Exploring the Potential of Mobile Health for Product and Process Innovation

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***Abstract*--Mobile Health or mHealth is an emerging concept of the use of mobile devices and wireless technology for healthcare purposes. Recently, mHealth-related technology is expected to form a new category of medical devices particularly in the monitoring of patients. This is also anticipated to improve the efficiency and effectiveness of pharmaceutical clinical trials. However, there are challenges to utilize this enabling technology to innovate healthcare business. Considering this context, we explore the potential of mHealth. First, we position mHealth with respect to current innovation theories based on intensive literature review. Second, we hypothesize that mHealth has two potential areas of innovation: product innovation in the medical devices industry and process innovation in the pharmaceutical industry. To test the hypotheses, we conducted a holistic observation on clinical trials to examine how large mHealth impacts a treatment pathway by innovative products. Consequently, we observed 193 studies are registered; however, most of these remain at a primitive level of information and communication technology such as text messaging and application, which suggests a significant gap to the market forecasts. This present study forms the basis of the trend of mHealth and a future outlook from the viewpoint of technology and innovation management.**

I. INTRODUCTION

A. Background of mobile health development

Mobile health or mHealth is an emerging concept referring to the use of mobile devices and wireless technology for healthcare purposes. mHealth is positioned as a branch of electronic health (eHealth) [3]. The term, eHealth, refers to "the healthcare practices assisted by communication systems and electronic processes." [3].The term, mHealth, broadly refers to "medical and public health practice supported by mobile devices such as mobile phones, patient-monitoring devices, personal digital assistants (PDAs), and other wireless devices" [70]. The technologies used for mHealth are text-messaging, phone calls, mobile tracking devices, wearable sensors that can be used for monitoring and measuring activities, applications (apps), wireless communications technologies, and so on. The coverage of mHealth includes the acquisition and transmission of healthcare-related information, telemedicine, electronic records, e-prescriptions, and the parallel industries of fitness and wellness [3].

The diffusion of mobile phones and smartphone technologies are expanding the possibilities of mHealth [51]. Today, mobile phones and smartphones have become an essential component of our lives. Current smartphones have been defined as "mobile telephones with computer features that may enable them to interact with computerized systems, send e-mails, and access the web" [17]. In 2014, the number of mobile phone users reached 5.2 billion, with a population penetration rate of 73% [43]. Further, the number of smartphone users worldwide is expected to surpass 2 billion in 2016 [24]. The healthcare and life sciences sector is understood to be one of the top three fields likely to experience new growth in the mobile-business model in the next five years [68].

Other than the mobile phone and the smartphone, a wide variety of wearable biometric sensors have also been developed, including watches, bracelets, skin patches, headbands, earphones, and clothing [59].The terms, "wearable devices" and "wearables," refer to electronic technologies or computers that are incorporated into items of clothing and accessories that can comfortably be worn on the body [41]. These wearable devices can perform many of the same computing tasks as those of mobile phones and laptop computers. A total of 72.1 million wearable devices were shipped in 2015, a substantial 173.3% increase from the 26.4 million units shipped in 2014, as new vendors, including Apple, entered the market [62]. Shipment volumes are expected to experience a compound annual growth rate (CAGR) of 42.6% over the five-year forecast period, reaching 155.7 million units in 2019 [62].

Especially, the field of mobile application for mHealth, mHealth apps, is rapidly growing. The number of mHealth apps that are published on the two leading platforms, iOS and Android, has more than doubled in only 2.5 years, reaching 165,000 by the third quarter of 2015 [5]. The market revenue reached 2.4 billion USD in 2013 and is projected to reach 26 billion USD by the end of 2017 [40]. Currently, the majority of mHealth apps have only simple functionality, mostly used for prevention and wellness [4].

The global healthcare Information Technology (IT) market is projected to reach 66 billion USD by 2020, driven by efforts to streamline critical workflow processes [32], and mHealth is expected to be one of the driving forces of the global healthcare IT market [71]. The global mHealth market was valued at 10.5 billion USD in 2014 and is expected to grow at a CAGR of 33.5% by 2020 [71]. In [71], it is reported that North America holds the largest market share, based on device type. With an increase in the prevalence of lifestyle-related diseases, the segment of blood pressure monitors holds a dominant share in the mHealth market, followed by blood glucose monitors and cardiac monitors.

B. Productivity of pharmaceutical industry

Recently, the pharmaceutical industry has struggled with high research and development (R&D) expenditure and high failure rates. The R&D activities of the pharmaceutical

industry are characterized by high levels of volatility because of the long-term R&D period, high costs, and increasingly demanding regulatory requirements, coupled with low success rates [33]. Between 1996 and 2004, in the United States of America (USA), the average number of approved new molecular entities (NMEs) was 36 and R&D expenditure was 65 billion USD per year [35]. From 2005 to 2010, the average number of approved NMEs was 22, but R&D expenditure climbed up to 125 billion USD [35]. In 2014, the USA and Japan approved the highest number of new active substances (NASs) were approved in a decade; 2014 saw the highest number of orphan drug approvals in the USA, EU, and Japan [13]. However, the costs of developing a new drug were estimated at 2.558 million USD in 2014 [20]. The estimated costs were 802 million USD in 2003 [21]. The growing R&D costs are attributable to drug manufacturers' transition from small molecule drugs to biomedicines [19]. The pharmaceutical industry is trying to improve productivity, so as to substantially increase the number and quality of innovative, cost-effective new medicines, without incurring unsustainable R&D costs.

C. The objective of this research

The main objective of this paper is to explore the potential of mHealth in the healthcare industry, based on the below-mentioned hypotheses. To test these hypotheses, we conducted a holistic observation of clinical trials, to examine how large-scale mHealth affects treatment pathways through use of innovative products. In the observation, we determined the current status of clinical trials that are registered in ClinicalTrials.gov using mHealth; we then analyzed trends in mHealth-related technology in clinical trials.

D. Previous research

In consideration of the standpoint of mHealth technology management, we postulated representative theories on technology and innovation management [1] [45] [54] [55] [66].

First, we considered the phase of innovation through reference to Rothwell's classification of technological transitions [55]. According to this classification, a linear model of technology push and demand pull prevailed in the first and second generations, a coupling model of R&D and marketing arose in the third generation, a parallel model or the Kline model represented the fourth generation, and a networking model arose in the fifth generation.

In order to observe the mode of innovation, we carefully considered Abernathy and Utterback's theory on product versus process innovation [1]. Process innovation refers to improvement in the production processes and production technology of existing products, and through new processes of production, reducing product costs, or improving quality and performance through technological innovation. Product innovation corresponds to technological innovation; it is presumed that technological innovation has the potential to produce revolutionary new products that did not previously exist [66].

Thirdly, we investigated the innovation process stage, according to Rogers' and Moore's theories [54] [45]. When recording the state of diffusion on a time axis, along with the number of adopters, with regularity, the normal distribution of adopters shows a bell-shaped curve [54]. The numbers relating to each adopter classification, which can be roughly determined from trends in either the number of people reached or the market share, show an S-shaped curve [54]. Moore argues that, with regard to the behavior of users in high-tech marketing, there are cracks between individual types of adopters in particular, and there is a chasm between early adopters and early majority [45].

Finally, we tested the applicability of the theory of disruptive innovation information [15]. Information and communication technology (ICT) is said to play two important roles in promoting a disruptive business model in healthcare. First, it reportedly promotes cooperation between doctors, nurses, and patients during medical treatment, and transitions healthcare towards being a network-style business. Second, by promoting cooperation between healthcare providers and digitizing medical information such as patient records, the efficiency of clerical work can be greatly improved. We believe that, with its expected growth, mHealth will help improve productivity in the development of pharmaceuticals. Through consideration of mHealth from the standpoint of technology management, in line with existing innovation research, we have developed three hypotheses, as described below.

E. Current understanding and hypothesis

For our first point, we will focus on the dissemination process of innovations. mHealth is in the introduction phase of the current medical market. Rogers reports the percentages of adopters during the diffusion of new technologies and services, in relation to the total market, to be at 2.5% for innovators; 13.5%, for early adopters; 34%, for early majority; 34% for late majority; and 16% for laggards [54]. According to this standard, healthcare businesses that use mobile phone and smartphone apps are currently considered to be early majority.

Meanwhile, mHealth has been progressing rapidly in terms of uptake and diffusion in the medical field. The global medical market size is said to be around 9.59 trillion USD [26]; within that, the market size for mHealth is 10.5 billion USD (0.11%) [15]. However, according to a survey, the number of people who use mobile phone and smartphone apps for self-tracking was approximately 7% in 2010 [29], and according to a 2012 survey, that percentage subsequently increased to 19% [28]. Additionally, with the spread of smartphones and wearable devices, a daily increase has been observed in healthcare-related IT products [25].

The implementation of mHealth is also progressing in clinical research and development. Clinical research related to mHealth has been on the rise since 2008 [27] [59]. In clinical research, mHealth has been used in many different

sub-fields, including health promotion and disease prevention, diagnosis, treatment, monitoring, and support for health services [6] [30] [59]. Based on the above, it can be said that mHealth is becoming a part of the clinical research through the uptake and diffusion of information and communication technology. In particular, based on the benefits of being able to access data in real time, advancements in the use of mHealth for drug development are also expected.

H1: mHealth including mobile phone, smartphone, and application technologies has a potential to be adapted for the improvement of productivity in the development of pharmaceuticals.

For our second point, we will be looking at the types of innovation. In the case of product innovation in pharmaceuticals, up until the 1970s, the utilization of natural compounds and the chemical synthesis of small molecules were mainstream. Since the 1980s, however, biological medicine using gene recombination technology has been developed, and research in the treatment of diseases that are difficult to cure is still in progress [19] [64]. In addition, the new innovation involving use of cell therapy and regenerative medicine to treat tissues and organs has also emerged, in place of use of substances in this regard [67]. As for process innovation, regarding small molecules, sophisticated rapid-screening technology and formulation technology has been developed. At the same time, developments in biological medicine require even more advanced technology, and the sharp rise in R&D costs has led to problems relating to a decline in productivity in this field [47]. That is to say, in light of previous research and observations [52], while small molecule-related matters are at a stage where they are being led by process innovation, biological medicine is considered to have remained at the stage of product innovation.

In the case of medical equipment, product innovations including devices such as catheters and portable blood inspection machines that can perform various analyses from a drop of blood [39]contribute to early detection and treatment of diseases, due to diagnostic equipment and the development of surgical instruments [12]. Process innovation involves improving equipment through miniaturization, making them lightweight and noninvasive, as well as increasing the degree of precision [15]. Additionally, in the development of products that primarily target developing countries, focus has been on features such as simplicity and low costs, and there are cases where such products even expand to developed countries, as well [38]. That is to say, while product innovation takes the lead, process innovation pioneers new therapeutic purposes and applications, such that the two innovations work mutually.

Product innovations in the cell therapy and regenerative medicine field include wound healing through use of cultured skin, cancer immunotherapy using dendritic cells, and regenerative medicine using stem cells, which are all on the market. In particular, the use of regenerative medicine to fundamentally restore the function of damaged organs and tissue has created new treatment possibilities for diseases and disorders that were previously difficult to treat [10]. Process innovation in stem cell-related technologies, such as safe and efficient production of cells of a consistent quality, achievement of cell separation, regeneration, conservation, and so forth, has advanced [34]. Essentially, although product innovation is still in the introduction phase, process innovation is simultaneously ongoing, as improvements in production costs in the diffusion phase are expected.

What about the case of mHealth? One possibility is that mHealth can, in itself, become a form of product innovation in the medical field. For example, Otoharmonics developed the LevoSystem app for the treatment of tinnitus, and obtained clearance from the Food and Drug Administration (FDA) 510(k)[50]. Doctors "prescribe" the app to patients, and through training of the brain to ignore tinnitus sounds, therapeutic effect is achieved.

Another innovation route for mHealth is improvement of existing therapies and the efficiency and effectiveness of pharmaceutical clinical trials[44]. WellDoc, Inc. developed BlueStar as a software application for guiding the treatment of Type 2 diabetes patients. BlueStar is the first application to achieve the trifecta of FDA-cleared, physician-prescribed and payer-reimbursed digital medicine product [58]. Patients download BlueStar, prescribed by their doctors to their smartphones and tablets. Patients' blood sugar levels are measured in real time; they also receive individual guidance concerning the content of their treatment and lifestyles from doctors and experts. The results of clinical trials showed improvement in hemoglobin A1c scores (HbA1c) over a 12-month period [53]. Moreover, WellDoc, Inc. has positioned BlueStar as mobile prescription therapy (MPT) [16]. Furthermore, real-time data gathering with respect to mHealth is expected to open the door for drug developers to improve drug development in the following ways: enhancing patient safety, strengthening the quality of data, and accelerating the duration of development [56]. Indeed, several leading pharmaceutical companies are adopting this technology for smarter development of new drugs in a faster, safer, clearer, and more cost-friendly manner [11] [48] [61]. However, there are challenges to the utilization of this technology to innovate the pharmaceutical and medical devices business. Based on the considerations mentioned above, we present the following hypothesis:

H2: mHealth reaches two potential areas of innovation: 1) product innovation per se, for medical use, and 2) contribution to process innovation in pharmaceutical product development.

As a third point, we will focus on the dynamics of innovation. Mowery and Rosenberg et al. classified technology push based on an innovation pattern set to improve the performance of technology, and demand pull as technological advances made in response to the needs of specific markets [46]. Against the background of the growth of mHealth in recent years, the technical aspects of devices

and within communication technology have shown substantial advancement. In the 1990s, Tarner et al. developed technology using compact and lightweight cameras and head mounted displays (HMDs) [57], and because of this, a mobile, wearable method for inexpensively collecting and storing data in real time became possible [31]. Moreover, through faster communication, it is now possible to quickly and safely share medical information [3], since sending and receiving large amounts of data, especially with the development of cloud services, became possible. From this, it is inferred that technology push has become a driving force behind innovation.

Meanwhile, the adaptation of mHealth to cognitive behavioral therapy for mental disorders has displayed different appearance. In this field, mHealth is expected to promote collaboration between doctors, nurses, and patients, and networking between patients and families. There are many recent apps available that are expected to work as tools to help improve patients' conditions [9] [60]. However, in actuality, although several apps are commercially available for the treatment of and therapeutic support for mental disorders, a lack of evidence proving their effectiveness should be pointed out [22] [42]. It follows from that, there are signs of innovation resulting not only from technology push, but also as a result of demand pull. Based on the considerations mentioned above, we present the following hypothesis:

H3: In order to implement mHealth in pharmaceutical R&D, technology push is the current driver for the innovation associated with mHealth.

II. MATERIALS AND METHODS

A. Database of holistic observation of clinical trials

In December 2015, two electronic databases of clinical trials (ClinicalTrials.gov and WHO International Clinical Trials Registration Platform) were systematically searched. In this study, we use ClinicalTrials.gov as a database, to determine the current status of clinical trials using mHealth. However, US federal law requires the registration at ClinicalTrial.gov to include information about federally or privately funded clinical trials conducted under investigational new drug applications, to test the effectiveness of experimental drugs for patients with serious or life-threatening diseases or conditions [36]. Therefore, ClinicalTrials.gov currently lists more than 200,000 studies, with sites in all 50 states and in 191 countries. Furthermore, the USA is a leader in the mHealth market [15]. ClinicalTrials.gov is a registration and results database of publicly and privately supported clinical studies conducted on human participants around the world. The website is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The information on ClinicalTrials.gov is provided and updated by the sponsor or principal investigator of each clinical study. For the reasons mentioned above, we decided to use ClinicalTrials.gov to cover many clinical studies around the world.

We could find wide-ranging information on the website, as each ClinicalTrials.gov record presents summary information about study protocol, including the following: Disease or condition, intervention (e.g., the medical product, behavior, or procedure being studied), title, description, study design, requirements for participation (eligibility criteria), locations where the study is being conducted, and so on.

B. Search strategy

Number: A list of keywords was created in the two domains of “mobile health” OR “mhealth;" our target was intervention studies.

C. Classification of Conditions

We classified the conditions of the mHealth clinical trials according to 23 categories of the International Classification of Diseases (ICD)-10 version 2015 [69]. The ICD is the standard diagnostic tool for epidemiology, health management, and clinical purposes. The ICD is used by physicians, nurses, other providers, researchers, health information managers and coders, health information technology workers, policymakers, insurers, and patient organizations, to classify diseases and other health problems recorded on many types of health and vital records, including death certificates and health records. The ICD-10 was endorsed by the Forty-Third World Health Assembly in May 1990 and came into use in WHO's member states, as from 1994 [69]. We decided to use the ICD-10 to understand the major categories of mHealth clinical trials.

III. RESULTS

A. Holistic observation of clinical trials

A search identified 199 studies with the two domains of [“mobile health” OR “mhealth"], on December 23, 2015. Of the 199 studies, 193 intervention studies were identified (6 intervention studies were blank). Clinical studies using mHealth are conducted all over the world. However, more than half are conducted in the US. We found that the registered status of 22 of the studies in the database was Phase[1]. The phase numbers for the different studies were as follows: Phase 0 in two studies, Phase 1 in five studies, Phase 1/2 in three studies, Phase 2 in four studies, Phase 2/3 in one study, Phase 3 in four studies, and Phase 4 in three studies. For three of the studies, the results status was “Has results,” but no statistical analysis was provided, to enable evaluation of the intervention impact of mHealth for each study. The results status of the other studies was “no results available.”

[1]Clinical trials are conducted in a series of steps, referred to as phases. There are four main phases of clinical trials, Phase 0 to 4. The earliest-phase trial aims to determine whether a drug is safe, or the type of side effects that it causes. A later-phase trial aims to test whether a new treatment is better than existing treatments.

B. The potentiality of mHealth for pharmaceutical product development

As for the starting date of clinical trials using mHealth, the number is increasing after 2012 (Fig. 1). According to "*Trends*, *Charts*, and *Maps"* of clinical.gov, there were 23,297 studies clinical studies registered between 2014 and 2015. To determine types of interventions in the registered data, we searched for major intervention keywords. We found the major keywords to be "application," followed by "text messaging," and "smartphone" (Table 1). In support of Hypothesis 1, the results showed that mobile phones, smartphones, and applications have already been used for clinical trials and that there is potential for the application of mHealth in pharmaceutical development.

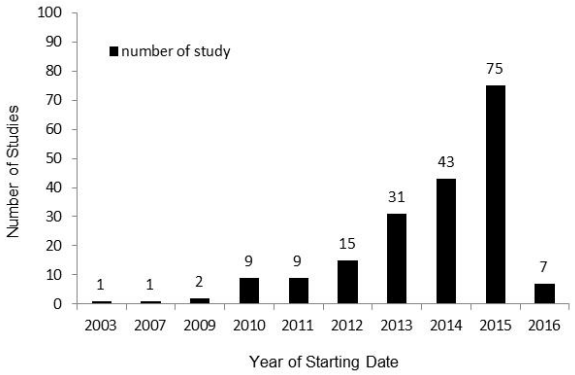

Figure 1. Starting date of Clinical trials with mHealth

TABLE 1. MAJOR KEYWORD OF THE CATEGORY OF INTERVENTION

Major key word of intervention	Number
application	34
text messaging	29
smartphone	18
SMS	18
fitbit	6
facebook	2

Note: the number of category was double-counting because there are some trials registered multiple conditions.

C. The mode of innovation with mHealth

We classified 178 of 193 studies according to conditions. Fifteen of the studies were not classified using the ICD-10 because the data were not related to conditions (i.e., attendance, sedentary lifestyle). Multiple conditions were registered for some of the trials; in such instances, we used double counting. Our results showed that mental and behavioral disorders (24.2%) were the most common condition, followed by diseases of the circulatory system (19.9%), endocrine, nutritional, and metabolic diseases (18.0%), certain infectious and parasitic diseases (11.8%), and pregnancy, childbirth, and puerperium (7.0%) (Table 2). Furthermore, we noted the disease types recorded in more than 10 studies. Diabetes mellitus was the most common disease (27 studies), followed by HIV (20 studies), hypertension (10 studies), cancer (10 studies), and obesity (10 studies).

TABLE 2. CONDITIONS OF CLINICAL TRIALS WITH MHEALTH

Category of ICD-10 version 2015	Number	%
V Mental and behavioural disorders	48	(24.2)
IX Diseases of the circulatory system	37	(19.9)
IV Endocrine, nutritional and metabolic diseases	34	(18.3)
I Certain infectious and parasitic diseases	22	(11.8)
XV Pregnancy, childbirth and the puerperium	13	(7.0)
II Neoplasms	10	(5.4)
X Diseases of the respiratory system	9	(4.8)
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	3	(1.6)
XIII Diseases of the musculoskeletal system and connective tissue	4	(2.2)
XIX Injury, poisoning and certain other consequences of external causes	4	(2.2)
VI Diseases of the nervous system	2	(1.1)
XXI Factors influencing health status and contact with health services	0	(0)
XVI Certain conditions originating in the perinatal period	0	(0)
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	0	(0)
VII Diseases of the eye and adnexa	0	(0)
VIII Diseases of the ear and mastoid process	0	(0)
XI Diseases of the digestive system	0	(0)
XII Diseases of the skin and subcutaneous tissue	0	(0)
XIV Diseases of the genitourinary system	0	(0)
XVII Congenital malformations, deformations and chromosomal abnormalities	0	(0)
XX External causes of morbidity and mortality	0	(0)
XXII Codes for special purposes	0	(0)

The primary purposes of 178 of 193 studies were registered on the database. Our results showed treatment (30.9%) to be the most common purpose, followed by prevention (25.8%), health service research (20.8%), supportive care (17.4%), basic science (2.2%), screening (1.7%), and diagnosis (1.1%) (Table 3).

Furthermore, we determined the breakdown of treatment studies. The most common purpose of treatment was medical adherence (45.5%) (Table 4). For medical adherence, reminders and a real-time feedback function with text messaging, as well as apps, were used to improve medical adherence. mHealth was related to other behavioral interventions.

To clarify how mHealth intervened in studies, we extracted the breakdowns of other behavioral interventions. We classified therapy or therapy support based on the primary endpoint of each study, regardless of whether it was combined with standard therapy. Our results showed that in 12 of 21 other behavioral intervention studies, interventions were examined as therapy and in 9 , interventions were examined as supplementary to therapy (Table 5). With regard to use of the intervention as therapy, we found potential for mHealth to be used as therapy for alcohol abuse, as cognitive behavioral therapy for depression, and for smoking cessation and drug dependence, without use of medicine. mHealth is

used to determine appropriate treatment for patients with mental conditions and addictions through use of mobile devices, in particular, text messaging and push notifications through apps. As a supplement to therapy, the inter-operability and remote function of mHealth are used to support existing therapy treatments; for example, the provision of rehabilitation program via mHealth, to implement a lifestyle intervention. Therefore, it becomes clear that mHealth has the potential for product innovation as a form of therapy, and also for process innovation as a means of support for existing therapy treatments. However, such potential has yet to be realized in pharmaceutical R&D. Currently, improvement of medical adherence predominates in clinical trials adopting mHealth. Overall, these observations are partially supportive of Hypothesis 2.

TABLE 3. PRIMARY PURPOSE AND INTERVENTION

Primary purpose	Number	%
Treatment	55	(30.9)
Prevention	46	(25.8)
Health Services Research	37	(20.8)
Supportive Care	31	(17.4)
Basic Science	4	(2.2)
Screening	3	(1.7)
Diagnosis	2	(1.1)

TABLE4. THE ITEMS OF TREATMENT

The items of Treatment	Number	%
Medication adherence	25	(45.4%)
Other Behavioural Intervention	21	(38.1%)
Monitoring	7	(12.7)
Improving workflow between physicians and other health care professionals	1	(1.8)
Education for health workers	1	(1.8)

D. The dynamics of innovation with mHealth

We found that many devices are used in a wide range of interventions not limited to medical devices only, but also applied to commercial uses for healthcare. In the registered data, we extracted the primary purposes and interventions relating to the most common conditions (mental and behavioral disorders, diseases of the circulatory system, and endocrine, nutritional, and metabolic diseases) as classified by the ICD-10 to identify intervention uses of mHealth. These results show that most mHealth interventions are based on simple device functions, such as text-messaging and apps, to improve adherence (Table 6). From this result, we concluded that current efforts relating to innovation using mHealth are not technology driven, which proves incompatible with Hypothesis 3.

We also examined the founders and sponsors/collaborators of the clinical trials that we observed. Approximately 75% of studies were funded by others, followed by the NIH (12%), "other" (13%), industry (9.2%), and U.S. Federal Agency (U.S. Fed.) (Table 7). Of the clinical trials using mHealth, 51% were sponsored by universities and colleges, 18% by institutes, and 15% by hospital and medical centers. No major pharmaceutical company was indicated as a sponsor/collaborator in the registered data. It is inferred that, with the growth of the mobile phone and smartphone, and the enforcement of the Mobile Medical Applications Guidance for Industry and Food and Drug Administration Staff in 2013 [63]. mHealth not only has potential for use in health tracking, but also offers a challenge to university and college centers regarding the use of mobile technologies to improve health outcomes. We identified few biopharmaceutical or other firms as sponsors in more than two clinical trials; these were RAND, Verizon Wireless, Proteus, Coherohealth, and Dimagi Inc. We also identified industries using mHealth in clinical trials (Table 8). Based on the results, we determined the type of study conducted by each industry and the type of technology developed. RAND, Verizon Wireless, Proteus, Coherohealth, and Dimagi Inc. conducted clinical trials to improve medication adherence. For example, Verizon, being the largest wireless telecommunications provider, determined the impact of an integrated mobile health system, Verizon Wireless's Converged Health Management (CHM), on heart failure and related quality of life [65]. Verizon Wireless's CHM, a remote patient-monitoring medical platform, is designed to help clinicians and patients manage patient health in-between doctors' visits; in 2014, the system received

TABLE5. THE ITEMS OF OTHER BEHAVIORAL INTERVENTIONS

The items of other behavioral interventions		Number
Therapy		12
	Alcohol abuse treatment	(3)
	Smoking cessation treatment	(3)
	Cognitive behavioral therapy (CBT) for depression, Schizophrenia	(2)
	Drug Dependence	(2)
	Adolescent Obesity treatment	(1)
	Traumatic Brain Injury care system	(1)
Therapy support		9
	Rehabilitation support	(3)
	Lifestyle interventions	(3)
	Self-management plus standard care	(2)
	Pain Coping Skills Training	(1)

clearance from the U.S. FDA 510(k) to run on the iOS (Apple, Inc.) mobile operating system [8]. Dimagi Inc. is a recognized social enterprise and certified benefit corporation committed to building mobile systems for local environments [37]. The enterprise conducted a clinical trial to evaluate a cellular phone-based system that assists patients with medication adherence. There is an intervention involving use of text-messaging or an interactive voice response (IVR), and an electronic pill container device. If the patient does not open the pill container, the system recognizes this as a failed dose and the intervention subject receives personalized reminder messages on his/her mobile phone. These results indicate industry-driven development of mHealth, with the use of devices, apps, and platforms. However, the current industry players remain at the stage of using only available technology to improve medication adherence, within the boundaries of clinical developments wherein telecom providers have diversified into healthcare.

TABLE 6. PRIMARY PURPOSE AND INTERVENTION: MENTAL AND BEHAVIORAL DISORDERS, DISEASES OF THE CIRCULATORY, ENDOCRINAL, NUTRITIONAL AND METABOLIC DISEASES

Category of ICD-10 version 2015	Primary purpose	Number	Intervention
V Mental and behavioral disorders	Treatment	17	application (6) text message(2) application and sensor (1) WatchPAT sleep monitor and CBT-i Coach mobile app (1) mobile phone(1) mobile phone(game)(1) therapeutic interactive voice response (1) application and Interactive Voice Response (1) website and SMS (1) Facebook and messaging (1) mobile health care system (1)
	Prevention	8	text message (5) application (3)
	Health Services Research	4	application (1) Ingestion Sensor and Wearable Sensor (1) mHealth (1) tablet (1)
	Supportive Care	2	text message (1) applications and web-based links (1)
	Basic Science	1	Misfit (1)
IX Diseases of the circulatory	Prevention	10	application (2) application and SMS(3) textmessage (2) iRhythm ZIO XT Patch and Wristband by Amiigo (1) SEEQ, Cardiocom and DocView(1) Fitbit Physical Activity Monitor, iHealth Glucometer, Withings Blood Pressure and application (1)
	Treatment	9	application (4) text message(3) bundled wireless real time medication reminder system and blood pressure monitoring system (1) wireless sensor monitoring and feedback (1)
	Supportive Care	5	text message (3) mobile monitoring system (1) phone call (1)
	Health Services Research	4	feedback via phone or email (1) application (1) mobiletechnology (1) textmessage and monitoring (1)
	Basic Science	1	iHealth BP7-Wireless Blood Pressure Wrist Monitor (1)
	Diagnosis	1	proteus(1)
	Screening	1	Converged Health Management (1)
IV Endocrine, nutritional and metabolic diseases	Treatment	10	application(6) application and feedback(1) application and fitbit(1) application, textmessageig and fitbit (1) textmessage, facebook and Physical Activity Monitor(1)
	Prevention	8	application (1) text message (1) SMS(1) application and SMS (1) monitoring (1) text message and social media(1) fitbit Ultra, Pedometer and application(1) website (1)
	Health Services Research	9	application (4) text message (2) on line self report (1) Mobile Health Care System (1) electronically-mediated CardioMetabolic Program (1)
	Supportive Care	6	application (4) text message (2)
	Basic Science	1	iHealth wireless scale, application and text message (1)

TABLE 7. FOUNDER OF CLINICAL TRIALS WITH MHEALTH

Founder	Number	%
Other	187	(75.1)
NIH	30	(12.0)
Industry	23	(9.2)
U.S. Fed	9	(3.6)

TABLE 8.SPONSOR/COLLABORATORS OF CLINICAL TRIALS WITH MHEALTH

Sponsor/Collaborators	Number
University of California, San Francisco	14
Boston University	8
Duke University	8
University of Washington	7
Massachusetts General Hospital	6
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)	6
National Institute of Mental Health (NIMH)	6
University of California, Los Angeles	6
Dartmouth-Hitchcock Medical Center	5
Johns Hopkins University	5
National Institutes of Health (NIH)	5
The Miriam Hospital	5
University of British Columbia	5
Icahn School of Medicine at Mount Sinai	4
London School of Hygiene and Tropical Medicine	4
National Institute on Drug Abuse (NIDA)	4
University of Nairobi	4
University of Pittsburgh	4
University of Southern California	4
VA Office of Research and Development	4
Yale University	4
Boston Medical Center	3
Children's Research Institute	3
CoheroHealth	3
Dimagi Inc.	3
George Washington University	3
Mayo Clinic	3
McKesson Foundation	3
Medical University of South Carolina	3
National Heart, Lung, and Blood Institute (NHLBI)	3
Patient-Centered Outcomes Research Institute	3
RAND	3
Rhode Island Hospital	3
University of Michigan	3
American Heart Associatio	2
Cedars-Sinai Medical Center	2
Columbia University	2
Department of Health and Human Services	2
Eunice Kennedy Shriver National Institute of Child Health and Human Developme	2
Institute for Clinical Effectiveness and Health Policy	2
Johns Hopkins Bloomberg School of Public Health	2
Johns Hopkins Bloomberg School of Public Health	2
Kenyatta National Hospital	2
Marie Stopes International	2
McMaster University	2
Medical College of Wisconsin	2
National Cancer Institute (NCI)	2
National Cancer Institute (NCI)	2
National Institute of Nursing Research (NINR)	2
New York University	2
Northwestern University	2
Proteus Digital Health, Inc.	2
Seattle Children's Hospital	2
Universidade Lusófona de Humanidades e Tecnologias	2
University of California, Davis	2
University of California, San Diego	2
University of California, San Diego	2
University of Cape Town	2
University of Copenhagen	2
University of Florida	2
University of Malaga	2
University of Miami	2
University of Oxford	2
University of Pennsylvania	2
Vanderbilt University	2
Verizon Wireless	2
Wellcome Trust	2
Scripps Translational Science Institute	2

Note: the number of founder was double-counting because there are some trials registered multiple founders.

IV. IMPLICATIONS

A. The potentiality of mHealth for pharmaceutical product development

In the innovation process relating to pharmaceutical development, we consider the positioning of mHealth (Hypothesis 1). Clinical trial data show that the number of studies conducted has increased since 2013. This overlaps with the spread of mobile phones and smartphones. Additionally, the FDA issued the "Mobile Medical Applications Guidance for Industry and Food and Drug Administration Staff," the guidelines of which have proved relevant for mHealth. Mental and behavioral disorders such as bipolar disorder accounted for 24.2% of disease classifications in the clinical trials, with cardiovascular disorders such as high blood pressure and heart failure followed by endocrine metabolic disorders such as diabetes. Based on these results and the "chronic quadrangle: behavior-intensive diseases with deferred consequences" shown in previous studies [15], schizophrenia, bipolar disorder, Type 2 diabetes, and so forth, are applicable. Each of these disorders requires a high degree of behavioral change, and it is difficult to determine the effects of their respective treatments; this points to a movement towards the use of mHealth. Additionally, it is suggested that ophthalmology and skin conditions, among others, are not suitable targets for mHealth, as they are proactively treatable and can be resolved through various other techniques.

Typically, there are some industries other than the medical and pharmaceutical fields as sponsors of clinical trials using mHealth. As sponsors, think tanks, telecommunications companies, and other companies developing sensor technology are building short message service (SMS) and feedback systems that use sensor technology, and conduct clinical trials aimed at improving patients' adherence. When the aim is improvement of adherence, the technological target becomes an application for communication between healthcare workers and patients, rather than providing of specialized medical knowledge. These technologies need not take a long time to measure effectiveness. Therefore, different industries may enter the field.

B. The mode of innovation with mHealth

Next, we consider the position of mHealth regarding innovations in pharmaceutical developments (Hypothesis 2). When examining the application-specific breakdown for the observed clinical trials, mHealth was introduced into trials to improve adherence; this aim accounted for 45% of the total. In the treatment of chronic diseases, the proportion of patient adherence does not exceed 50–60% [49], and due to insufficient adherence, there is an estimated 100 billion USD in hospital expenses annually [2]. Although there is an urgent need for improvement in adherence, from the standpoint of the medical economy, the establishment of a care system that takes care of individuals is challenging. However, current hospital profit models are optimized to manage peak

symptoms and acute phases. Under these circumstances, mHealth is considered to meet the needs of lower healthcare costs and duration of guidance in the provision of proper treatment to patients. In particular, as a complementary treatment tool for these diseases, mHealth is setting the standard for product innovation.

Meanwhile, with regard to the concerns of this study, the feasibility of mHealth to support process innovation in the development of pharmaceuticals could not be confirmed. However, pharmaceutical companies also sense the allure of taking advantage of possibly cheap and large-scale data collection. Based on the concept of "beyond the pill" [14], pharmaceutical companies are trying to fuse drug development and digital technology, and considering building a business model of digital medicine [23] [58] . On this basis, in innovative drug development, the fusion of IT and devices is considered the way to a prosperous future.

C. The dynamics of innovation with mHealth

Finally, let us consider the position of mHealth, with regard to the innovation dynamics of pharmaceutical development (Hypothesis 3). The results of this study showed that mHealth has been studied in relation to improvement in adherence through, for example, reminding individual patients when to take their medication, so as to encourage behavioral change in this regard. The intervention methods use the functionality of mobile phones and smartphones such as SMS, or alternatively, social media such as Facebook. Across the board, improvements are not based on the advanced level of the technology in sensors and devices, but the convenience of always being able to easily make contact. As a result of that, mHealth can be expected to fill the gap with regard to aspects that are outside the reach of medical institutions, such as maintaining patients' motivation levels regarding treatment and improving communication between patients and healthcare workers [7]. However, current trends cannot deny the innovation resulting from technology push in future. In the USA in 2015, the top category for digital health funding was healthcare consumer engagement (613 million USD), followed by wearable bio-sensing devices (489 million USD), and personal health tools and health-tracking tools (407 million USD) [18]. These results suggest that there is an increase in the attention paid to the field of sensing and tracking. It is assumed that, in future, the so-called major analyses and Internet of Things (IoT), which represent trends in the ICT sector, will continue reflecting the spread of mHealth.

D. Study limitations and future perspectives

A few aspects of the limitations of our research should be considered. First, we made a particular focus on mHealth-related interventional studies to examine how mHealth affects treatment pathways. However, we made a particular focus on mHealth-related interventional studies that are usually conducted as clinical trials thus more likely registered to the ClinicalTrials.gov, rather than non-interventional studies. Second, it could not significantly impair the quality of the present study since the ClinicalTrials.gov is the largest database that registers more than 200,000 studies from 192 countries including all the studies conducted in the United States that is by far the leading country of mHealth[2], it is required for further improvement to take notice of other data sources. Third, the current keyword settings ('mobile health' or 'mhealth') excluded searching the records that are using mHealth but not using these wordings in the study description. Forth, there was no uniformity with regard to the trials' characteristics on the database. The extent of the information registered on the database depends on the sponsors. Therefore, we are aware of the lack of uniformity in, for example, the words and terms used. This report provides only the registration status of clinical trials using mHealth because outcomes were registered for only three studies on the database. To evaluate the outcomes of mHealth interventions, we will try to analyze the results of the clinical trials.

V. CONCLUSION

In this present study, we observed the current status of clinical trials related to mobile health or mHealth; we also characterized the related innovations from the viewpoints of stage, mode, and dynamics. First, we confirmed that mHealth has shown double-digit growth in the number of clinical trials for a wide range of indications, including mental and behavioral disorders, and circulatory, endocrinal, nutritional, and metabolic diseases, in order to improve drug adherence. Second, through in-depth analysis of these clinical trials, it was shown that mHealth has two potential areas of application: product innovation in pharmaceutical R&D, as a form of therapy in itself, and process innovation, as a supportive tool for existing therapies. With regard to product innovation, therapies using mHealth are oriented towards cognitive behavioral therapy for mental conditions and addictions, implying that mHealth are expected to enhance patient engagement. With regard to process innovation, mHealth contributes towards improved medical adherence in a considerable number of clinical trials, whereas a dominant design has yet to appear. Third and last, we observed that the current usage of mHealth in pharmaceutical clinical trials remains at a preliminary level of technology, such as bidirectional communication using text messaging or applications. This suggests a need for further technological developments and implementation around mHealth in future. The present study forms the basis of the trend of clinical trials using mHealth and a future outlook from the viewpoint of technology and innovation management.

[2] The US Federal Law requires the registration of all the clinical studies with human volunteers to the ClinicalTrial.gov.

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