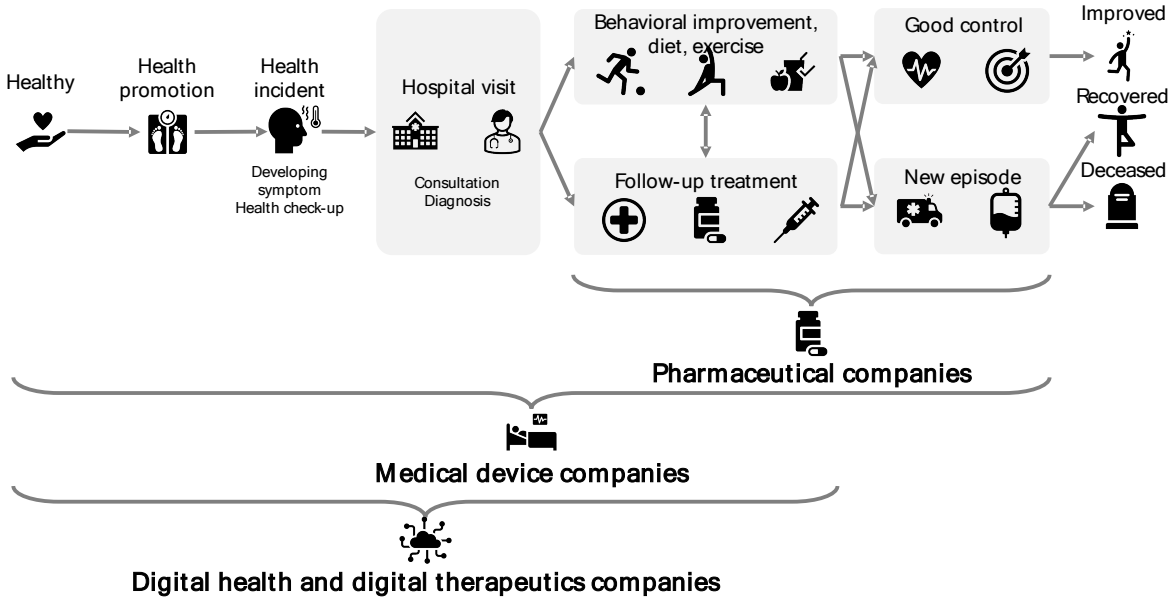
3) It is also necessary to build a bridge between academia and the private sector – as there is a so-called "Death Valley" between seeds and applications – and thereby to create an environment in which new seeds from academia can be implemented in society as concrete products.
4) Moreover, it is crucial to build a venture ecosystem consisting of the following actors: challengers who are trying to overcome "Death Valley," supporters such as angel investors and venture capitalists who provide risk money, lawyers, and experts in intellectual property, finance, and accounting, who support the challengers.
5) In order to intentionally reduce the aforementioned deadweight and increase the utility in society, the government should take a proactive role to foster an enabling-environment for DH/DTx throughout society, including the above (1) to (4), rationalizing the current regulations, and providing subsidies, among other things.

## 8.2. Facilitation of competition and collaboration

According to the mapping exercise conducted in this paper, coverage of a variety of industries on the journey of diabetic patients can be mapped out as in Figure 7. The observations arising from the figure are as follows:

1) The coverage of DH/DTx service providers overlaps with that of medical-device manufacturers. However, as there is a clear difference between software and hardware, there is a possibility to create synergies between them through collaboration.
2) There is also a possibility that medical-device manufacturers will enter the market by expanding their business to include DH/DTx.
3) If DH/DTx succeeds in preventing diseases, it is expected to reduce the demand for medical drugs and curb the rising cost of healthcare. On the other hand, DH/DTx poses a threat for pharmaceutical companies, because it will shrink their market. At the same time, some are proactively seizing the opportunities created by DH/DTx under a strategy called "beyond the pill" (Cattell, Chilukuri and Knott, 2012).

**Figure 6.** Coverage of a variety of industries on the journey of diabetic patients




## 8.3. Challenges for administrative framework

Practical implementation of DH/DTx poses administrative framework challenges in terms of regulatory approval. The key issue is that, in the realm of pharmaceutical and therapeutic development, securing regulatory approval requires the execution of clinical trials. These trials are pivotal in ascertaining the safety and efficacy of novel drugs or treatments. Typically, clinical trials involve the segregation of participants into two cohorts: an experimental group that undergoes the novel treatment, and a control group that receives the established standard of care. Such a bifurcation facilitates comparative analyses, crucial for assessing the new treatment's effectiveness. The gold standard in clinical trial design is the Randomized Controlled Trial (RCT), characterized by the random allocation of participants to either the experimental or control group, thereby reducing potential biases. Moreover, clinical trials may employ placebo controls and double-blind methodologies to enhance their scientific rigor.

However, the distinctive nature of DH/DTx, predominantly delivered through application-based platforms, poses challenges in establishing

traditional placebo-controlled groups, a staple in pharmaceutical trials. The unique format of DH/DTx, often encompassing apps, smartphones, and wearable technologies, enables the collection of a diverse array of biomarkers through inbuilt sensors, alongside user-inputted data. This aggregation of real-world data paves the way for analyses that can support causal inference, a significant leap in understanding therapeutic impacts.

Given this context, the utilization of real-world data in DH/DTx necessitates the evolution of an administrative framework capable of critically evaluating evidence derived from these data. Such a framework will be instrumental in ensuring that DH/DTx maintains rigorous standards of safety and efficacy, akin to its pharmaceutical counterparts, while also navigating the unique challenges posed by its digital nature.

## 8.4. Japan's policies for DH/DTx with behavioral economics as an example

In this section, again using Japan as a case example, we succinctly delineate the initiatives undertaken by the country in the domain of DH/DTx, shedding light on its strategic approach to fostering the growth and integration of DH/DTx within its healthcare paradigm. We focus on the consideration that, when advancing DH/DTx, it is imperative to address several critical factors that contribute to the effective development and implementation of these technologies. These factors encompass the encouragement of research and development (R&D), clarification of the developmental process, assurance of regulatory predictability, acceleration of review procedures, establishment of cost reimbursement frameworks and promotion of international cooperation, all of which necessitate the active role of national governments.

In an endeavor to foster the progression of DH/DTx within the Japanese healthcare system, the government of Japan released a seminal document titled "DASH for SaMD 2 DX (Digital Transformation) Action Strategies in Healthcare for SaMD (Software as a Medical Device) 2" in September 2023 (Ministry of Health, Labour and Welfare Japan, and Ministry of Economy, Trade and Industry Japan, 2023). While having been delayed compared to the US-FDA which introduced a new scheme called the "Digital Health Software Precertification (Pre-Cert) Program" to facilitate the innovation of DH/DTx as early as 2017 (US-FDA, 2021), this Japanese strategic

framework takes a holistic approach to the promotion, practical application, and global dissemination of Software as a Medical Device (SaMD). It meticulously articulates a comprehensive strategy aimed at accelerating the development and regulatory approval of programmed medical devices in Japan. Furthermore, the document details an array of policies, objectives, and specific actionable steps, underlining the government's commitment to not only enhancing the domestic DH/DTx landscape but also positioning Japan as a pivotal player in the international DH/DTx market. This initiative reflects a concerted effort to integrate innovative digital solutions into healthcare, thereby advancing the overall efficacy and accessibility of medical care.

Furthermore, in order to bolster the development of programs that catalyze behavior change, such as DH/DTx, through the application of behavioral economics insights, Japan's Ministry of Economy, Trade and Industry (METI) and the Japan Agency for Medical Research and Development (AMED) introduced a principal document in March 2023. This document, entitled "Development Guideline on Medical Device Programs to Promote Behavior Change in the Medical and Health Fields," serves as a foundational guide for entities venturing into the DH/DTx domain, particularly those new entrants who are navigating the complex terrain of medical-related legislations and regulations (Ministry of Economy, Trade and Industry Japan, and Japan Agency for Medical Research and Development, 2023).

The guidelines meticulously elucidate the conceptual design and functional module approach integral to program development. They provide clarity on the legal definitions of medical devices and picture criteria for their applicability. Furthermore, the document offers comprehensive guidance to developers and operators, assisting them in formulating product development policies and understanding the critical legal and regulatory frameworks pertinent to DH/DTx. This initiative underscores the commitment of the Japanese government to facilitate innovation in the healthcare sector by providing clear, actionable guidance to foster the development of behavior-changing medical device programs.

## 8. Conclusion: Way forward to the promotion of DH/DTx

This paper has proposed that an interdisciplinary and sectoral approach among the government, business and academia needs to be promoted in the area of DH/DTx with a strong initiative taken by the government. Such an approach includes interdisciplinary research and development environment, a mechanism to apply behavioral economics to DH/DTx-related policies and business, further creation and use of evidence for applications, and building of regulatory frameworks and a venture ecosystem. It also highlights the importance of facilitating multi-industrial competition and collaboration, such as among pharmaceutical companies, medical-device manufactures, DH/DTx specialized ventures and others.

Innovation in the medical sector, especially developing new drugs, is now extremely advanced and expensive. Therefore, the number of countries in the world capable of creating new drugs is limited to developed countries such as the US, Switzerland, Japan, the UK, and Germany. Moreover, the global trend is that the business risk of developing innovative drugs and medical devices in-house is increasing, even for these developed countries. Open innovation, in which start-up companies develop innovative technologies and major companies commercialize and market them, has become the global norm.

Under this situation, there is an emerging trend of startups focusing on development and innovation within the domains of DH/DTx. This trend is subsequently followed by mergers and acquisitions (M&A) by pharmaceutical companies and other entities eager to integrate and capitalize on these DH/DTx solutions. Given the rapid advancement and increasing significance of DH/DTx in healthcare, it is plausible to anticipate a rise in such M&A activities in the future. This trend not only reflects the growing importance of digital technology in healthcare but also highlights the strategic moves by pharmaceutical companies to stay at the forefront of innovation in this sector. Therefore, it is more necessary than ever for governments to swiftly take a proactive role as mentioned above.

Before concluding, we would like to point out the limitations of this paper and the necessity for further study. In this paper, our review of literature was based on a medical research database. However, private companies do not necessarily publish papers on their own technologies in the form of research results. They tend to refrain from publishing them and to protect their technology by applying for a patent. While this paper did not extend its search to the patent database, such extensive research might enable a

more comprehensive market evaluation. In addition, the evaluation in the quantitative analysis was conducted based on bold assumptions. By breaking down these assumptions into finer granularity, it might be possible to identify the critical variables, that is, the most effective drivers, to maximize the benefits of DH/DTx.

Furthermore, this paper does not provide a detailed discussion of who, among the various stakeholders and beneficiaries, will bear which costs, as outlined in the previous section. Previously, the only sales channel for pharmaceutical companies was through prescription by doctors in medical institutions; however, digital health can now also be provided through general apps. It can be offered by not only doctors but also health insurers to encourage disease prevention among their customers, as insurers have a strong incentive to reduce their reimbursements. DH/DTx can also be provided by companies in order to maintain the health of their employees, with a view to reducing absenteeism. They have different monetization methods and incentive structures, which may lead to the development of different business models.

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