

Review Article**mHealth For Aging China: Opportunities and Challenges**Jing Sun¹, Yutao Guo², Xiaoning Wang^{3,*}, Qiang Zeng^{1,*}

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ABSTRACT: The aging population with chronic and age-related diseases has become a global issue and exerted heavy burdens on the healthcare system and society. Neurological diseases are the leading chronic diseases in the geriatric population, and stroke is the leading cause of death in China. However, the uneven distribution of caregivers and critical healthcare workforce shortages are major obstacles to improving disease outcome. With the advancement of wearable health devices, cloud computing, mobile technologies and Internet of Things, mobile health (mHealth) is rapidly developing and shows a promising future in the management of chronic diseases. Its advantages include its ability to improve the quality of care, reduce the costs of care, and improve treatment outcomes by transferring in-hospital treatment to patient-centered medical treatment at home. mHealth could also enhance the international cooperation of medical providers in different time zones and the sharing of high-quality medical service resources between developed and developing countries. In this review, we focus on trends in mHealth and its clinical applications for the prevention and treatment of diseases, especially aging-related neurological diseases, and on the opportunities and challenges of mHealth in China. Operating models of mHealth in disease management are proposed; these models may benefit those who work within the mHealth system in developing countries and developed countries.

Key words: mHealth, aging-related neurological diseases, developing countries

Population aging has become a global problem and exerted heavy burdens on the healthcare system and society. By 2030, the world is likely to have one billion people aged 65 years or older, accounting for 13% of the total population [1]. As the world's most populated country, China is facing a major challenge due to the aging population. China's aging population is estimated to increase at a rate of 5.96 million per year from 2001 to 2020 and then 6.2 million per year from 2021 to 2050, and is expected to exceed 400 million by 2050, accounting for 30% of its total population [2].

In the past 30 years, the spectrum of diseases in China has also altered dramatically due to changes in people's lifestyle and the environment. The population with chronic diseases, such as hypertension, diabetes, and

cardiovascular disease, has increased substantially. In 2012, the Chinese Cardiovascular Report[3] indicated that there were 290 million cardiovascular patients in China and forecasted that 50% of the adults aged between 35 and 84 years will have cardiovascular disease in the coming twenty years and that the number of cardiovascular disease patients will increase by 21.3 million. Due to the prevalence of hypertension, metabolic syndrome and cardiovascular disease, stroke has become a major cause of death in China. Approximately 70-80% of cerebral apoplexy patients lose their ability to work to some degree, 40% have moderate dysfunction, and 15-30% have severe disabilities, the treatment of which costs nearly 40 billion yuan [4]. In addition to the incidence of disease, the prevalence of disease among young people is an

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additional issue in contemporary medicine. For example, a 2012 survey on young people with high blood pressure (HBP) in Shandong Province of China showed that 1 out of 7 young people had HBP at the age of 14 [5]. In addition to cardiovascular and cerebrovascular diseases, psychiatric and cognitive disorders caused by aging are main features of the diseases. According to statistics, 47% of Chinese adults and 70% of the population over the age of 60 have a sleep disorder [4]. Lastly, chronic disease is not effectively managed and is resulting in heavy economic burdens to both families and society. For example, the incidence rate of Alzheimer's disease is approximately 5% in the population over 65 years, i.e., over 8 million patients; the incidence rate of Parkinson's disease is approximately 1.7%, i.e., over 2 million patients in China. It is estimated that China's annual economic burden of these diseases will be more than 200 billion yuan by 2050, assuming per capita patient costs of 10000 yuan each year [4]. Because of her large population, China has the world's largest population with chronic diseases; therefore, China will play a major role in the control of chronic diseases.

The growth of China's medical sector is unique. First, there is a serious imbalance in the distribution of medical resources in China due to the unbalanced development of economy in urban and rural areas. Medical resources are in short supply overall, especially high-quality resources, which are mainly distributed in large and medium-sized cities. Rural and remote areas remain underserved. Most people seek medical services in large hospitals, and small hospitals lack patients. As an example, the General Hospital of the People's Liberation Army (PLAGH) has over 4000 beds, and the total outpatient volume reached 4 million in 2014. More than 3000 patients wait to be admitted each day, and medical personnel experience long-term work overload. Facing the present situation of chronic disease, greater efforts are needed in chronic disease promotion, education and sustainable intervention [2]. Second, as chronic diseases are difficult to control at home and in the community, many resources will be spent on emergency services, which may reduce the efficiency of treatment and cause patient suffering.

However, in contrast to its state with regard to medical resources, China has advantages in the development of mHealth. mHealth refers to the use of information and communication technology, such as computers, mobile phones, and satellite, to deliver medical service and information [6]. Mobile communication and Internet service are as well established in China as they are in other developed countries. According to the 2014 data [7], there are 1.17 billion mobile phone users and 80 million Internet users. The Chinese population has the highest renewal enthusiasm for mobile phones, tablets and other electronic

equipment in the world. The Chinese people enjoy trying different types of new devices and software, and the penetration rate of smartphones is even higher than that in the United States (U.S.). The rapid development of e-commerce further promotes the construction of networks in China. At present, the 4G broadband penetration rate has reached 80% and mobile broadband has entered the era of 4G. In the near future, both urban and rural areas in China will move into the 5G era [7]. In China, most of the stations, ports, airports, canteens, and shopping malls provide free WIFI, which is even called a "trick" in reference to Starbucks' first location in China. The high penetration rate of mobile devices and communication networks provide an excellent foundation and great opportunities for mHealth development, which may aid in the management of chronic diseases in China and provide an opportunity to achieve healthy aging. To meet these challenges, a medical service and healthcare system suitable for the elderly has been building up in Beijing. By gaining supports from all of society, the implementation of the system will benefit millions of elderly people and also will promote the sustainable financial development and social harmony of Beijing.

In the past 10 years, there have been tens of thousands of studies on the concepts of mHealth, medical devices and applications in disease management and business models [8]. mHealth is growing rapidly not only in developed countries but also in developing countries such as Asia, Africa, etc [9]. A substantial amount of experience has been accumulated in terms of the application of mHealth for the prediction and diagnosis of cardiovascular diseases, e.g., myocardial infarction and stroke and vascular thrombolysis, which not only enhances treatment rates but also reduces costs [10-13]. mHealth has developed into an independent discipline, and new terms such as telestroke and teleneuroscience are coined.

Generally speaking, mHealth is currently at its initial stage of development. There are many issues in the technology and operating system that must be improved. Because mHealth is a new medical model, many aspects of mHealth, including ethics, policy and culture, need to be addressed. The issue of how to utilize mobile medical resources to solve the shortage of physical medical resources in developing countries or poor areas, especially the shortage of high-quality medical resources, remains a great challenge.

In this review, we focus on clinical applications of mHealth foraging-related neurological diseases and the problems and challenges that mHealth faces in the management of these diseases. This review focuses on the experience of China, which may serve as a reference for developing countries that would like to build a mHealth system and a new medical cooperation model.

Developing trend of mHealth

mHealth activities have grown in popularity worldwide. A global survey of 114 nations that the World Health Organization conducted in 2011 found that many countries have established mHealth initiatives. The most common activity was using health call centers, followed by using SMS for appointment reminders, using telemedicine, accessing patient records, measuring treatment compliance, raising health awareness, monitoring patients, and supporting physicians' decisions. Not surprisingly, there were large differences between developed and developing nations. North America, South America, and Southeast Asia showed the highest adoption levels. Africa had the lowest rate of mHealth adoption. Analysts predict that Europe and the Asia-Pacific will have the largest markets, followed by North America, and that Latin America and Africa will have the smallest markets. Within the Asian region, China and Japan will account for the largest percentage of the market, with 37 percent and 21 percent, respectively [7].

Remote monitoring devices represent a fast-growing aspect of the mHealth sector. According to a report that was jointly authored by Global System for Mobile Communications Alliance (GSMA) and PricewaterhouseCoopers (PwC), the Chinese medical monitoring services market will reach \$1.2 billion by 2017, with over 90 percent of the revenues coming from chronic disease management solutions. They also predict that monitoring services will dominate the worldwide mHealth market. The second- and third-largest market sub-sectors are diagnosis and treatment, respectively.

mHealth has attracted heavy investment in China due to its potential to bring revolutionary changes to the medical system and large market. The research firm iiMedia predicts that the mobile medical market in China will exceed 10 billion RMB by the end of 2017. They also predict rapid growth in the Chinese wearable medical devices market, which will exceed 5 billion RMB by 2017. Internet giants such as Alibaba and Baidu have announced their plans to enter the market. Because there are approximately 1.17 billion phone users in China, the market of smartphone applications has the potential for substantial growth. By using smartphone, the healthcare provider and the user can be easily connected, which not only saves time and traveling fees but also allows doctors to treat their patients more efficiently. A survey by Cube Labs finds that 30 percent of smartphone users are expected to use healthcare applications by 2015. In 2014, the High Light Capital invested \$20 million in QuYi's APP "to the hospital"; Tencent invested \$170 million in Ding Xiangyuan (the online medical network) and Guahao (Registered network); Temasek's affiliated company Pavilion Capital invested \$500 million in Spring

Rain Doctors (Omnipresent mobile "doctors"; the application has the ability to link users to more than 5,000 doctors in China's leading hospitals, and users can consult doctors by paying a nominal fee of up to 25 yuan and generally receive a professional consultation within minutes).

As mHealth allows patients to directly contact medical institutions or doctors anywhere, wearable or portable medical equipment has become a major area of investment. A wearable medical device can be described as an autonomous, non-invasive system that performs a specific medical function such as monitoring or support. The term "wearable" implies that the device is either supported directly on the human body or a piece of clothing and has an appropriate design that enables its prolonged use as a wearable accessory. In broad terms, the device must have minimal size and weight, functional and power autonomy, and be easy to use and wear in comfort. However, it should be emphasized that the value of wearable devices in the mHealth system is due not only to its portability but also to its capability to continually collect and manage patients' vital signs. Medical providers can make more precise decisions through real time evaluation and adjust patients' treatment based on the collected information, resulting in improved diagnosis and treatment efficiency as well as the avoidance of unexpected serious adverse reactions. This model breaks the traditional model of "Visit doctors on-site, take the prescription off-site, re-visit the doctors on-site again" by expediting the decision-making process of medical professionals without affecting their role in diagnosis. Therefore, regardless of the form that wearable devices and operation systems take, if they lack the strong support of medical resources as a backup, they will eventually become a "toy" in the market and quickly disappear. Business models should largely focus on this key issue. In July 2011, the Wireless Heart Health program operated by Life Care Networks in collaboration with the Community Health Association of China and Qualcomm was implemented in remote areas. 96 community doctors and 11,012 patients in four Community Health Clinics are using the system. The 3G enabled system includes smartphone with built-in electrocardiogram (ECG) sensors, web-based, electronic medical record software and internet ready workstations located within the clinics. Each workstation includes a computer terminal with internet access, providing health care workers with instant access to electronic patient records, including ECG data. Smartphone automatically send patient data over China Telecom's 3G network for fast analysis to a cardiac specialist in the Beijing Life Care Networks Call Center. Doctors provide rapid feedback to patients and clinic staff via a phone call. The facility has over 60 physicians who record and analyze the ECG information and provide

rapid feedback to the users. Out of all of the patient participants, 1,171 have been screened for serious cardiovascular conditions and referred to higher-level clinics for further evaluation and testing. The users have benefitted from Wireless Heart Health because wearable devices have a strong backup of medical professionals.

The increase in incidence of aging-related pathologies observed in the recent years has greatly emphasized the need for a personalized care system that can be extensively and effortlessly integrated into a patient's daily life. Thus far, most research efforts in this direction have been focused on the adaptation of miniaturized wearable designs based on relatively mature technologies such as motion tracking, bio-electrical signals analysis and temperature detection. Blood is by far the most understood sample for diagnostic measurements; other biological fluids, such as sweat, saliva, interstitial fluids, tears and breath, are more readily accessible and, thus, are attractive targets for non-invasive or minimally invasive wearable sensor platforms [14]. Chemo/bio-sensors face multiple challenges during their normal use. For instance, due to continuous exposure to the fluid of interest and to wear and tear, portable sensors that target biological fluid analytes need frequent recalibration to correct for signal drift over time, and in some cases, they have relatively high energy demands.

Perhaps most striking is multinational IT companies' recent dramatic movement into the wearable sensor space, including the first signs of attempts to integrate chemo/bio-sensors. For example, Google Glass is a wearable spectacle-based electronics platform that can be used to harvest body sensor data. Google has announced a novel project to integrate a glucose sensor into a contact lens that, due to the close proximity to the spectacles, could be powered inductively to enable glucose measurements and short-range communications. Currently, blood pressure, heart rate, and sleep-related and epilepsy-related body surface potential can be measured through real-time wearable devices. At the same time, there are some breakthroughs in real-time collection of biochemical indicators through implantable devices. For example, in January 2014, Echo Therapeutics Company launched a new product named Symphony Continuous Glucose Monitoring (CGM) System, a non-invasive (needle-free), wireless, continuous glucose monitoring system that is designed to provide accurate, real-time blood glucose data conveniently and continuously. Symphony's glucose sensor does not need to be inserted into the patient and, thus, does not give rise to the risks or discomfort associated with needle-based CGM systems. Symphony will provide continuous access to glucose values and changes and should identify prolonged excursions into the hyperglycemic and hypoglycemic zones [15].

Wearable devices are of emerging interest due to their potential influence on certain aspects of modern healthcare practices, most notably delivering point of care service, by providing remote monitoring, ambulatory monitoring within the health care environment, and support for rehabilitating patients, the chronically ill and the disabled. Apart from providing useful tools, the trend toward the wide spread use of personal health assistants is also viewed as a helpful step toward the transition of healthcare management into a more preventative model rather than the reactive, episodic model that is currently used. Furthermore, wearable healthcare devices can aid in changing the public's attitude toward personal healthcare in the sense that individuals are both asked and enabled to play a more active role in their care. It is expected that in the near future, these devices can be combined in a patient measurement kit for mobile rescue or primary healthcare at anytime and anywhere.

Although wearable devices have attracted more attention, there is still insufficient. One issue concerns ensuring the precision and accuracy of the devices [7]. As mentioned above, mHealth aims to change the traditional diagnosis process, treatment process and efficiency of medical professionals but not the decision-making process. All diagnoses by doctors must be made using reliable evidence. In most situations, wearable medical devices should not be used as a diagnosis tool; rather, it should be used as a tool for disease management. Wearable medical devices should focus on dynamic data acquisition, transmission of personal health data and the provision of real-time data to medical professionals, which will facilitate more timely and accurate medical decisions. Therefore, it is important for the devices to show acceptable accuracy and stability. Recently, the Food and Drug Administration (FDA) released a draft regulation on mobile medical and wearable devices. Developers and users can assess the wearable devices' performance reliability according to the guidelines.

An additional important parameter that should be considered for wearable devices is the experience of the users, especially elders. For example, the most widely used and practical wearable device is a blood pressure - ECG - sleep monitoring device named Holter. Previously, measurements of 24-hour ambulatory blood pressure and ECG were separate, and the equipment was large, inconvenient and expensive. Other problems also needed to be considered, as follows: the cuff sphygmomanometer needed high power and, thus, it was difficult to further reduce the size of Holter; and the inflation process disturbed the users during the night in a manner that was unbearable at times. Hence, continuous monitoring for more than 3 days is nearly impossible. An additional problem is that it is difficult for users to attach sensors to the designated body sites to collect accurate and reliable

data. Therefore, it is difficult to use this type of equipment for the long-term monitoring of patients. To solve the former problem, the device electrode can be weaved into a wearable “T-shirt”, allowing subjects to select the size of the T-shirt, enhancing the precision of electrode positioning and greatly improving comfort [16]. The latter problem will be solved by replacing the cuff sphygmomanometer with a cuffless technique. This technique includes 4 parts: the pulse wave measurement, data processing, extraction and mathematical modeling of feature points. A single chip microcomputer will calculate part of the output pulse wave and transfer the measurement data after processing in asynchronous serial communication mode to the host computer. The host computer will receive the pulse wave, calculate the pulse wave transit time, and establish the model of relationship between pulse wave transit time and blood pressure to achieve a cuffless blood pressure measurement [17]. An international standard for evaluating this technology has been published. Research and development of equipment for the long-term continuous measurement of blood pressure without the need for inflatable cuff compression and decompression is becoming increasingly mature. It can greatly improve patients’ compliance and reduce the cell pressure. It can also result in equipment that is more compact, portable and easily adopted by the public. At the same time, based on the principle of this equipment and the tension, “vascular age” can be evaluated. Hypertension-induced myocardial infarction and stroke remain the top causes of death among elderly patients. Thus, fusion of the wearable technology and the telestroke system may help save tens of thousands of lives and reduce social burden. These types of devices and medical models would truly reflect the revolution initiated by mHealth.

In contrast to such a sophisticated design of wearable devices, a simple design may be the most practical. For most geriatrics diseases, such as acute myocardial infarction and stroke, timely rescue is the most important aspect of the whole process of treatment; thus, it is crucial to have a disease onset alarm and to find the patients. In China, based on the size of the community, different types of clinics are established and responsible for people’s daily basic medical needs. In some relatively developed cities, elderly families are equipped with “red button” telephones or mobile phones. The key feature on the phone is the ability to set up a quick dial function through the “red button”. The user can make an emergency call immediately to obtain assistance from medical institutions. Using the telephone or mobile phone’s positioning system; emergency personnel can quickly reach the patient location. These low-cost and easy-to-use mobile facilities should be promoted in developing countries.

Clinical applications of mHealth for aging-related neurological diseases

mHealth shows promising applications for health and disease management. The available evidence has demonstrated that mHealth could optimize the care and recovery of patients with myocardial infarction and stroke, aid in the screening and management of cognitive impairment, and facilitate sleep monitoring and intervention [18-19]. Moreover, mHealth may offer solutions to accessible and good quality individualized health management services to improve the management of chronic diseases through remote monitoring and enhance awareness and diseases-specific education. However, it still needs to be validated in a large cohort in a real-world setting.

Here, we summarize the clinical application of mHealth mainly in neurology diseases. We aim to address the advantages and disadvantages of mHealth development in Western and Eastern countries and to provide alternative solutions to reduce medical burden in developing countries.

Stroke

Stroke is the second-leading global cause of death following ischemic heart disease, and accounts for 11.13% of all deaths worldwide [20]. In the past 40 years, the global incidence of stroke in developed countries was reduced by 42%, with the most dramatic decline in the U.S., where the mortality of stroke declined from the third- to fourth-leading cause of death [21]. However, in developing countries, the incidence of stroke increased by more than 100% [22]. In China, stroke remains the leading cause of death. In 2010, the cerebrovascular disease mortality rate in cities of China was 125.15/100,000 and that in rural areas of China was 145.71/100,000. According to the sixth census results of China [3], it is estimated that 833 thousand urban residents and 982 thousand rural residents died of cerebrovascular diseases in 2010.

Stroke is also the main cause of disability in the elderly. Stroke can lead to movement disorders and vascular cognitive impairment with great medical burden. Stroke can occur at anytime and anywhere, and the window period for treatment (3 to 4.5 h) is very short [23, 24]. It is critical for mobile medical attention and practice to transfer patients promptly, to make appropriate medical decisions to save the lives of patients, and to reduce sequelae. Over the past ten years, a large number of literature reports and summaries have shown that mobile medical technology can greatly improve the efficiency of emergency patients with stroke center and can help to improve the management of rehabilitation.

The stroke mortality rate in China is declining through intervention and proper control of hypertension [3]. An effective mobile medical system that covers a large area is under construction. At present, there is only a small difference between China's and developed countries' handling of calls to monitor patients' vital signs, diagnosis and interventional treatment technology and system. The largest difference concerns the determination of when and whether to give the patient intravenous thrombolytic therapy of tissue plasminogen activator (tPA). Doctors are generally reluctant to use thrombolytic therapy without imaging and neurological doctors' support [25]. Therefore, the core problem of telestroke is determining what type of stroke can be confirmed on the scene and on the road. Recently, Germany launched the stroke unit "The Stroke Emergency Mobile (STEMO)" that includes brain CT equipment and a vehicle laboratory, which can be used to complete brain imaging during the transport process. Hence, patients' stroke type can be quickly and accurately diagnosed, and thrombolytic therapy can be used during the transport process [26]. According to a random survey of the equipment, the implementation of STEMO pre-hospital treatment can shorten median medical decision-making time from 76 minutes to 35 minutes [19]. Obviously, this type of luxury equipment is not suitable for developing countries. Therefore, pre-hospital diagnosis, that is, pre-notification, is recommended by the stroke guidelines [27,28]. An intelligent mobile phone advance notification system can strengthen hospitals' preparations and shorten door to needle time. At present, large cities in China, such as Beijing, have established 200 to 300 cardiocerebrovascular and nerve specialists, who are distributed across different regions. These specialists are connected with hospitals through the mobile phone, tablet or real-time broadband to improve the identification rate of thrombolysis in stroke patients and the rate of tPA treatment. Unfortunately, because of the public culture, patients and their families lack trust in grassroots medical staff and insist on being sent to large hospitals, even if the hospitals are far away. A number of stroke patients delay visits to a doctor and miss the golden period of intravenous thrombolysis. The quality of medical institutions organized by the alliance must be unified through training rules and clothing labels, which could be useful in gaining the patient's or family's trust at first sight [29].

Diagnostic techniques play an important role in the diagnosis and differential diagnosis of stroke. Some progress has been made due to the trend of replacing CT technology with ultrasound technology [30]. It reported the use of manual control of a transcranial Doppler ultrasound diagnostic system for diagnosis and thrombolytic therapy in 20 cases of ischemic stroke

patients. The result shows that the system is safe and effective. Using easily identified anatomic landmarks (e.g., the pinna, bridge of nose, and occipital protuberance), medical professionals without neurosonology training will be able to place a device quickly in an emergent setting. The device can be effectively applied to emergency doctors and shorten the time of medical decision making.

Transcranial ultrasound scanning technology (transcranial duplex sonography) and helmet-type ultrasonic scanner technology (simple helmet transducers and transmission of ultrasound imaging via telemedicine) also allow the rapid diagnosis of ischemic or hemorrhagic stroke, but the operator requirements are extensive, and these technologies are difficult to popularize. The ultrasound scanner can be very small and easy to carry, demonstrating a potential future trend in equipment [31,32].

In addition to imaging techniques, biomarkers for early diagnosis and prognosis of stroke have received further attention. The STEMO first aid car equipped with a portable laboratory (Point of Care Laboratory) with biochemical indicators also plays an important role in early medical decisions. Biomarkers that can be used to improve pre-hospital stroke medicine decision-making ability may also be a direction of development in the future. Currently known natriuretic peptide, neuroendocrine hormone, and plasma glial fibrillary acidic protein plasma markers may be used in the pre-hospital diagnosis of stroke; these markers which can not only aid medical decision making but also be used as a monitoring index in the treatment of stroke [33,34]. Cheng Jing, as a pioneer of Lab on a Chip, led the team that developed a portable biochemical detector, which is very small in size and can automatically extract blood from a patient's fingertip. This equipment can automatically complete the whole process, from the centrifugation, detection and interpretation of the result. The result can be transferred in real time through a mobile phone or network to the hospital. In the future, the above mentioned biomarkers, which remain to be validated, may be used for the diagnosis and differential diagnosis of stroke by a clinical study cohort and for the implementation of on-site detection. Pre-hospital medical decisions concerning stroke will be greatly improved, and biomarkers can be used widely in China or other developing countries. The Hong Kong Applied Science and Technology Research Institute (ASTRI) has developed a portable cardiovascular monitoring device that can be worn at the wrist to obtain a radial augmentation index and continual blood pressure measurement. The radial augmentation index informs medical professionals of the stiffness/vascular age of the user, while the continual blood pressure measurement results indicates the user's quasi-static blood pressure

variability, which cannot be collected using a cuff-based blood pressure meter.

Besides in emergency treatment, mobile medical technology has also been successfully used in the rehabilitation treatment of patients with stroke. Smartphone can easily be used to assess the rehabilitation of stroke patients. A virtual reality system is established through the remote system, which can simulate real objects and processes using a computer to generate a simulation environment through a variety of sensing devices that users "input" to the environment and to realize interaction between the user and the environment. The system can monitor the whole interaction process of training data and compare these data to determine whether patients reached the requirements of the subject [35]. The rehabilitation training on stroke patients with disabilities shows good results, and patients rated their experience as very positive.

Telerehabilitation is an emerging method of delivering rehabilitation services which uses technology to serve clients, clinicians, and systems by minimizing the barriers of distance, time, and cost. The driving force for telerehabilitation has been as an alternative to face-to-face rehabilitation approaches to reduce costs, increase geographic accessibility, or act as a mechanism to extend limited resources. A rationale for telerehabilitation is the potential to enhance outcomes beyond what may result from face-to-face interventions by enabling naturalistic, in vivo interventions. There is considerable support for the value of interventions delivered in the natural environment, ranging from addressing efficacy concerns by addressing problems of generalization, to increasing patient participation, including environmental context in rehabilitation, and increasing patient satisfaction. Rehabilitation training after stroke can achieve cross national network through this technology may improve the efficiency of patients' recovery [36,37].

Sleep disorders

Sleep disorders are a common issue in aging. The average proportion of sleep disorders in the elderly population is much higher than that in the adult population. In the U.S., approximately 70 million people have sleep disorders, of which approximately 50 million people have chronic sleep disorders [38]. In China, the incidence reaches as high as 70% [4]. Sleep disorders can induce and aggravate many diseases and can become a barrier to treatment for diabetes and tumor primary chronic disease [39]. Similar to other chronic diseases, sleep disorders need a long treatment process. Therefore, mobile medical technology can improve the curative effect and reduce the cost of treatment. Because of the high rates of sleep-related disorders, enthusiasm for devices that detect and manage

the disease has been very high. As a result, a wide variety of "health management" wearable bracelets have sleep quality detection or intervention functions. However, most of these devices can only collect simple sleep movement data without direct support from medical staff; the medical benefits for the users or patients are vague. Sleep disorders are categorized as organic, such as obstructive sleep apnea, or non-organic, such as insomnia. The former can be treated using a continuous positive airway pressure (CPAP) ventilation device to improve the quality of breathing and blood oxygen saturation. The latter mainly needs psychological treatment or drug treatment [40]. Some types of sleep disorders cannot be diagnosed without a complicated process. Therefore, in the specification of the sleep disorder diagnosis, intervention and treatment process, mobile medical technology is only a supplement. In the diagnosis stage, a sophisticated polysomnography scanner and psychological evaluation system should be used to make accurate differential diagnoses [38] and properly address the treatment of the diseases. To overcome patients' lack of comfort in hospitals, patients can rent mattresses with sleep-monitoring sensors to assess the primary sleep disorders at their home. Then, the effect of the treatment is evaluated through real-time surveillance of the patients via wearable devices. In this way, the therapeutic effect can be evaluated and adjusted at all times and in any location. No return visit is needed.

Although the population with sleep disorder-related diseases is large, China lacks a professional treatment center. Until recently, sleep disorder treatment centers were established in West China Hospital. The Hong Kong ASTRI has been developing a wearable device with integrated functions for simultaneously measuring continual heart rate, heart rate variability, pulse oximetry and body motion, which provides medical professionals with valuable overnight data. A remote sleep disorder diagnosis-in-hospital, treatment-out-of-hospital model that uses such devices and the cloud is under operation.

In addition to paying attention to patients' sleep state, telemedicine technology has been proposed to solve problems caused by overnight medical personnel. Globally, medical staff members are experiencing work overload, which is particularly prominent in China and other developing countries. Night shift work can lead to the reversal of medical staff's sleep disorders, reduce their work efficiency and cause damage to their body [41]. A 24-hour mode was proposed, in which hospital medical staff's night shift work is done by colleagues who work at sister hospitals that have a 12-hour time lag using remote medical technology [38]. This may reduce the work intensity of medical staff and improve the overall diagnosis and treatment quality that patients receive. This mode is not limited to the interpretation of the image data;

it can also be extended to other aspects of medical management, such as the management of an intensive care unit. The night flipping model can also be used in pension institutions of developed and developing countries to improve the efficiency of the monitoring of elderly accidents at night through wearable wrist devices.

Cognitive dysfunction

Cognitive dysfunction has become one of the most serious diseases affecting the elderly health and quality of life [42]. Cognitive dysfunction includes memory disorders, aphasia, apraxia and visual spatial disorder and is accompanied by intense emotional and behavioral disorders such as anxiety, depression, agitation, and impulsivity. These emotional and behavioral disorders can be the causes of patients' disability [43]. The incidence rate of cognitive impairment increases with age and is expected to become 1/85 by 2050 [43]. At present, the prevalence rate of mild cognitive impairment in the elderly population of China is 3% to 19%, the incidence rate is 5 to 58/1000 per year, and the dementia conversion rate is 11% to 33% every two years. A total of 7.7 million patients are given a first diagnosis of dementia each year, which exerts a heavy burden on the family and a great economic burden on society [44].

In the 1990s, to quantify cognitive function impairment, Bowler and Hachinski presented the concept of vascular cognitive impairment (VCI) [45]. VCI is a syndrome that is caused by risk factors for the cerebral vascular diseases (such as hypertension, diabetes and hyperlipidemia). Obvious cerebrovascular diseases (cerebral infarction and intracerebral hemorrhage) or unobvious cerebrovascular diseases (leukoaraiosis and chronic cerebral ischemia) with clinical characteristics have been associated with mild cognitive impairment to dementia. The population that is at high risk for stroke is also at risk for cognitive impairment. VCI is the only currently available prevention indicator for cognitive impairment. The screening of this population's cognitive status and analysis of possible risk factors can aid in the early diagnosis, intervention and prevention or delay of dementia.

The traditional assessment of cognitive impairment needs to be conducted in a face-to-face manner, including a basic physical examination and an evaluation of the subjects' nervous system. In the face-to-face cognitive assessment process, one can ask the patient or agent to answer some questions or to perform certain tasks to determine the patients' cognitive status. However, most of the patients with cognitive disorder are scattered across different communities and different regions and not all patients with cognitive impairment can receive a timely and effective assessment, which will lead to missing of the

best time of early intervention. It has been shown that smartphone use for early screening of cognitive impairment is convenient and efficient for the completion of assessments; it can especially facilitate the early screening and effective assessment of elderly patients [46]. A study conducted in Hong Kong showed that smartphones can be efficiently used in the screening and management of VCI. Assessment was completed by smartphones with voice, image and face-to-face interaction functions, which can be used to store images, transmit data and complete automatic cognitive assessments without a professional guide [47]. This approach can be duplicated in the mainland and other developing countries. However, due to differences in cultural and education backgrounds, this technology may need to be adapted to these areas.

mHealth can also play a major role in the rehabilitation management of patients with cognitive dysfunction [48]. Most patients with cognitive disorder need continual treatment after they are discharged from hospitals. However, they cannot regularly go to professional rehabilitation centers for rehabilitation therapy. Computer-aided training has become an effective means of cognitive rehabilitation. Javier Solana [49] developed a new intelligent rehabilitation system for intelligent assistant (The Intelligent Therapy Assistant, ITA). The cognitive evaluation system provides an automatic analysis of patients' cognitive status and arranges rehabilitation content. According to a clinical observation of 528 cases with cognitive disorder, ITA can improve the rehabilitation effect of patients with cognitive impairment [49].

Virtual reality (VR) technologies can promote the combination of computer technology and cognitive science at a higher level. The rehabilitation assessment and training of cognitive impairment showed great advantages compared with the traditional methods. Virtual reality technology used for cognitive dysfunction after brain injury, which is based on virtual reality modeling, cognitive rehabilitation evaluation of human-computer interaction and cognitive rehabilitation training, can overcome disadvantages of traditional treatment, such as its time-consuming and laborious nature. Hannah C et al. reported that virtual reality cognitive training and rehabilitation training can effectively improve the cognitive level of patients with mild cognitive impairment and dementia [50]. At present, the 4G network can solve the technical bottleneck of image transmission. The 5G network will promote all-round development of the virtual reality interface, which will greatly enhance the efficiency of mobile health and the opportunity to create remote training center-based international corporation networks for the rehabilitation of patients in developing countries.

Epilepsy

Epilepsy is a common disease of the nervous system; it is also known as chronic recurrent brain dysfunction syndrome. The abnormal discharge of neurons in the brain is the main cause of epilepsy. The Epilepsy Foundation reports that the epilepsy incidence rate reaches as high as 1/26, 70% of which can be controlled via timely treatment and control. Telemedicine plays an important role in the treatment and follow-up of patients with epilepsy, especially those in remote areas [51].

Epilepsy is a random phenomenon that occurs without warning. The amount of time within which this disease should be treated is not fixed. It is difficult to control the duration of the disease and collect the onset data of patients even when 24-hour monitoring is used in hospitals. Undoubtedly, epilepsy may occur suddenly while patients are on the way to work, shopping or travel; thus, it is difficult to control quickly. To solve this problem, an implanted monitor coupling anti-epileptic drug can be used for the treatment of seizures with continued effectiveness [52].

Dialog is a wrist recorder that can be connected through Bluetooth and smartphones. It can remind patients to take medicine and issue a warning at the disease onset period, simultaneously notifying the patient's family, friends or nursing staff. Patients with the onset of the disease can trigger the alarm by simply holding the device. Because there will be an alarm before the onset, patients can double-click the equipment and record the alarm so that they can predict the onset of the seizures. At present, Dialog is only a concept; it should be available in two years. A similar wearable device that developed for the treatment of epilepsy can detect and provide early warning of epileptic seizures and promptly inform patients' family members of preventive measures. This device uses an algorithm to calculate epilepsy patients' respiratory frequency and heart rate, which will facilitate effective preventive measures and treatment methods [53].

Another form of wearable device is also under development. For example, Venture Company Bio Serenity has designed a smart shirt, called Wearable Epilepsy Monitoring Unit (WEMU), which can be used with big data to diagnose and treat patients with epilepsy. WEMU smart clothes can provide patients with timely and effective monitoring and treatment, especially patients with cognitive disorders.

Elderly fall prevention

Falls are an important threat to the health of the elderly. Falls can cause injuries and reduced activity, self-care ability and social ability [54]. Accidental falls are one of

the important factors that cause injury in elderly people over 65 years old and area major cause of death in the elderly over 85 [55]. Slips and falls accounted for approximately 40% of all falling cases of elderly over the age of 70. Hip fracture caused by slipping is closely related to death [56].

Effective slip prevention trainings have been conducted with the elderly. Of these trainings, anti-disturbance training, such as perturbation training [57], which is based on repeated sliding training adaptation and long-term memory, has proven to be most effective. Adaptive training allows the subjects to conduct anti-slipping training in a protected environment and improve their ability to control their body's motion and quickly respond to environmental disturbances in the process. This approach is adopted to improve individuals' dynamic stability and physical support to reduce their risk of slipping. Studies have shown that through repeated training, the young and the elderly have similar stability recovery ability and adaptability [58,59]. Long-term changes caused by movement and posture control systems through the perturbation of training will also produce the actual effect on the slip intervention and reduce government expenditure on healthcare due to falls [60].

The Fraunhofer Institute in Berlin has developed a rehabilitation training system, called myrehab that patients can use for rehabilitation training at home. The whole system consists of a special camera, a television set and a chest strap with a plurality of sensors. A virtual character guides the patient through exercises using a guidance system characterized by corrective action. The system also allows doctors and therapists to communicate with patients through Internet video.

As elderly fall prevention is needed for a large population, even if experts can guide patients through fall prevention training via a remote monitoring system, the resources remain limited. Recently, we carried out tens of thousands of elderly fall prevention trainings in different areas of China in collaboration with Yi-Chung Pai from the Department of Physical Therapy, University of Illinois at Chicago, to establish an effective database and associative parallel processor (APP) platform for patients' remote self-evaluation via mobile phones. Patients can input their physiological, pathological data and past life experiences (such as whether they were brought up in the mountains, had sports experiences and other information) through the APP. The computer provides the fall risk assessment value following the analysis of data. Patients with low risk can be arranged to basically learning through a telemedicine system and those with high risk may be recruited to the training centers. Through triage via this APP, fall prevention knowledge can be promoted effectively and resources can be greatly saved and used for the necessary people. This is a new model that will

properly connect mHealth with the public.

Issues related to mHealth services

The technical aspects

mHealth based on wearable medical devices helps achieve a high-quality and evenly distributed system. Additionally, it will change the traditional face-to-face consultation model. In addition to the battery life and accuracy of the device and users' experience with the device (which can be resolved at some point), the most important core issue in the development of mHealth is how to ensure that patients and medical providers can benefit from these devices and systems. In China, the construction and investment of devices and databases are often separate; thus, the measured parameters from individuals are isolated and are difficult to gather and centralize as big data to assist doctors in making decisions. Therefore, data isolation is the largest problem that medical providers and investors face. At the present stage, features of mobile medical equipment should be highlighted in terms of mobile technology, and the goal and model of the application should be set in a relatively limited range. From our point of view, the current mobile devices, especially wearable devices, cannot meet the demand of disease diagnosis and, therefore, should mainly be used in disease management. As mentioned above, treatment and rehabilitation outside of the hospital is one of the most important factors for senile diseases. After the disease has been diagnosed via the traditional method, wearable devices can be used to assess efficacy, monitor therapy-related toxic and side effects, and guide remote rehabilitation. For example, we recently designed a study for patients with hypertension by adjusting the initial use of medication with the new Holter mentioned above. The patients' daily medications, activities and self-reported possible drug-related side effects, such as headache, can be easily recorded through an APP on their smartphones. Doctors can monitor blood pressure, heart rate, respiration and sleep information after treatment in real time using a smartphone or tablet.

According to the data collected after a few days, doctors can easily determine whether the prescription is reasonable and adjust the treatment as appropriate. Most importantly, doctors can terminate the treatment in sufficient time if patients experience a serious adverse effect, such as drug-induced bradycardia. Through this model, a comprehensive evaluation of effects, severe toxicity and side effects and drug economy can be quickly obtained to effectively determine the dosage regimen for patients. Similarly, the use of wearable devices for the monitoring and management of sleep disorders can also maximize the drug effect and communication between

doctors and patients and minimize the medical costs. Through this mode, a large database can be established and used as a decision-making system.

Issues surrounding policies, regulations and culture

In addition to technical problems, the development of mHealth is affected by culture, policies and regulations. Of these, a government's policies are the most critical. At present, the Chinese government is supportive of the development of mHealth, but the corresponding regulations and standards lag behind. Although many hospitals have implemented HIS systems for many years, thus far, there is no state standard, and the hospital data cannot be shared. Data islands can be found everywhere. Some local governments have made efforts to change this situation. For example, the municipal government of Xiamen city launched the intelligent medical city project and has invested heavily in unified medical information and established an alliance with the people's Liberation Army General Hospital to implement the city's medical card. Individual medical information can be shared among all hospitals in the city, which not only improves the efficiency of treatment and reduces the medical burden caused by repeated inspection but also provides a foundation for realizing health and disease management based on mHealth.

An additional obstacle in developing mHealth in China is the lack of regulations and standards. In the U.S., the FDA always takes a flexible policy to keep recommending regulations to coincide with the development of new technologies and new biomedical markets, securing the U.S.'s leading position in the field of biological medicine, even during the global recession of the past 20 years. Regulatory sciences and regulatory reform have also played a significant role in the development of mHealth. In July 2011, the FDA issued a report on the mobile medical app guidance draft regulation. After debates, on September 23, 2013, the FDA officially released the mobile medical applications (MMAs) regulatory guidelines, focusing on the supervision on two types of mobile medical Apps: 1) those used as an accessory of a regulated medical device and 2) those used to transform a mobile platform into a regulated medical device. At present, hundreds of mobile medical applications received by the FDA and dozens of APP have been approved. As mentioned above, in the U.S., a clinical APP for diagnosis and data transmission will be regulated by FDA. Therefore, most of the multinational or transregional telemedicine services only provide recommendations to patients or other medical personnel to bypass the regulation.

However, the regulations always lag behind the emerging new bio-pharmaceutical technologies and

market demands in China. On January 15, 2015, China Health and Family Planning Commission issued a "remote medical information system construction technology guide" and defined the basic function of the national and provincial remote medical service and resource monitoring centers and the remote medical service site architecture and construction standards. It put forward the construction of remote medical treatment, as follows: 1) the proposed information system should be planned in a standardized manner with hierarchical and stage construction; 2) adhere to the government's lead, effectively promote the cooperation between all levels of medical institutions and medical resource sharing; 3) adhere to uniform standards, technical barriers to restrict and exclude artificially construction, and an open system to achieve interoperability between all levels of remote medical system information, resources and services; 4) include telemedicine construction and management tasks in the government work plan and evaluation index; 5) encourage the active participation of social forces and promote the construction and application of telemedicine. However, the new mobile medical services and hospital charges are not covered by medical insurance. Furthermore, the guideline was issued by the Health and Family Planning Commission rather than the direct regulatory authority, China Food and Drug Administration (CFDA), which caused further confusion in the field. This situation should be changed, and many motions have been submitted to the central government.

Operation model of mHealth

Mobile health can improve the efficiency of disease treatment and health management and will be helpful for achieving the accessibility and equality of high-quality medical resources. However, a poor operation model may lead to low efficiency. For example, some large hospitals have established many telemedicine networks distributed in different regions in the same province or among provinces in China. Such networks play a significant role during disaster relief, emergency care and health providers' tele-education. However, if they operate in a daily model, many problems exist. The First Affiliated Hospital of Zhengzhou University, China's largest general hospital, which owns nearly 8,000 patient beds, has built a telemedical platform from Huawei. The system provides telemedical solutions for patients in remote areas through a consultation center of experts. The system can not only provide real-time audio and video communication but also combine the Hospital Information System (HIS) and different types of endoscopes, B ultrasound monitoring instruments, and medical equipment integrated with communications systems. However, as the virtual "face-to-face" consultation takes a substantial amount of time,

experts are reluctant to participate in the telemedical consultation, which lowers its effect and return.

Therefore, if we take into consideration the fact that the core of mHealth is to maximize the efficiency of high-quality medical resources and adopt a proper operating model, mHealth can break the regional and national medical resource restriction, resulting in an expansion that forms a global alliance of high-quality medical resources. It also brings major business opportunities to the health market.

The value of medical practice is universal, regardless of whether one lives in the West or East, is rich or poor, or is a resident of a city or a remote area. mHealth technology provides a hitherto unknown opportunity to solve these problems. However, the investment must be large to achieve the technology, system and network goals. Following the government, the power of the market is the second most important factor. Therefore, it is worth exploring how to promote the development of the market, how to maintain the enthusiasm for investment, and how to establish and perform an effective mHealth system and model, especially in the early stage of the development of the technology. Several suggestions for the development of mHealth are provided below.

The unified practice doctors model

As mentioned above, the resources of medical experts are always scarce; thus, the establishment of a unified clinical pathway and a unified computer-aided decision training and triage medical decision-making system is very important. In this system, patients on the mHealth interface are first exposed to a trained unified doctor (TUDoc) or even digital doctors. Here, if their claims are easily diagnosed and managed, they can be treated by the TUDocs or even answered by the digital doctors. The TUDocs or digital doctors provide patients with the basic medical recommendations and follow up via a standard clinical pathway. Therefore, one TUDoc may be in charge of 10 or more patients. Behind every 10 TUDocs, there is a medical specialist who is responsible for the problems that the TUDocs cannot solve or provide emergency medical support. Above the experts is an expert cloud, which gathers national or worldwide experts, who are able to join the diagnosis and treatment process at any time through their mobile phone, tablet or laptop computer APP by request. This system ensures not only the overall quality of the mHealth platform but also the consistency of healthcare quality in the system. In this way, one specialist can easily be responsible for 10 TUDocs, while a network of TUDocs can easily be managed and the specialist's capability can be magnified 10 times (Figure 1). "Experts Cloud" will provide reliable medical support for the whole system. Because all of the doctors do not

need to provide face-to-face serve in the process, for patients, the brand effect of the mHealth system is the same whether the doctor is a TUDoc or a specialist. Patients' compliance can be greatly improved.

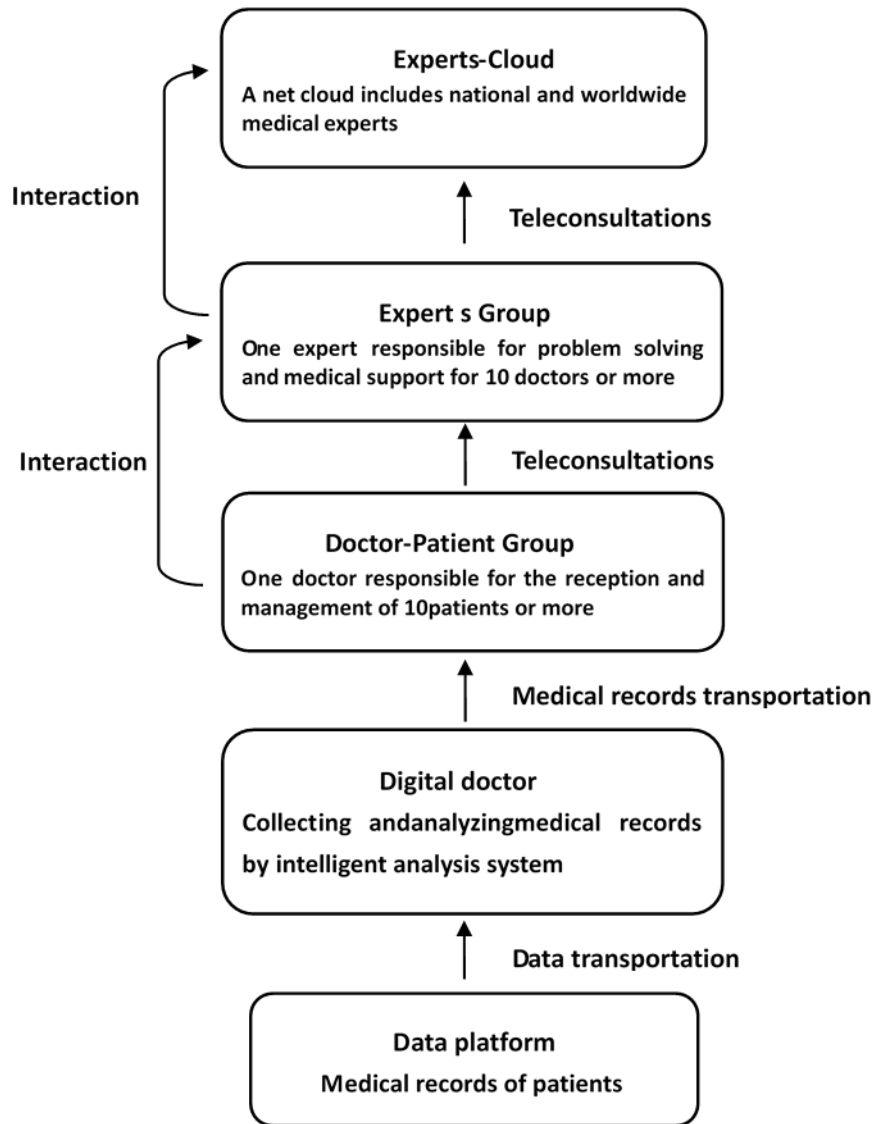


Figure 1 Classification Treatment System Model. (1) A digital doctor utilizes big data platform on medical health to collect all types of medical records of patients. After automatic classification and the intelligent sorting of history and risk factors, it generates a mobile electronic health medical record, which finally realizes the customized health risk factors management; (2) Doctors are trained and unified (TUDocs) by the standard clinical pathway and put forward the basic treatment recommendations for patients. They provide basic medical service and follow-up service. They can refer patients to medical experts; (3) The experts and networking experts group is responsible for the problems that general doctors cannot solve and provide emergency medical support. Above the experts, there is an experts-cloud, with national or worldwide experts, who are able to join the diagnosis and treatment processes at any time through a mobile phone, tablet or laptop computer. Experts can interact with other experts and experts and doctors can interact with each other in the network.

Redistribution of wealth from the rich to the poor

Due to the large investment and high requirement of fundamental infrastructure, a profit model that is in an early stage should enhance the activeness of investors and maintain the market's enthusiasm. Therefore, even in developing countries, the initial service target should focus on the niche of social elite and wealthy people. These people have the greatest demand and desires for quality healthcare, with the greatest enthusiasm for participation and most financial resources. The social influence of the effect of implementation is also fastest and most obvious in this niche. It is not difficult to understand the implications of this model following a view of the history of the mobile phone in China. If the price of the first-generation mobile phone "Big Brother" in the early 1990s is held constant, its popularity might be a hundred fold.

The internationalization of mHealth

mHealth can not only be used to achieve the accessibility and equality of medical resources but also used to integrate high-quality medical resources globally, especially in developed countries, which can increase the level of disease prevention and treatment. A new remote cooperative medical alliance can be formed through international remote medical institutions. Through this alliance, patients in developing countries could receive medical recommendations from doctors in developed countries. For example, the business of the American Image Interpretation Center can be extended to China or other developing countries, which will improve the quality of image interpretation and solve the problem of the low efficiency of partners who work the graveyard shift on the other side of the world. In turn, the medical institutions in developed countries can organize the substantial clinical resources from developing countries to expand and enhance their existing medical decisions database. Therefore, their cooperation would be mutually beneficial and complementary. To achieve this goal, rules or relevant standards and regulations of globalized mobile medicine should be drafted in the early stage to provide opportunities for international medical resource sharing.

Prospect

Following the global trend of population aging, China has become a heavy aging society. Healthcare for the elderly should be an essential part of the basic medical service and should focus on health promotion, chronic disease treatment, rehabilitation, long-term care, and hospice care. Medical services for the elderly in China are faced with an unprecedented challenge and a rare opportunity, which

will have a profound influence on sustainable financial development and social harmony. The improvement of the geriatric healthcare system is a long-term and arduous task. It entails the vigorous support of governments at all levels and the active participation of the entire society. The current mHealth for geriatric health literature throughout China is quite limited. To ensure patients have access to the best possible resources, there is a critical need for rigorous research that will produce high quality and evidence-based mHealth programs. In developed countries, information technology will likely continue to improve existing systems of mental healthcare. But in developing countries, technologies may play an even more crucial role – serving as the primary conduit to introduce training, resources, and services that might otherwise remain nonexistent or out of reach for the vast majority of the population. Therefore, encouraging greater cooperation among network operators, equipment manufacturers, and health care professionals would encourage the adoption of mHealth. It would be easier to innovate and speed up the growth of the mHealth market by improving discussions across these groups.

Mobile health applications offer unique opportunities for monitoring patient progress, providing patients and family members with education materials, receiving personalized prompts and support, collecting ecologically valid data, and using self-management interventions when and where they are needed. Mobile health application services for mental illness have evidenced success in Western countries. However, they remain in the initial stage of development in China. The promotion of mobile health application development in China is much needed. With the advancement of wearable health devices, cloud computing, and the mobile technologies and Internet of Things; mHealth is rapidly developing and shows a promising future in the management of chronic diseases. Its advantages include its ability to improve the quality of care, reduce the costs of care, and improve treatment outcomes by transferring in-hospital treatment to patient-centered medical treatment at home. mHealth could also enhance the international cooperation of medical providers in different time zones and the sharing of high-quality medical service resources between developed and developing countries.

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