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**TECHNICAL AND BEHAVIORAL
INTERVENTIONS FOR MEDICATION
ADHERENCE THROUGH M-HEALTH**

BY

XINYING LIU

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree

Of

Doctor of Philosophy

In the Robinson College of Business

Of

Georgia State University

GEORGIA STATE UNIVERSITY

ROBINSON COLLEGE OF BUSINESS

2020

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Acknowledgement

First and foremost, I would like to express my deep and sincere gratitude to all the special people who have supported my pathway toward this dissertation. I am tremendously fortunate to have Dr. Upkar Varshney to be my advisor and mentor. His dynamism, vision, sincerity, and motivation have deeply inspired me. Not only he guided my research, but also his patience and encouragement always provide me with mental comfort. It was a great privilege and honor to study under his guidance and work with him.

I would also like to thank my wonderful committee: Dr. Aaron Baird, Dr. Yu-kai Lin, and Dr. Anu Bourgeois. They all shared invaluable advice and feedback throughout this dissertation's development. I am extremely grateful for what they offered me to enrich this research.

I express my thanks to my parents. Their love and caring provide me with great courage to pursue my dream. Many thanks to them for keeping themselves healthy as well. And special thanks to my friends, especially my roommate. They were the ones who add different colors to my life when I need them.

This dissertation is also a gift to my deeply loved grandfather. I feel sorry that I was unable to sit by his bed and hold his hands when he misses me in those days. I know he is now a star that winks at me from the sky, and I can still talk to him.

ACCEPTANCE

This dissertation was prepared under the direction of the *XINYING LIU's* Dissertation Committee. It has been approved and accepted by all members of that committee, and it has been accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Business Administration in the J. Mack Robinson College of Business of Georgia State University.

Richard Phillips, Dean

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ABSTRACT

TECHNICAL AND BEHAVIORAL INTERVENTIONS FOR MEDICATION ADHERENCE THROUGH M-HEALTH

BY

XINYING LIU

08-JULY-2020

Committee Chair: *Dr. Upkar Varshney*
Dr. Aaron Baird (Co-chair)

Major Academic Unit: *Computer Information Systems*

In this research, we present a novel intervention, Carrot and Stick, to improve the outcome of one of the self-management tasks, medication adherence (MA), among patients with chronic disease(s). Our design incorporates the growing importance of mobile health (m-health) in Health Information Technology (HIT) with the users' dependency on mobile phones to facilitate valuable behavioral changes. Drawing on Social Cognitive Theory, Social Exchange Theory, Goal-setting Theory, and people's dependence on smartphones, we develop the functionalities in our intervention, including positive and negative reinforcement, goal-setting, and social connections. The iterative process of our development follows the Design Science Approach.

In the evaluation and validation of our intervention, we not only examine the intervention's impacts on patients through analytical models and simulation but also demonstrate the possible

active support of the intervention from healthcare providers based on the current pay-for-performance (P4P) scheme. Our results suggest that (1) with the help of electronic medication container, appropriate reminder design can reduce the patients' chances of forgetting doses, overdosing, and intaking doses at the wrong time, (2) positive reinforcement can help increase the probability of the patient achieving expected MA, while negative reinforcement has a further impact that is added to the increment, (3) our intervention can assist the patient in saving more than \$600 per year, and (4) under the current P4P scheme, physicians with the exceptional performance or with bad performance are likely to invest in the intervention to change their patients' behaviors, while physicians with good performance are less likely to participate.

Our research is the first to utilize negative reinforcement in intervention design to enhance MA; it is also the first to provide corresponding interventional solutions that are customized according to elements derived from theories. Besides, the focus and understanding of healthcare providers' involvement in the incentive program can facilitate the adoption, prescription, and implementation of the proposed intervention.

Keywords: Medication adherence, m-health, pay-for-performance, intervention, reinforcement, chronic disease management

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Chapter 1. Introduction

According to Centers for Medicare & Medicaid Services (CMS) report, U.S. spending on healthcare has been kept to more than 17% of the GDP since 2009 (Figure 1). The 2017 data shows the total healthcare spending was approximately \$3.5 trillion dollars and spending per person on average has reached \$10K¹. And the RAND Corporation's report in 2017 shows within the spending, 90% is for patients with chronic and mental health conditions (Buttorff et al. 2017). Over the coming years, the prevalence of chronic diseases is predicted to increase as a result of the rapid aging of the population and the greater longevity of people with chronic conditions (Tunstall-Pedoe 2006). Healthcare systems struggle with coordinating care for people with chronic conditions. However, with significant spending on chronic diseases, we have not seen the desired quality of care in the outcomes. Heart disease and stroke have led to about one-third of all deaths every year in the U.S. It is approximately 86,000 in total, and 235 persons per day (Benjamin et al. 2018). More than 26.9 million Americans are diagnosed with diabetes, with another 7.3 million people are undiagnosed, and both the numbers keep increasing every year. The related complications caused by diabetes, such as kidney failure and blindness, also become more serious problems over time (Control and Prevention 2020).

The reasons behind this situation are complicated, but one of them is the re-active approach, which predominates the healthcare system. The healthcare providers react to patients' requests, and the patients just get the treatment or prescriptions from the professionals. The patients are passive in their healthcare decisions, and it has been observed to be not effective enough in managing chronic conditions. Besides receiving appropriate clinical care, the patients and their

¹ Data source: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf>

family members should take the central role in making informed decisions and managing their chronic health conditions on a day-to-day basis.

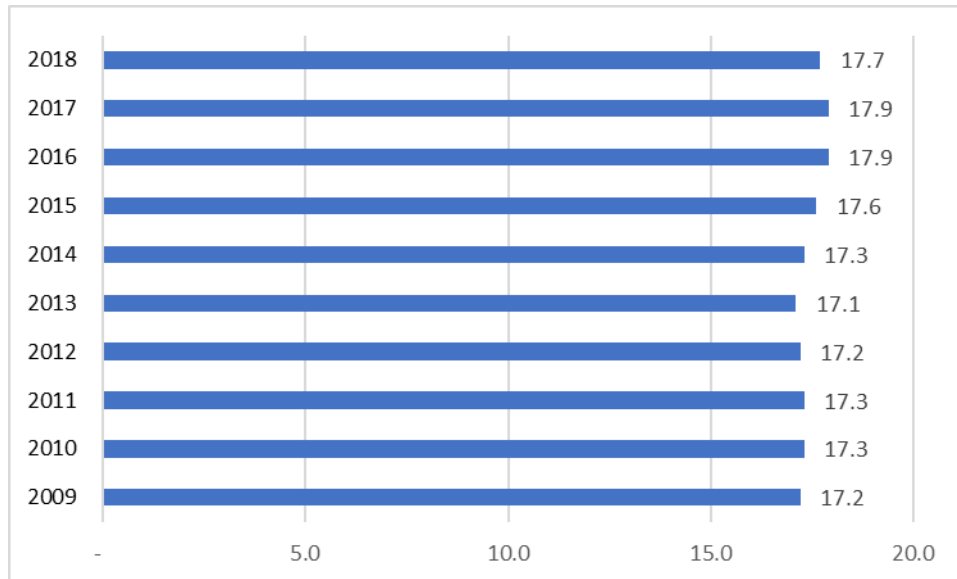


Figure 1: U.S. National Health Expenditure as Percent of GDP

The concept of self-management captures the patient’s involvement in managing their own care. It is defined as “the individual’s ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition” (Barlow et al. 2002). There are four task categories in self-management according to Clark et al. (1991):

- Engage in activities that promote health, such as exercise, healthy diets, and social activations.
- Interact with healthcare providers and systems, as well as adhere to the recommended treatment protocols.

- Monitor physical and emotional status and make informed decisions based on symptoms and signs.
- Manage the impact of the illness on emotions and self-esteem, and relations with others.

Even though the patient is central in accomplishing these tasks successfully, the achievement of optimal outcomes requires the redesign and involvement of more parties. The Chronic Care Model (CCM) outlines how should the interactions among six interrelated components be facilitated and successfully implemented (Wagner 1998). The self-management support component lies in the center of the model, and the other five parts are community resources and policies, organization of healthcare, delivery system design, decision support, and clinical information systems. The model has been found effective when it is implemented as a whole or only partially (Bodenheimer et al. 2002; Tsai et al. 2005).

Recently, critical changes are taking place in the organization of healthcare component. The national Quality Payment Program (QPP) modifies the healthcare provider's payment structure. The reform, which shifts from the emphasis on the number of services providers perform to reward outcomes for patients, requires the providers to pay more attention to patients' self-management to achieve higher quality outcomes of chronic disease treatments. It facilitates increased participation of healthcare professionals in supporting patients' self-management. Also, within the program, the interoperability of health information is encouraged. The integration of health information captured from multiple sources, especially the patient-generated data, can provide deeper insights into the patient's behaviors and better support self-management.

Section 1.1 Research Context

Within the four self-management task categories, the poor adherence to recommended treatment protocols, especially the prescriptions, is shown to be an ever-present and complex problem for decades. Medication adherence (MA) is defined as “the extent to which a patient act by the prescribed interval, and a dose of the dosing regimen.”(Cramer et al. 2008). According to an estimate in 2011, more than half of Americans with chronic diseases do not take their medications as prescribed and are said to be non-adherent with therapy (Brown and Bussell 2011). This situation persists as 40% to 50% of patients are not adherent to their prescribed medications for the management of chronic conditions (Kleinsinger 2018). In addition, MA works as “the key mediator between medical practice and patient outcomes” (Kravitz and Melnikow 2004). Positive associations between poor MA and clinical outcomes such as re-hospitalization, morbidity, and mortality have been demonstrated in previous studies (Smith et al. 2011). The poor MA is a significant public health problem that imposes a considerable financial burden and leads to worsening of diseases. In general, 80% of medication adherence is desired for chronic conditions; however, a higher level (95%) may be needed for acute conditions (Osterberg and Blaschke 2005).

To resolve this critical barrier that hinders healthcare outcomes, a lot of efforts have been spent by researchers and healthcare professionals to examine the reasons behind poor adherence. Four groups of factors have been identified. The first is inadequate dose frequency and/or scheduling (Eisen et al. 1990; Paes et al. 1997); the second is insufficient patient education about the disease or poor health literacy (Seltzer et al. 1980); the third includes patients’ demographic factors (Beardon et al. 1993; Ren et al. 2002), their beliefs about the effectiveness of treatment (Horne et al. 2005), or their motivational factors (DiMatteo et al. 2000); and the fourth is lack of

social support (DiMatteo 2004). In practice, the factors that influence medication adherence behavior are usually a combination of the above categories. They are sophisticated and could be unique to individuals, thereby requiring numerous multifactorial strategies to remove barriers and promote adherence. A large number of interventions have been proposed by researchers and healthcare professionals to improve the patient's self-management performance in following the prescription. However, effective interventions have been complex and expensive (McDonald et al. 2002).

In recent years, mobile health (m-health) solutions have been introduced to enhance the adherence factor in self-management. M-health is broadly defined as “medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices” (Kay et al. 2011). It is said to be “healthcare to anyone, anytime, and anywhere by removing locational and temporal constraints while increasing both the coverage and the quality of healthcare” (Varshney 2009). M-health facilitates many self-management interventions in practice based on its supportive functionalities, inexpensiveness, and constant accessibility. It is not a replacement for traditional healthcare services, but it can change the way healthcare services delivered to be more patient-centered. It provides patients with healthcare information to help them make better decisions, giving them instructions to follow physicians' advice, and supporting the overall quality of their healthcare (Varshney 2014). A systematic review of m-health self-management intervention using text messages, including educational information and reminders, to increase MA has shown that text messaging is a highly acceptable and feasible intervention. And a majority of studies (18 out of 29) found significant improvement in patients' MA (Park et al. 2015). Elderly patients, using a tablet application to enable behavior tracking, are found to have higher MA than

patients writing a diary to keep track of their performance (Mertens et al. 2016b). In a program enabling patients' consistent connection with health professionals through m-health, there was a significant decrease in the number of hospitalizations during patients' participation period. The essential contributing reason was increased MA (Španiel et al. 2008).

Section 1.2 Research Questions

Although there are promising results from previous intervention studies, there are also major weaknesses. An earlier systematic review of m-health interventions has pointed out that there was a lack of long-term studies, appropriate statistical and economic analysis, and test of theory-based interventions (Thakkar et al. 2016). Our review of publications within the last ten years has found the lack of theory-based interventions, and the short-term estimation of effectiveness are still drawbacks. In addition, even though the motivational factors have been identified among significant factors that impact patients' behaviors, m-health interventions that are designed to promote patients' self-management by influencing their motivations have not been studied. Money, voucher, and lottery have been all examined in a clinical setting for their effectiveness in promoting MA as the reward, also known as the positive reinforcement. However, short-term observation and a small number of participants lead to less than reliable results (Barnett et al. 2009; Moore et al. 2015; Sen et al. 2014). M-health provides a solution to overcome these obstacles because interventions delivered through the mobile platform have significant potential to impact the decision-making process of a large population worldwide. Also, a critical characteristic of the mobile phone, especially the smartphone, was ignored in the previous studies. Smartphone users are highly dependent or almost addicted to mobile applications, such as Facebook, Twitter, and many games. This aspect can be used to change patients' behaviors as well.

Thus, this leads to our first three research questions

***RQ 1:** How can motivational factors and users' dependency on mobile phones be incorporated in self-management intervention to promote MA through m-health?*

***RQ2:** What is the theory base of such an intervention? How should the intervention be applied to different patient types?*

***RQ3:** Will the intervention be effective and cost-effective?*

Based on what we have discussed in the healthcare provider's payment structure transformation and the interoperability of health information, healthcare providers are expected to participate in supporting patients' self-management increasingly. Our fourth research question is:

***RQ4:** When would a healthcare provider choose to be an active supporter of the intervention?*

Section 1.3 Research Approach

The critical prospect of our research is the development of an m-health intervention to address the problem of poor MA among patients with chronic diseases. We follow the Design Science Approach to utilize theories to generate, evaluate, and improve our novel intervention, terms as Carrot and Stick. The functionalities of our intervention are built up based on theories. In the validation of our design, we deploy analytical models to assess effectiveness. We also leverage the analysis results from a public healthcare dataset, Medical Expenditure Panel Survey, to initialize a simulation model to estimate the savings due to our intervention. The participation of healthcare providers is also evaluated by testing analytical models.

Section 1.4 Research Contributions

Our research contributes to the literature in two ways. First, we establish a theoretical foundation that helps in narrowing the gap in reinforcement intervention in m-health. Our research investigates the utilization of both positive and negative reinforcements. It is the first one that utilizes negative reinforcement in intervention design to enhance MA. This unique element of negative reinforcement complemented the application of reinforcements in behavior change literature. Second, we develop the scenarios of our intervention to cover a variety of patient types and illustrate how to set system parameters for these scenarios. The theory base of our design facilitates the scenarios to be reliable. From a practice perspective, our study contributes a well-designed and valid novel intervention, which fully utilize mobile characteristics in modern life to enhance patients' medication adherence. Also, we transform the users' dependence on smartphones into a promising solution to the long-existing medication poor adherence problem. According to our simulation, the intervention can help patients with diagnosed diabetes save more than \$600 in medical expenditures per year. Our discussion of application scenarios provides healthcare professionals baselines to adjust the intervention to meet various patients' needs. And we also examine the participation of healthcare providers in delivering the intervention.

Chapter 2. Background

Section 2.1 Chronic Care Model (CCM)

Based on the recognition of the critical role of self-management among patients with chronic diseases, some deficiencies in the traditional culture and structure of the healthcare system have been identified as barriers to effectively meeting patients' self-management needs. One main deviation is that the traditional system, especially the primary care system, is acute care oriented. The emphasis on diagnosing, ruling out serious diseases, as well as overwhelming workload to treat acute patients diminish healthcare providers' ability to differentiate the clinical approaches for patients with chronic disease (Wagner et al. 1996).

In a review of programs to improve chronic care quality and outcomes in western countries in the 1990s, the initial CCM was proposed. Focusing on facilitating and supporting patients' self-management from the practice team's side, the model recognized the importance of "evidence-based care" from four significant areas. The four areas are increasing healthcare providers' awareness, expertise, and skills of different methods in treating chronic illness, educating and supporting patients, redesigning care delivery to be more team-based and planned, and making better use of registry-based information systems (Coleman et al. 2009; Wagner et al. 1996).

Later, these four areas were renamed to be "decision support," "self-management support," "delivery system design," and "clinical information systems" in the revised model, along with other two additional contextual components, "community resources and policies," and "organization of healthcare." Together the six components cover the influence of the healthcare community, organization, supporting information systems, and practice team in assisting productive interactions between informed, activated patients and the prepared, proactive

healthcare professionals (Wagner 1998). They fall into two spheres that interact and influence systematic change for chronic disease management (Figure 2). Self-management support is on the edge between the organization of healthcare and the community, and it is the key to achieve informed and activated patients (Wagner et al. 2005).

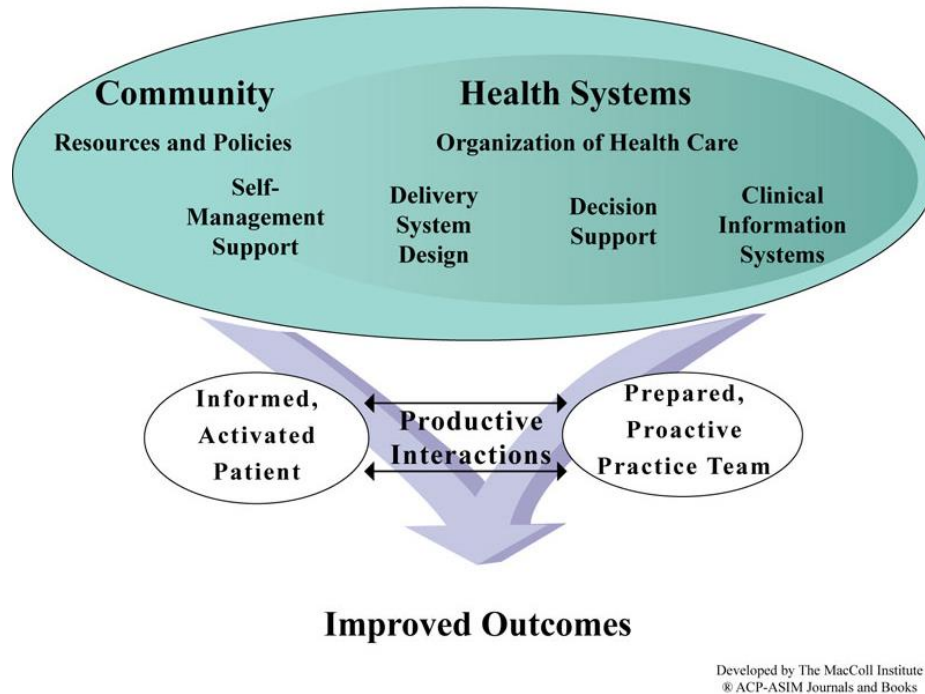


Figure 2: Chronic Care Model (Wagner 1998)

- The Community Resources and Policies component emphasis on developing partnerships with community organizations to support and meet patients' needs. Example actions include (a) identifying effective chronic disease management programs and encourage appropriate participation of patients, or (b) referring patients to relevant community-based services.

- The Health System – Organization of Healthcare component focus on the role of the healthcare organization in program planning that includes measurable goals for better care of chronic illness. An example is offering incentives for care providers.
- Self-Management Support component emphasizes the critical and central role that patients have in managing their own care. Example actions include providing educational resources, behavioral change interventions, and psychosocial support to patients to assist them in managing their care.
- Decision Support component advocates the integration of evidence-based guidelines into daily clinical practice. Actions could be wide dissemination of practice guidelines, or providing education and specialist support to the healthcare team when needed.
- Delivery System Design focuses on an expanded scope of practice for team members to support chronic care, as well as allocate tasks appropriately among all team members to reduce the overwhelming workload of physicians. Practical actions include clearly defining roles of the healthcare team and keeping planned visits and sustained follow-up of patients through nonphysician personnel.
- Clinical Information Systems component encourages the development of registry-based information systems targeting on chronic ill patients to provide relevant client data. Examples include a surveillance system that provides alerts, recall and follow-up information, and identification of relevant patient subgroups requiring proactive care through patients' data (Bodenheimer et al. 2002; Wagner 1998).

Evidence indicates that the application of the model in major chronic disease management programs reached significant success (Bodenheimer et al. 2002; Wagner et al. 2001). The organized and multifaceted support for primary care teams positively affects the care of diabetic

patients (McCulloch et al. 1998). When applying the CCM to the care of people with diabetes, decreased levels of HbA1c and a decrease in smoking rates among patients are shown as results in functional and clinical outcomes (Baptista et al. 2016). Patients with chronic obstructive pulmonary disease who received care under the instruction of CCM were found to have lower rates of hospitalizations and a shorter length of stay compared with control groups (Adams et al. 2007). The impact of a more quality-focused payment structure on the four elements contained in the health system oval, self-management support, delivery system design, decision support, and clinical information systems, has also been examined. The results show positive effects on increasing quality of healthcare (De Bruin et al. 2011).

Since the implementation of the whole model requires abundant resources and efforts, most quality improvement teams working with this model focus their efforts and interventions to promote one or more of the four components within health system oval, especially on self-management support. And it has proven to be a useful framework for patient empowerment, self-management support, and improving clinical and behavioral outcomes (Siminerio et al. 2005; Stellefson et al. 2013; Tsai et al. 2005).

With more advanced technology, analytic capabilities, as well as support from national programs such as the Health Information Technology for Economic and Clinical Health Act (HITECH Act), IT-based systems, such as mobile health applications and web-based patient portal, are being increasingly used in facilitating self-management over the past decade (Kitsiou et al. 2017; Or et al. 2011). Unlike others, mobile technologies enjoy more extensive usage in racial and ethnic minorities and low-income groups and thus have the potential to address health disparities in chronic disease management (Mallow et al. 2014).

Section 2.2 Reforms in Healthcare Provider's Payment Structure

There are fundamental transformations taking place in healthcare, where instead of rewarding the number of services providers perform, outcomes for patients are rewarded. Pay-for-performance (P4P) is the scheme behind the transformation. P4P is a payment model that rewards healthcare providers for meeting pre-established targets and/or punishes them for not meeting the objectives in delivering healthcare services by financial incentives (Conrad and Perry 2009). Based on their performance, healthcare providers receive either additional or reduced payment. P4P is designed to help reach the goal of improving the quality of care as well as reducing health expenditures.

Several P4P programs were designed to impact one or more of the four components within the health system oval in CCM using incentives for healthcare providers. They aimed at improving chronic care quality through disease management. Most of the programs were estimated according to the effects on healthcare quality measures defined by Donabedian (1980): structure measures, process measures, and outcome measures. Table 1 shows measure definitions and examples.

The studies showed positive effects of P4P on the quality of care delivered. In a study examined one P4P program, which targeted on self-management support, decision support, and clinical information system components, the result revealed that the program increased the probability of an HbA1c test being ordered (Scott et al. 2009). The result implies a positive effect on the quality of care in diabetes management. In another study that focused on the same P4P program, results indicate that financial incentives promote better clinical management of diabetes patients. Physicians who claimed financial incentives were more likely to comply with all requirements than those who did not claim incentives when they were asked to what extent they

implemented the nationally established minimum requirements to diabetes care (Saunders et al. 2008). In another program that aimed at changing delivery system design, decision support, and self-management support, the majority of the participating physicians improved their performances on process indicators and patient outcome indicators. The process indicators include the screening of clinical parameters, and an example of the patient outcome indicator is blood pressure $\leq 130/80$ during the measurement period (Beaulieu and Horrigan 2005). Additionally, one other study also found the P4P program was positively related to improved delivery of clinical processes of care (Damberg et al. 2010).

Measure Category	Measure Definition	Example
Structural Measures	Measure the healthcare provider’s capacity, system, and process to provide high-quality care.	Whether the healthcare organization or individual professional uses EHR
Process Measures	Measure what a provider does to maintain or improve health. It also supports patients with information about the medical care they may expect to receive for a given condition that contributes toward improving health outcomes.	The percentage of people receiving preventive services such as immunizations.
Outcome Measures	Measure the impact of the health care service or intervention on the health status of patients. Risk-adjustment methods are often required in assessing this kind of measure to minimize the misleading or even inaccurate information about health care quality.	Surgical mortality rates

Table 1: Healthcare Quality Measures

Policymakers and other stakeholders have confidence in the outcomes of which P4P program can provide. Started in 2017, CMS initialized the Quality Payment Program (QPP)², which includes the Merit-based Incentive Payment System (MIPS) and the Alternative Payment Models (APM) as the two major P4P programs. According to CMS’s report, which summarizes the

² Program overview: <https://qpp.cms.gov/about/qpp-overview>

participation status and performance of eligible clinicians in 2017 (Medicare and Services 2017), more than one million clinicians are eligible to participate, making the program extraordinarily influential.

The MIPS program has four categories of outcome measurements: Cost, Improvement Activities, Promoting Interoperability, Quality. The clinician's payment adjustment is determined by the score they gain in meeting the established standards of measurements. The four measurement categories have different weights in calculating the physician's performance score. The adjusted rate spectrum varies across the year, the adjusted rate for clinician's 2017 performance ranges from - 4% to 4%, and the rate for clinician's 2020 performance ranges from - 9% to 9%. The clinicians will receive their adjusted payments based on year X 's score in year $X+2$.

CMS sets two performance thresholds for each MIPS performance year. The two thresholds create four financial adjustments for eligible clinicians: penalty, neutrality, reward, reward + exceptional adjustment (Figure 3). Within the penalty group, a fragment of clinicians would receive the maximum penalty if their scores are too low to reach the score baseline. The Medicare Access and CHIP Reauthorization Act (MACRA) legislation provide CMS with funds specifically for exceptional performance until the performance year 2022.

Table 2 illustrates how the payments are adjusted for the performance year 2017. MIPS is a budget-neutral program, which means CMS pays rewards using the money it collects through penalty. Therefore, a scaling factor is applied to positive adjustment to ensure budget neutrality, and the actual adjustment rate may be lower than the designed rate. Even though the additional adjustment for exceptional performance is not budget neutral, another scaling factor is required to distribute the available funds proportionately.

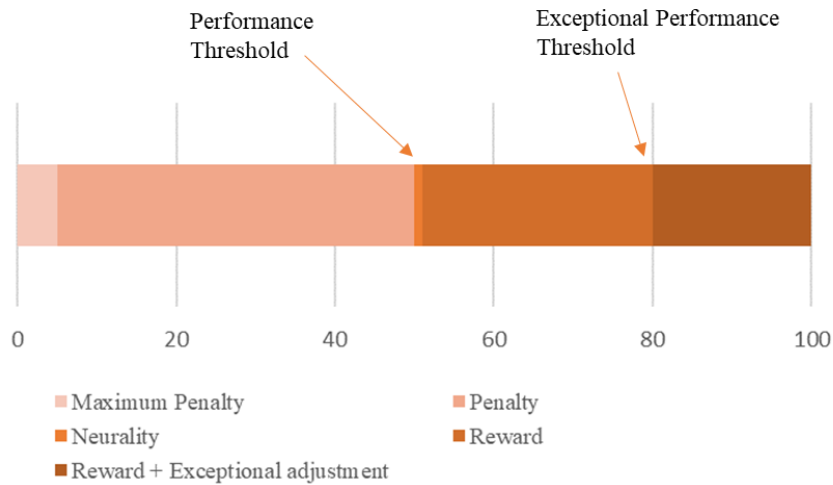


Figure 3: Payment Adjustment Conditions

Score Points	0-0.75	0.76-2.9	3.0	3.1- 69.9	70.0 - 100
MIPS Adjustment Rate	-4%	-4% < Adjust Rate < 0	0	$0 < \text{adjust rate} \leq 4\% \times \alpha$ to preserve budget neutrality	$4\% \times \alpha < \text{adjust rate} \leq 4\% \times \alpha + 10\% \times \beta$ to proportionately distribute the available funds for exceptional performance

Table 2: Illustration of the MIPS system of the Year 2019 Payment Based on the Year 2017 Performance

Section 2.3 M-health in Promoting Interoperability of Health Information

The “promoting interoperability” category of measurements in MIPS (details in Appendix A) evolves from the electronic health records (EHR) incentive program, also known as the Meaningful Use program. Table 3 shows a summary of the objectives of meaningful use program across several stages. Following the achievement of the high adoption of EHR systems, nearly 9 in 10 (86%) of office-based physicians had adopted an EHR system as of 2017³; the

³ Data source: <https://dashboard.healthit.gov/quickstats/pages/physician-ehr-adoption-trends.php>

promoting interoperability category moves beyond the existing requirements of meaningful use to a new phase of EHR measurement. It emphasizes the patient’s access to health information and the exchanging of health information among different providers. It also encourages patients’ self-management of their disease conditions and integration of patient’s health-related data from multiple resources, including EHRs, m-health Apps, and wearable devices.

Stage	Effective Years	Main Objectives
Stage 1	2011 - 2014	<ul style="list-style-type: none"> • Collect health records electronically and in a standardized format. • Communicate the collected information to improve care coordination processes. • Enable reports of clinical quality measures and public health information. • Engage patients and their family members in their care processes.
Stage 2 (include modified Stage 2)	2014 - 2018	<ul style="list-style-type: none"> • Achieve more rigorous health information exchange (HIE) than Stage 1. • Broad adoption of e-prescribing. • Transmit patient care summaries across multiple settings electronically. • Allow more data to be controlled by patients.
Stage 3	From 2017	<ul style="list-style-type: none"> • Improve quality, safety, and efficiency to improve health outcomes. • Enable patient access to self-management tools. • Establish patient-centered HIE. • Improve population health.

Table 3: Stages of Meaningful Use Program

With the legislation supporting EHR meaningful use, patients are granted accessibilities to view, download, or transmit their EHR through the patient portal or other eligible platforms. There is an increasing number of m-health Apps which are providing such functionalities to enhance the patient experience in self-management (Silva et al. 2011). They allow patients to access records in EHRs containing current medications, allergies, lab test results, and medical treatment. In order to improve the overall quality of users’ healthcare, some of the Apps also

provide healthcare information and tools, including disease-related educational information, instructions to follow physicians' advice and medical regimen, and supports in monitoring and tracking their own disease conditions. They can help patients make more informed decisions. The compatible wireless or Bluetooth-enabled devices, such as wearable devices and electronic medication container, add to the capability of capturing consistent patient-generated daily data (Lopes et al. 2011). Also, the Apps assist users in forming two-way communication and sharing the records with specialists to get timely feedback (Ahmed et al. 2011).

Wearable devices include wristbands, smartwatches, wearable mobile sensors, and other mobile hub medical devices. They can collect data ranges from exercise routines and sleep status (Kim 2014) to blood pressure (Milani et al. 2017) and blood glucose (Heintzman 2016) through either user reporting or sensors in Apps that communicate with devices through application programming interfaces (APIs) passively. Due to the development of platforms such as Google Fit and Apple HealthKit to aggregate data from multiple health Apps, the patient-generated data available for self-management rises (Grundy et al. 2017). Also, users can then choose to share these data with healthcare providers to give them deeper insights into users' behaviors and status to get better support in future treatments.

The electronic medication container, also known as electronic pill container and smart pill container, has an advanced setting in preventing multiple dosing and capturing patients' medication intake patterns. The container stays locked beside pre-set time windows for the patient to take medication doses. When it is time for the patient to take a dose, the associated App will remind the patient. The data of the patient's medication intake behavior can be tracked

and communicated with healthcare professionals if the user agrees⁴. The data allows the patient to adjust actions and enables the healthcare provider to plan interventions if needed.

Besides the assistance of patients' self-management and accessibility to EHRs enabled by these m-Health Apps, they also offer another unique capability to integrate patient-generated data in their everyday life into EHRs. Combined with API enabled secure data transmission and more advanced analytic abilities, this meets the needs of precision in healthcare, which emphasis finding the right treatment for the right person at the right time. The role of m-health Apps in assisting the interoperability of health information is shown in Figure 4.

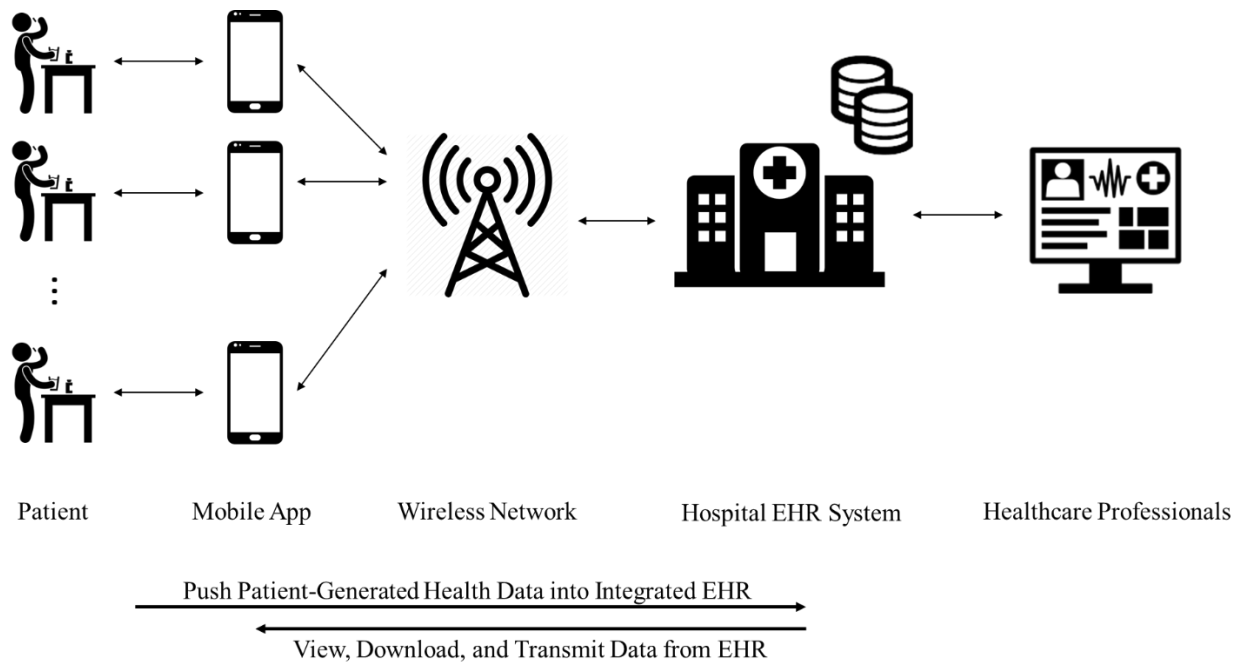


Figure 4: Data Transmission Between Patient and EHR

⁴ A container example: <https://www.elucid-mhealth.com/index.html>

Even though the lack of systematic development of integration standards has hindered the interoperability of health information in past years (Kohli and Tan 2016), the efforts from the Office of National Coordination (ONC) and many other stakeholders have achieved some valuable outcomes. They have established standards, specifications, and additional implementation guidance to facilitate effective HIE. Table 4 shows the up to date standards and specifications of HIE between patients and EHRs. The syntactic interoperability, which requires standard to “define the data format and syntax for data exchange” (Kohli and Tan 2016), is supported by HL7[®] FHIR[®]. And the semantic interoperability, which requires “data encoding standard to deal with the content or meaning of the message as interpreted by humans rather than machines” (Kohli and Tan 2016), is assisted with the Current Procedural Terminology (CPT) Consumer Friendly Descriptors (CFDs). The HL7[®] FHIR[®] DSTU 2 and SMART on FHIR are implementation specifications that support the HIE between mobile Apps and other systems.

Combined the payment structure reforms with the emphasis on health information interoperability, m-health is playing a role with increasing importance in health information technology (HIT) and patients’ self-management. Next, we will review the interventions delivered through m-health to support patients’ self-management. We focus on the medication adherence phenomenon because it has been identified as the critical mediator between medical treatment and outcomes for chronic illnesses (Kravitz and Melnikow 2004).

Standard or Specification	Facilitated Data Transmission		Objective
	<i>View, download and transmit data from EHR</i>	<i>Push Patient-Generated Health Data into Integrated EHR</i>	
Direct	√	√	Establish universal health addressing and transport for participants to send encrypted health information directly to cryptographically validated recipients over the Internet.
HL7® FHIR® DSTU 2	√		Support patients or clinicians use the provider-approved web or mobile application to access health data.
HL7® FHIR® R4	√		FHIR aims to simplify implementation without sacrificing information integrity. It leverages existing logical and theoretical models to provide a consistent, easy to implement, and rigorous mechanism for exchanging data between healthcare applications.
Current Procedural Terminology (CPT) Consumer Friendly Descriptors (CFDs)	√	√	It is developed to simplify the highly technical CPT code descriptors into something more patient-focused and patient-friendly.
SMART on FHIR	√	√*	Designed as a universal API to transform EHRs into platforms for substitutable mobile Apps.
HL7® FHIR® RESTful API		√*	It defines a set of common interactions, Create/Read/Update/Delete, performed on a repository of identified resources.
HL7® FHIR® Patient Reported Outcomes Implementation Guide		√*	It focuses on capturing and exchanging patient-reported outcome data electronically and making the data available to both providers and authorized researchers.

* These three are emerging implementation specifications for pushing patient-generated health data into integrated EHR

Table 4: Standard or Specification for Health Information Transmission

Chapter 3. Literature Review

Assist patients' adherence to treatment guidelines and medications, and to improve their quality of life is one task of effective self-management. To achieve the goal, diverse education programs, as well as community initiatives, have rolled out. However, their effectiveness was observed to be mixed (Barlow et al. 2002; Janson et al. 2009). To better facilitate self-management in attaining required MA, we must get a more in-depth insight into the reasons why patients are not ideally adherent to their medications and what have been done in previous research in promoting MA using interventions. Partial of the content in this and following several chapters has already been published in Liu and Varshney (2020), whereas significantly more contributions have been made in addition to what has been included in the publication.

Section 3.1 Reasons of Poor Adherence

After examining the related literature, we come up with a classification of various factors behind low adherence into four major types, despite the individual differences in their medication intake behaviors:

1. Dose frequency and medication regimen;
2. Patients knowledge about the disease, also refer to patient education;
3. Patient characteristics, including
 - a) demographic factors, such as gender and age;
 - b) beliefs about the effectiveness, side effects, and necessity of the treatments;
 - c) motivational or psychological factors;
4. Social support.

In the research establishing the relationship between dose frequency and medication regimen, results have been found that the prescribed number of doses per day is inversely related

to MA (Paes et al. 1997). Also, the MA improves dramatically as prescribed medication dose frequency decreases (Eisen et al. 1990). However, reduced dose frequency can induce unexpected outcomes as well. Even though the reduction of dose frequency may decrease the number of doses that are missed, it may also increase the risk of overconsumption if patients try to make up the dose he/she missed (Claxton et al. 2001). Studies consider the effect of educating patients about the disease on patient's medication-taking behavior has found that "educated" patients tended to be more adherent on outpatient follow-up and were less fearful of side effects and addiction (Kripalani et al. 2007; McDonald et al. 2002).

There are also many studies that focus on the effect of patients' characteristics on their behaviors. Patients who are older and less active in their treatment decisions have been found to be less adherent to medications because they are more likely to forget doses (Ren et al. 2002). Meanwhile, no significant variation of MA has been found across different gender, general practitioner, exemption status, and with a day of the week the prescription is written (Beardon et al. 1993). Moreover, research shows that patient beliefs are important predictors of MA. If a patient believes in the effectiveness of his/her medication, he/she is more likely to have a higher MA (Horne et al. 2005). The patient's mental status also impacts an individual's MA, compared with non-depressed patients, the odds are three times greater that depressed patients will be non-adherent with medical treatment recommendations (DiMatteo et al. 2000). Also, clinical trials using monetary incentives as external motivation to encourage patients to follow their prescriptions have found significant improvement in MA in 12-weeks examination (Moore et al. 2015) and also a reduced risk of re-hospitalization (Messina et al. 2003). Social support is an important factor in promoting patients' MA as well; for example, adherence is 1.74 times higher in patients from cohesive families and 1.53 times lower in patients from families in conflict.

Marital status and living with another person also increase adherence modestly for adults (DiMatteo 2004).

Indeed, in practice, the factors that influence MA behavior are not usually single, but a combination of different aspects. The complexity and individual-level differences behind poor adherence require multifactorial strategies to remove barriers and promote adherence.

Section 3.2 M-health Interventions

With researchers' efforts in developing appropriate interventions to address patients' poor adherence behaviors, four intervention categories have been examined to be effective in behavioral change: (a) informational interventions, (b) behavioral interventions, (c) family and social interventions, and (d) combined interventions (Kripalani et al. 2007).

Informational interventions focus on cognitive strategies designed to educate and motivate patients by instructional means. The basic idea is that patients who understand their conditions and the treatments will be more informed, empowered, and likely to be adherent. Informational sessions conducted individually or in a group setting, as well as didactic and interactive approaches, were included. Examples of informational interventions are face-to-face oral, telephone, written, or audiovisual education; didactic group class; and mailed instructional material (not including reminders or prompts to be adherent) (Kripalani et al. 2007; Liu and Varshney 2016).

Behavioral interventions are strategies designed to influence behavior through shaping, reminding, or rewarding desired behavior (reinforcement). The examples include skill-building by a health care professional; pillboxes, calendars, a change in packaging, or other steps intended to remind the patient; changes in dosage schedule to simplify the regimen or tailor the regimen to

the patient's daily routine (i.e., reduce its behavioral demands); and rewards and reinforcement (e.g., assessment of adherence with feedback to the patient) (Kripalani et al. 2007).

Family and social interventions involved social support strategies, whether provided by family or another group. The examples are support groups and family counseling. Group sessions that were primarily didactic or educational, rather than supportive, were categorized as informational intervention (Kripalani et al. 2007).

The combined interventions include combined features of two or more of the preceding categories of the interventions. While being more complex, the combined interventions are usually more effective than single interventions (Kripalani et al. 2007).

As we have discussed, the role of m-health has become more critical in assisting patients' self-management. To present the current research on m-health interventions for MA and to discover the gaps in the literature to provide us an opportunity to make our contributions, we conduct a comprehensive literature review.

3.2.1 Literature Search

We conduct a review of m-health interventions which used to promote adherence to chronic disease treatments and mediations. We do not try to discover the impact of interventions on broad self-management of chronic diseases but only focus on MA because of its important role in achieving desired clinical outcomes.

We searched PubMed, Web of Science, and IEEE digital library databases for relevant studies. Titles and abstracts, or titles and topics of English-language articles published in peer-reviewed journals and conference proceedings from January 2010 to March 2020 were searched. The search terms include: “medic* adherence,” “medic* compliance,” “drug adherence,” “drug compliance,” “intervention,” “mHealth,” “mobile health,” “m-health,” “mhealth,” and “mobile.”

3.2.1.1 Study Eligibility

We include original empirical research that evaluated m-health interventions for their effect on patient adherence to chronic disease treatments or medications. We also include quantitative studies that primarily examine the impact of m-health interventions on disease-specific clinical outcomes, e.g., hemoglobin A1c (HbA1c) or blood pressure (BP), if they contain the analysis of effects on medication adherence as secondary outcomes. Allowing for the variation in the outcomes measured is because it is necessary to have a comprehensive view of the effectiveness of interventions delivered through mobile platforms in different stages.

We exclude articles that evaluate the intervention on the population of age less than 18, in the military, or institutionalized since these groups' health-related behaviors are significantly influenced or even controlled by others. We exclude studies that focus on the usability, feasibility, and acceptability features of interventions because of the absence of evidence that supports their effectiveness. We also exclude interventions delivered through Web-based platforms with mobile access portals if the patients cannot get full functionalities through the mobile portal. If the article does not have a specified test or evaluation protocol for the effects of the intervention, we exclude it. Besides, literature review articles, commentaries, poster presentations, abstracts only, research proposals, study protocols, descriptive articles without examining scientific relationships and results, intervention designs without testing, conceptual papers are excluded.

The full list of inclusion and exclusion criteria is presented in Table 5.

Inclusion Criteria
<ol style="list-style-type: none"> 1. Empirical research articles 2. Studies that examine a specific chronic disease, or management for those with a chronic condition. 3. Studies that examine at adherence to treatment or medication as primary or secondary outcomes.
Exclusion Criteria
<ol style="list-style-type: none"> 1. Non-empirical articles (e.g., literature review articles, commentaries, poster presentations, abstracts only, research proposals, study protocols, descriptive articles without examining scientific relationships and results, intervention designs without testing, conceptual papers). 2. Only focus on chronic mental illness (e.g., bipolar disorder, schizophrenia). 3. No human data related to treatment or medication adherence collected (e.g., the descriptive analysis of intervention features without showing their impacts). 4. Studies that only focus on examining usability, feasibility, and acceptability of interventions. 5. Studies only providing descriptive statistics without further investigating any relationships (e.g., the increase in the number of doses that are taken by the patient). 6. Testing population under age 18. 7. Testing population is in military or institutionalized (e.g., patients who live in care homes). 8. Not testing with patients who are diagnosed with chronic diseases (e.g., studies which focus on primary prevention among healthy or at-risk groups). 9. Interventions delivered through web-based platforms, and the accessible mobile portals do not have full functionalities (e.g., patients can only receive text reminder through a mobile phone or other mobile device but cannot check behavior history). 10. The testing of the intervention does not follow a clear protocol (e.g., no specific testing population assigned, no description of intervention frequency)

Table 5: Inclusion and Exclusion Criteria

After removing duplicated research from the database search result, articles were screened for potential inclusion based on reviewing of title and abstract. After that, reference lists of those articles were screened to ensure a comprehensive inclusion of related research. Then, we screen full texts of included articles. We exclude articles based on our inclusion and exclusion criteria in the detailed screening.

In all, we retrieved 575 articles from the database search. 368 research left after removing duplicates. Based on the inclusion criteria of empirical research which focus on adherence to treatment or medication of chronic diseases, 233 records were excluded. Through screening reference lists, we added 33 articles in our records. We assessed the full text of 168 articles, including those added through the reference lists screen. In them, a total of 143 articles were further excluded, about 1/3 (45 articles) of them is excluded because they only studied usability, feasibility, or acceptability. Another 27 research were excluded because they only had descriptive analysis or descriptive statistics. In meeting other exclusion criteria, an additional 71 publications were excluded, leaving 25 research included in our final review list. The detailed selection process is shown in Figure 5.

We extract information including research objectives, the chronic disease type of the research, types of mobile intervention used, design of the evaluation, study samples, outcomes measured, and results. Studies were organized for analysis based on the objective of the study and the key outcomes measured. The detailed information of our included articles can be found in Appendix B. We perform analyses of the data and summarize the findings from these studies.

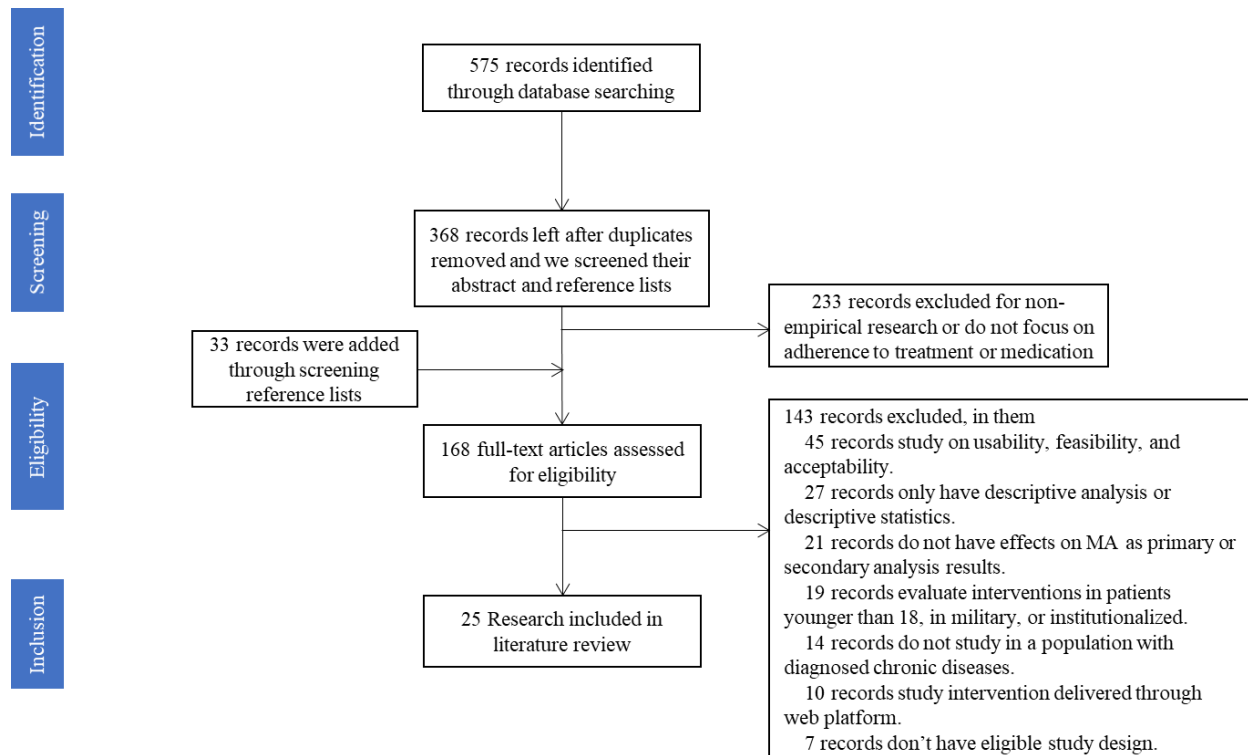


Figure 5: Selection Process

3.2.1.2 Results Summary

The number of publications by year is shown in Figure 6. Since no publication from January 2020 to March 2020 met our inclusion criteria, we do not exhibit the year 2020 in the figure. The 25 articles examined patient samples from 15 countries, including the United States, India, China, South Korea, Australia, and several European countries. Ten of them were conducted in the United States, two were in India, and all other countries had 1 for each (Figure 7). It implies that the poor MA is not only a problem in the US but also a global concern. The sample sizes and study durations both varied widely. The sample sizes ranged from 18 to 1372 participants, and the study duration ranged from 2 weeks to 12 months.

All articles can be categorized into four study designs: randomized controlled trial, longitudinal or pre-test and post-test comparison, quasi-experimental, and crossover (Table 6). In

them, randomized controlled trials (RCTs) account for 18 (71%) studies. They assessed differences between interventions or differences between intervention and standard care.

Several studies focus on the high-risk, vulnerable, or underrepresented patient populations, including elderly patients (Mertens et al. 2016a; Yu et al. 2015), members of minority ethnic groups (Chandler et al. 2019), and low-income adults (Schnall et al. 2018). In most of the 25 studies, mobile phones or other related devices were either provided to receive interventions or required for study participation. In the research which also examined usability and acceptability, the targeted elderly, minority groups, and low-income groups were highly satisfied with m-health interventions (Chandler et al. 2019; Schnall et al. 2018; Yu et al. 2015).

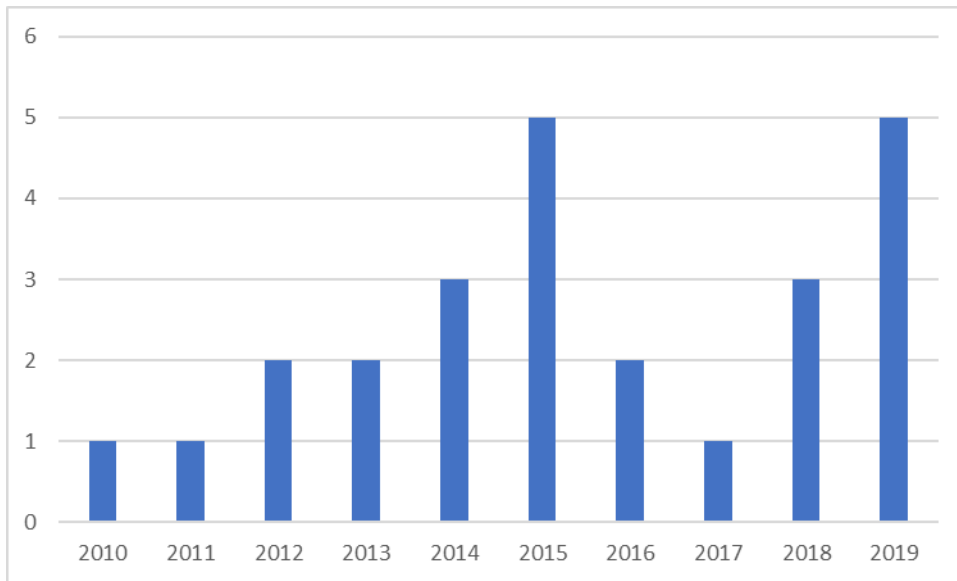


Figure 6: Number of Publications by Year



Figure 7: Geographic Information of Publications

Study Design	Diabetes	Hypertension	Coronary artery disease	HIV	Other or no specific diseases
Randomized controlled trial	4	5	5	1	3
Longitudinal/Pre- and Post-test	1	0	0	0	2
Crossover	1 ^a	1 ^a	1	1	0
Quasi-experimental	1 ^b	1 ^b	1 ^b	0	0

Note: ^a One article included here examined both diabetes and hypertension

^b One article included here examined diabetes, hypertension, and coronary artery disease

Table 6: Studies by Study Design and Disease Type

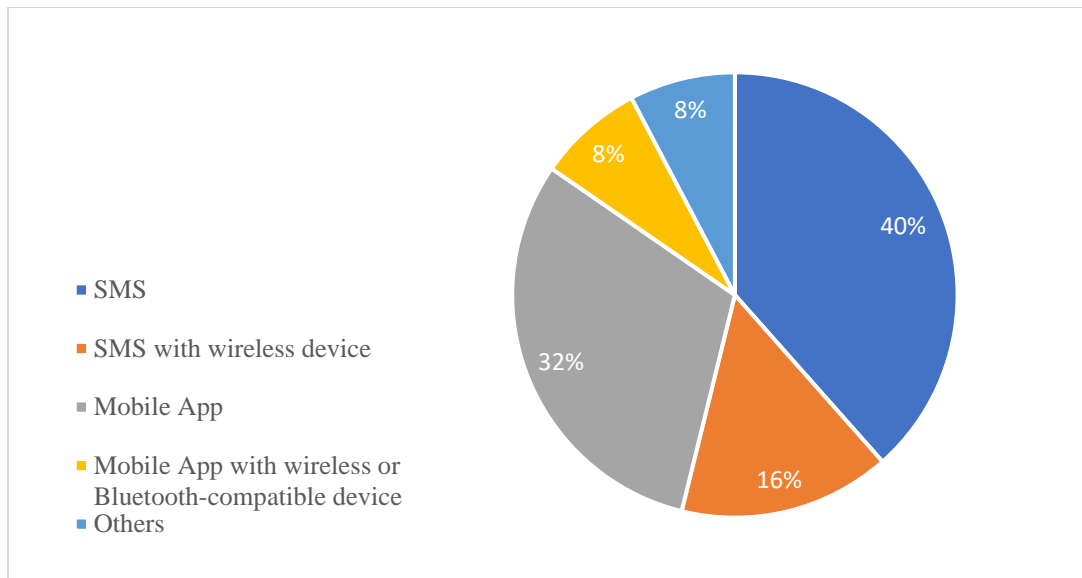


Figure 8: Intervention Tools Used in Studies

We classified the intervention tools into five categories: SMS, SMS with wireless device/system, specialized mobile App, mobile App with wireless or Bluetooth-compatible device, or others such as voice or video messaging. We summarize the categories to minimize the overlap in methods to facilitate interventions in studies, but there are still studies that used more than one category of the method. For example, Chandler (2019) used both SMS and mobile App with Blue-tooth compatible device. The proportion of each category is shown in Figure 8.

SMS comes with the smartphone or even non-smartphone as a default function. It is the least sophisticated method to transmit information to the patient’s mobile device as interventions. Nevertheless, more complex interventions, such as contextual dependent messages, can be fulfilled when combining SMS with other wireless devices or systems, e.g., electronic medication monitoring device. A specialized mobile App is generally designed to meet the requirements of intended interventions. Besides delivering interventions, the mobile App also helps to track the patient’s behavior changes. If used alone without sensor function or other

wireless or Bluetooth-compatible devices, patients need to manually input information into the mobile App. However, with the rapid development of wearable devices and sensor technology, more data can be captured automatically and synthesized with the mobile App to keep a record. These records can be viewed for decision support by both the patient and health care providers.

3.2.1.3 Impact on Adherence

Self-report is the most commonly used method to assess MA (Arora et al. 2014; Bobrow et al. 2016; Khonsari et al. 2015; Mertens et al. 2016b; Park et al. 2014), followed by patient's behavior monitoring system (Vervloet et al. 2012; Yu et al. 2015) and pill count based on electronic pill container's record (Brath et al. 2013). Of the 18 RCTs that measured the effect of interventions on adherence behaviors, a statistically significant change or difference between groups ($P < .05$ to $P < .001$) was observed in 10 studies (56%).

In the studies we reviewed, simple SMS was the most commonly used intervention delivery method. It facilitated medication reminders, patient education, as well as patient-provider communications. The message content is predominantly dose reminder (Khonsari et al. 2015; Quilici et al. 2013; Shetty et al. 2011; Singh and Varshney 2014; Strandbygaard et al. 2010; Vervloet et al. 2012), while some of them also include educational medical information (Arora et al. 2014; Kamal et al. 2018; Zolfaghari et al. 2012). The variation in text message intervention characteristics is considerable. Most of the studies (8 out of 10) send text messages at a fixed frequency (Cook et al. 2015; Ojo et al. 2015). Two studies compare the effect of simple text message reminders and personalized text message reminders (Cook et al. 2015; Singh and Varshney 2014). In one study, no difference in MA has been found whether messages are based on patients' emotional status or not (Cook et al. 2015). In another study, personalized reminders have been found to be effective in increasing MA without increasing undesired drug events, such

as taking more doses than prescribed (Singh and Varshney 2014). In the ten articles examined the effect of simple SMS on MA, 6 of them found statistically significant differences (Arora et al. 2014; Chandler et al. 2019; Khonsari et al. 2015; Myoungsuk 2019; Quilici et al. 2013; Strandbygaard et al. 2010). Two articles also found significant improvements in MA using SMS with wireless devices (Park et al. 2014; Park et al. 2015).

The functionality of sending reminders and educational messages tends to be a more integrated function in mobile Apps during more recent years. Besides the simple messages which are supported in SMS, mobile Apps facilitate other formats. For example, interactive video messages have been examined to help promote MA significantly (Schnall et al. 2018). The mobile App-enabled connection to the social network or out-of-home supporter besides healthcare providers helped reduce stress caused by the disease and improve MA (Mayberry et al. 2019; Yu et al. 2015). However, if the patient does not have family support, social support has been found associated with worse test results (Mayberry et al. 2019). Meanwhile, information sharing preference has also been found to exist among elderly patients. Some of them are willing to share their profile but not their dose loggers with others in the same community, but some are willing to share all information (Yu et al. 2015). Also, a study shows that intervention which combines both social support and text messages is more effective in improving MA and other self-management behaviors as compared to text messages alone (Chandler et al. 2019).

Behavior tracking and monitoring through mobile Apps receive increment attention because of the emphasis on patients' self-management. The growing accessibility of EHR from the patient side promotes the importance of patient-centered treatments. How to assist the process through mobile Apps have significant potential with the development of advanced technology (Serlachius et al. 2019). So far, besides the great success of mobile Apps in the work-out

industry, it has been found that using the mobile application for following prescription instructions shows a higher MA among elderly patients than using diary (Mertens et al. 2016b). Additionally, the mobile application that associates with electronic medication container not only provides more accurate MA data than self-report but also helps to increase adherence (Yeung et al. 2017) and leads to improved control of health indicator such as blood pressure (Brath et al. 2013)

In-home monitoring and monitoring through devices or smartphones support analysis of the patient's behaviors with more information. In-home monitoring utilizes large scale sensors to monitor detailed activities and analyze the patient's behaviors. It enables condition-based medical treatment to increase MA and decrease possible side-effects (Sugumaran et al. 2014). Nevertheless, it is expensive and requires strong infrastructure support, so more work needs to be done for broader feasibility and adoption (Morak et al. 2012). Monitoring through wearable devices or smartphones, as we discussed, is developing rapidly. It supports the mobile App in improving MA among patients (Yu et al. 2015). The monitoring of electronic medication containers also assists patients' self-management. Even though currently the monitoring only covers a set of simple vital signs with doubts about their constant accuracy, the scope of patient data would expand as health systems strive to meet new care models, leverage innovative digital technologies, and improve patient outcomes.

3.2.1.4. Limitations

Despite the promising results from the above interventions in changing the patient's MA, there are still some weaknesses. Our review of m-health interventions shows that the median intervention duration was three months, while the shortest duration is only two weeks. Also,

post-trial follow-ups are insufficiently conducted. Comparing with the nature of chronic illness as a life-long condition, the consistency of examined interventions is doubtful.

One reason for the widespread of IT-based self-management tools or platforms, especially m-health, is that they are thought to make it easier to facilitate communication and information exchange between patients and healthcare providers, as well as enable continuous patient monitoring and more timely feedback from professionals (Ahmed et al. 2011). Nevertheless, previous studies rarely discussed the participation of healthcare provider's in the delivered intervention and their potential benefits from the enrollment.

Moreover, compare to the four categories of behavior change intervention types, we observe that even though reinforcement has been identified as an effective intervention method, it has rarely been studied in m-health. In clinical trials, different positive reinforcements, also known as rewards, have been tested for their effectiveness in changing patient's medication intake behavior. The examined reward types include money, voucher, and lottery. A significant increase in MA was presented in several trials, along with a lower possibility of re-hospitalization (Barnett et al. 2009; Messina et al. 2003; Moore et al. 2015; Sen et al. 2014). Similar to the positive reinforcement, negative reinforcement, also known as punishment, could help change an individual's behavior too. However, due to its "negative" nature that could lead to resistance from patients, there was no intervention that integrates it based on our best knowledge. As we mentioned in the preceding discussion, the user's dependency or addiction to specific mobile apps can be utilized to design an intervention that incorporates negative reinforcement to encourage users to take their medications. If we build a causal relationship between patient's poor medication adherence behavior and disconnection to the patient's favorite mobile apps, the

patient's intention to re-connect to the app can lead to changes in the patient's behavior and achieve better self-management result.

Another weakness of previous research is that the design of intervention lacks discussion of theoretical support. Even though the evidence of effective chronic disease management and patients' self-management largely grow from practice, the design of elements in a specific intervention could still leverage the intelligence of established theories to increase the feasibility and validate the impacts.

3.2.2 Our Design Targets

We discover several effective interventions delivered through m-health from previous research in this chapter. However, the lack of evaluation about the impacts of both positive and negative reinforcements, the short intervention period, and the absence of discussion about healthcare professionals' participation as well as the short of underlying theories that support the interventions leave us a great opportunity to develop our novel intervention. In which, we would like to incorporate the reinforcements with other effective elements which are supported by theories. In addition, not only the impact of the intervention on patients but also the involvement of the practice team will be a part of our evaluation of the designed intervention.

Chapter 4. Theoretical Background

In this chapter, we discuss the theories that can support our intervention design. Also, these theories provide us with guidelines in creating multiple scenarios of intervention application.

Section 4.1 Social Cognitive Theory and Health Promotion

Based on Social Learning Theory, Social Cognitive Theory (SCT) posits that learning occurs in a social context with a dynamic interaction of the person, environment, and behavior (Bandura 1986). One unique feature of SCT is its emphasis on social influence on external and internal social reinforcement. SCT is widely applied in public health because it considers the maintenance of behavior and not just the initiation of behavior. SCT explains how people regulate their behavior through control and reinforcement to achieve goal-directed behavior that can be maintained over time (Bandura 1986). The five core determinants that SCT specifies in health promotion behaviors (Bandura 2004) are

1. Knowledge of health risks and benefits of different health practices. This is the precondition for any changes in behaviors because it is unlikely that people will change their habits if they lack knowledge about how these behaviors would affect their health.
2. Outcome expectations about different health habits. The outcomes include not only the positive or negative effects of the behavior on an individual but also consider social reactions of the behavior. Besides, self-evaluative reactions are also a form of outcome.
3. The health goals people set for themselves and the concrete plans and strategies for realizing them. Cognitive goals provide further self-incentives and guides to health behavior. In self-motivation through goal setting, people monitor their behavior and react to their attainments.

4. Perceived facilitators and social/structural impediments to the changes. The smoothness of change would be partly determined by the perceived facilitators and obstacles.
5. Perceived self-efficacy that one can exercise over one's health habits. Self-efficacy is a focal determinant because it affects health behavior both directly and by influencing other determinants. Self-efficacy beliefs can help shape people's outcome expectations and determine how obstacles are viewed.

The intervention categories we examined in the literature review can be traced back to these five determinants in SCT. The developed approaches which encourage people to adopt health-promoting behaviors based on these five determinants in SCT are parallel to our previously discussed interventions. The first approach is to inform people about the health risks of detrimental habits and the benefits of healthy behaviors. This approach shares the same core with informational intervention.

The second approach tried to reward people into regular health-promotion behaviors by linking those behaviors to extrinsic reinforcements. Behavioral interventions are the exact applications of this approach. The use of extrinsic reinforcements as an intervention has its theory support by the operant conditioning model, which was first proposed by Skinner in 1948 (Skinner 1948). The model considers how positive and negative reinforcement should be used to modify an individual's behavior. A review article in 2012 examines 19 papers using positive reinforcement, including cash, voucher, lottery, and candy for kids. It shows that this incentive type can effectively promote MA (a mean of 20% percentage but with significant variance) under a variety of disease types. These include children with TB, HIV patients, and opioid dependency patients. The reviewed articles also find a positive relationship between the value of incentive and the impact of the intervention. However, post-intervention evaluations are rare,

while the adherence effects are found to have an immediate diminish after the interventions are discontinued (DeFulio and Silverman 2012). One possible reason is that the effects of rewards are solely examined in almost all studies, but the combined effects of both positive and negative reinforcements are rarely tested. Besides, there is research showing punishment has a more significant effect on people's behavior than the reward (Gray and Tallman 1987). Another possible explanation is that the benefits patients get from following the good practice are only reflected in gaining rewards. Nevertheless, only when the benefits are internalized to be perceived health condition improvement, the patients will continue their activities despite the incentives are discontinued.

The third approach treats personal change as occurring within a network of social influences. Family and social interventions are representatives of this approach. Social relationships can help bring satisfaction to one's life and relieve the adverse effects of stress. Also, perceived social support and self-efficacy can strengthen each other in both directions. One weakness of this approach is that social support is not a self-forming entity. People have to go out and find or create supportive relationships for themselves (Granfield and Cloud 1996).

We can conclude that each of these three approaches has its advantages and limitations. Also, our identified research gap, negative reinforcement (punishment), has theoretical support for it to be a promising intervention type.

Section 4.2 Goal Setting Theory

As we discussed in social cognitive theory, goals people set, and the plans they make are important determinants of the behavior change process. Furthermore, in goal setting theory, one central tenet is that for many tasks, setting specific goals to achieve a task, in combination with performance feedback, leads to higher performance than does no goal or a vague goal (Latham

and Locke 1991; Mento et al. 1987). Three motivational mechanisms have been found beneficial for performance: effort, persistence, and concentration (Latham and Locke 1991). Goal setting encourages a person to try harder and for more extended periods of time, with less distraction from the task at hand. Based on this, another central tenet of goal setting theory is the linear goal difficulty-performance relationship. The higher the goal set, the better people perform, even when the goal is very high (Latham and Locke 1991; Mento et al. 1987). Of course, there are conditions for which the goal difficulty-performance relationship is not strong: (1) tasks that are too complex for an individual are set as goals, (2) the individual is not capable of performing tasks related to the goals, and (3) the individual is not committed to the goals (Cervone et al. 1991).

Therefore, to ensure a strong goal difficulty-performance relationship in the designed intervention process for health-promotion behaviors, one question needs to be answered: which one is better, self-set goal or system-assigned goal? In previous research, contradictory findings have been shown. Alexy (1985) found that letting patients select their own health behavior change goals did not lead to a different result from behavior change with provider-assigned goals. In another weight loss experiment, the assigned goal group was found to be statistically superior to the self-set goal group (Boyce and Wayda 1994).

One can think of situations in which self-set goals would result in poorer outcomes than counselor-assigned goals. A self-set goal might be either too easy or too difficult, while a counselor-assigned goal based on a counselor's experience can be more appropriate. On the other hand, the counselor may not always possess knowledge of the real difficulties a user is likely to experience and consequently may set goals that are inappropriate for the user. Also, individuals may sometimes have a greater commitment to self-set goals (Tesser et al. 1984).

Section 4.3 Social Exchange Theory

Homans defined social exchange as the exchange of activity, tangible or intangible, and more or less rewarding or costly, between at least two parties (Homans 1958). He studied social exchange on an individual level and argued that “there was nothing that emerges in social groups that cannot be explained by propositions about individuals as individuals, together with the given condition that they happen to be interacting” (Fiske et al. 2010). Reinforcement principles derived from the behavioral research were used to explain the persistence of exchange relations. Behavior is viewed as a function of payoffs, whether the payoffs are provided by the environment or by other humans.

Homans had five key propositions that examined social behavior regarding both positive and negative reinforcement. His first proposition, or the success proposition, states that a behavior which generates rewards is likely to be repeated. The second proposition, or the stimulus proposition, states that behavior which has been rewarded under certain circumstance in the past will be performed in similar situations in the future. The third proposition, or the value proposition, states that an individual is more likely to perform an action if the action has a more valuable result to him/her. The fourth proposition, or the deprivation- satiation proposition, introduces an idea of diminishing marginal utility: the more often an individual has recently received a particular reward for an action, the less valuable is an additional unit of that reward. Finally, the fifth proposition considers that individuals will react to different reward situations emotionally. People will become angry when they do not receive what they anticipate (Homans 1974).

Following these propositions, we can reasonably assume that using the financial reward as positive reinforcement in our intervention design could encourage the patient to repeat his/her

praised medication-taking behavior if we reward the patient with each on-time-taken dose. We also need to consider the diminishing marginal utility of our designed reward. Repetition of most affectively relevant stimuli eventually leads to an attenuation of response. That is, at some point, people respond less and less to every additional exposure to a stimulus. Thus, in our design, the most appropriate solution to avoid this diminishing effect is to provide increasing reward value to the patient over time. However, individual variance exists, so it is not necessary for us to provide an increasing reward to every patient. More details related to reward design and its suitable patient types will be discussed in the Scenarios chapter.

From these three theories we discussed and the comprehensive literature review we conducted, we could conclude that no single intervention approach can meet the requirements of all different patients. To generate an intervention that targets broadly, we need to combine several approaches. From previous literature, reminder and social support are evidence-proved effective intervention types. Thus, in our design, we should include them. Reinforcement is another intervention type we should incorporate since it has already been tested to be impactful in clinical trials, and it is one of the approaches supported by Social Cognitive Theory. Goal-setting is a function that should be involved in our design to arouse the patient's intention to achieve goals. Additionally, as we internalize several simple interventions in our design as functions, we should offer enough choice options for patients and/or healthcare professionals to choose whether they want all or only part of them. Because all patients have individual differences that lead to various acceptances of each function or element within functions. In this way, the combination of a set of different function choices can work as a scenario that effectively targets a specific type of patient.

In our following System Design chapter, we will introduce how we include all functions that are supported by theories to generate our novel intervention. We will also illustrate how our intervention operates in details.

Chapter 5. System Design

Section 5.1 Method

Our design of the system utilizes the Design Science Approach (Vaishnavi and Kuechler 2015). We start with the awareness and definition of the problem. Then we suggest our solution to the problem based on the established knowledge and theories. A design guideline is generated in this step, followed by developing an artifact and evaluate its effectiveness in solving the problem. The suggestion, development, and evaluation steps are iterative until our designed system meets its performance goal. We implement modifications to our artifact to resolve any limitations in effectiveness evaluation. This iterative design science approach enables us to meet the system's requirements. Figure 9 illustrates the process and outputs of the Design Science Approach.

The requirements we derived from theories and empirical observations using the above design science approach are:

- a. Allow personalized setting of goals, reinforcements, and social connection.
- b. Generate reminders to patients.
- c. Monitor patients' adherence.
- d. Record patients' medication intake behavior data and generate the corresponding report for patients and healthcare professionals.
- e. Interact with healthcare professionals.
- f. Implement positive and negative reinforcement interventions for patients.
- g. Allow patient's access to their EHRs.
- h. Assist in integrating patient-generated data into their EHRs.

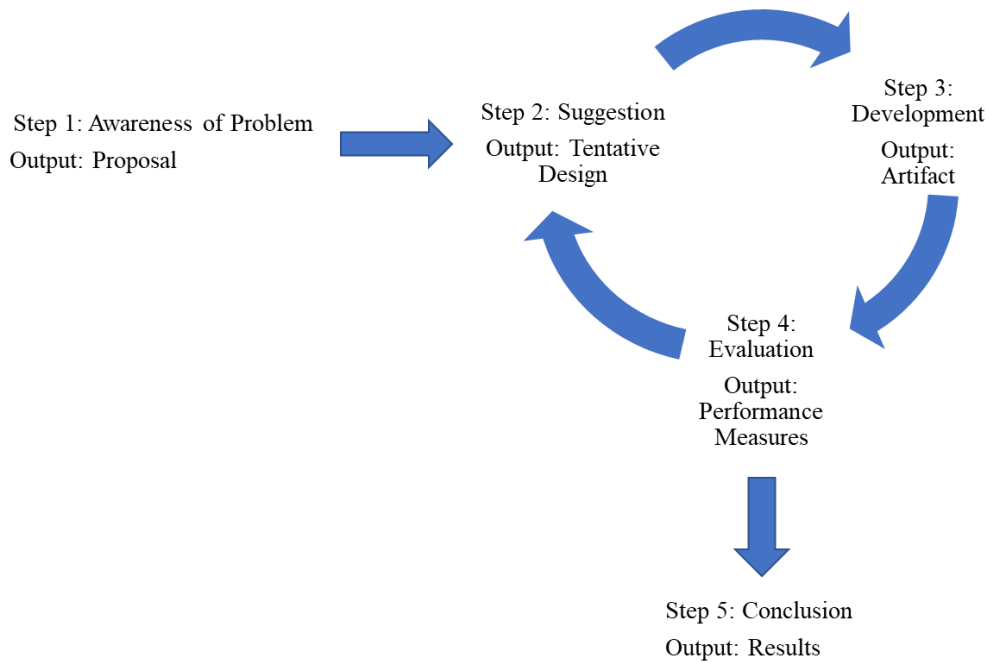


Figure 9: Design Science Research Process and Output

Section 5.2 Intervention Process for Patients

Our designed system interacts with patients' medication intake patterns in five steps to fulfill the above requirements. We name our designed intervention Carrot & Stick system (C&S) because we take advantage of both positive and negative reinforcements. The five steps are:

First, we need to set several initial parameters of the system. Namely, we need to set the desired MA, reinforcement type (reward and/or punishment), whether the reward should be fixed or increasing, and a threshold number, which is the number of doses a patient can miss without receiving extreme negative reinforcement. MA goal should be allowed to be set by the patient or the physician since individual variances exist in reactions to a self-set goal or assigned goal. The reinforcement type can be selected by multiple factors: the type of medication, the patient's past medication-taking behavior, the patient's current status, MA goal, and level of dependence on apps and smartphones. Whether rewards should be fixed or increasing should also be a choice

made based on the patient's characteristics. If the patient has multiple medications to record in the system, we can also optimize the frequency of doses by communicating with healthcare professionals. In addition, the social connection capability should also be set at this stage. Users can choose whether to add authorized user(s) to help monitor their behavior and access their records. For example, a user can authorize a third person to receive notification of his/her missing dose to assist in the behavior monitoring. More details of an authorized user(s) will be discussed later.

Second, we need to specify two different reminder windows, which should be set through discussion with a healthcare professional. Reminder windows are available time intervals for a patient to take his/her medication dose(s). We design these two reminder windows in such a way that the first reminder window covers the period during which the taken dose will fulfill its full function, and the second reminder window specifies the last possible period for a taken dose to not interfere with the effect of next on-time-taken dose. At the beginning of the first reminder window, the system will send a reminder to the patient, if the patient takes the dose during first reminder window, no further reminder will be sent; if the patient doesn't take it, then a second reminder will be sent to the patient at the beginning of the second reminder window. We can prohibit the potential of dose overconsumption due to the patient's catch-up behavior to take doses at an inappropriate time to make up for their skipped or delayed doses by utilizing an electronic medication container. Occasionally, this catch-up behavior comes as one of the side effects of reducing dose frequency (Claxton et al. 2001).

The implemented association between the patient's behavior and reward is as follows. If the patient takes his/her dose within the first reminder window, he/she will get full reward; if the patient takes the dose within the second reminder window, he/she will get reduced reward; if the

patient doesn't even follow the second reminder window, then he/she will get no reward. More parameters about reminder windows design and intervals between reminder windows will be discussed in the next chapter.

Third, we will only implement negative reinforcement if the patient initializes the system as he/she would like to receive it, or the responsible healthcare professional thinks it is appropriate for a specific patient. Two conditions are designed to implement negative reinforcement: the first condition is when the patient's MA drops below the expected MA for medication to be effective in treatment, the second condition is when the patient has missed a specific number of doses consecutively even though his/her MA stays equal or higher to the expected MA. Healthcare professionals decide the maximum number of possible consecutive-missing-doses. We will start by blocking the most used social media or entertainment app in his/her mobile and move on to the second most used app, and so on. However, every blocking action could be reversed automatically if the patient takes his/her subsequent doses to bring back the adherence rate to the desired MA. An example will be given later.

Fourth, if a patient's missing doses reach the threshold number, we will execute the extreme action, which is blocking multiple applications (besides our app) but allow the phone calls or text from family, friends, police as well as healthcare professionals.

Fifth, our application will provide daily, weekly, and monthly adherence data to the users and allow them to send the report to the healthcare professional for analysis and any further adjustments. This personalized patient-generated data could facilitate more informed decision makings of physicians in prescribing the treatment.

The entire process of intervention is shown as a flowchart in Figure 10, where rewards for taking doses during the two reminder windows with system generated reminders, as well as

blocking and unblocking of the most commonly used apps are included. The positive and negative reinforcement cycle can also be utilized for numerous other self-management tasks, including keeping the appointment time, consuming healthy food, doing exercise, managing weight-loss goals instead of meeting MA goal, but we focus on MA.

Section 5.3 The Authorized User(s)

To provide the social connection to patients, we allow them to add authorized user(s) to help monitor their behaviors, access their records, as well as receive system-generated reports. The authorized user can help in ways:

1. If being allowed by the patient in settings, a notification would be sent to the authorized person at the beginning of the second reminder window instead of sending another reminder to the patient. The notification will indicate that the patient has missed the medication dose and allow the authorized person to text or call the user to take the dose. The alternative process is shown in Figure 11.
2. The authorized user(s) have access to view the patient's tracking records and take actions to help the patient.
3. The authorized user can receive the system-generated history reports automatically. To avoid damage of information leakage to the patient's privacy, all detailed information of the medication is excluded from these reports, only information about rewards and/or punishments can be shared. The patient can set whether both reward and punishment information or only either one of them can be shared.

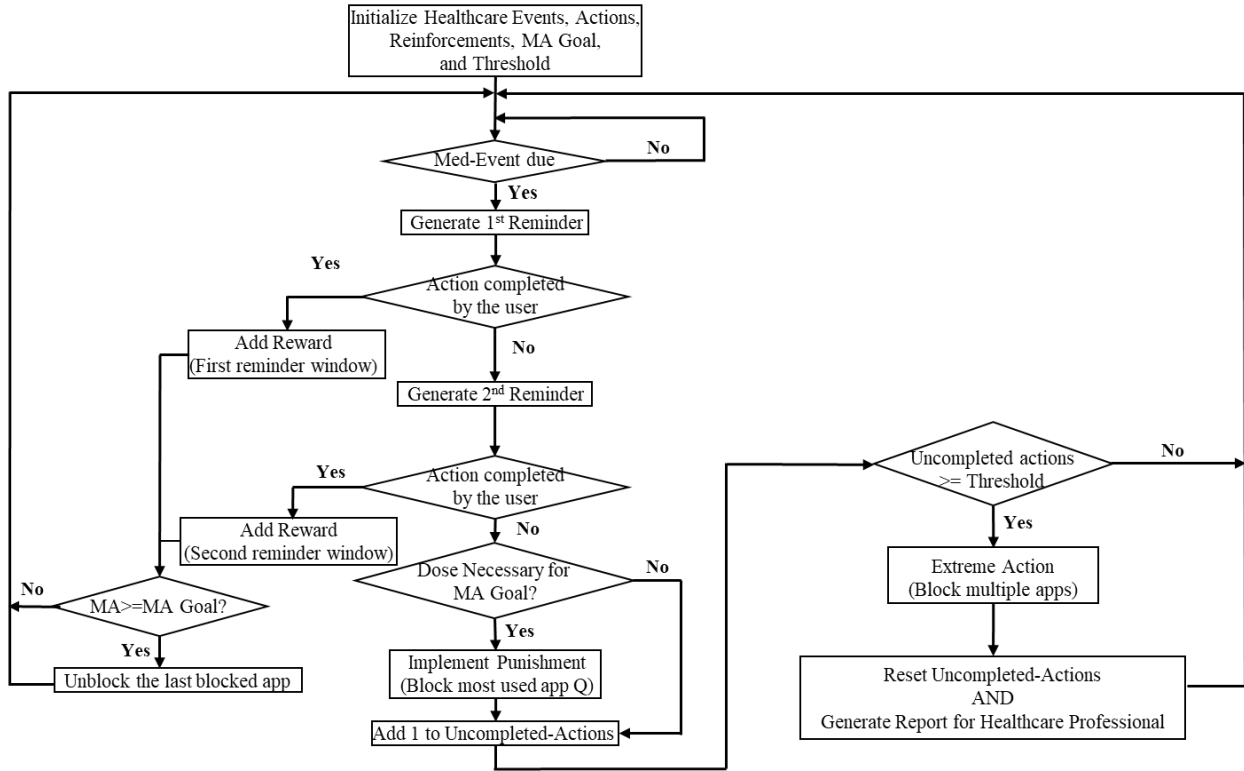


Figure 10. The Process of Carrot & Stick Intervention

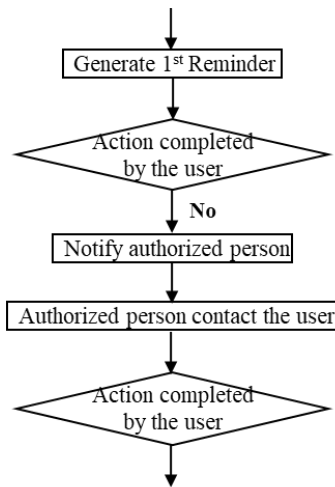


Figure 11: Process of Contacting Authorized Person

Section 5.4 Intervention Operation

Figure 12 shows the mobile interface for positive reinforcement. It demonstrates how reminders, daily medication list, and reward record would be displayed. From left to right, the first interface represents how a reminder will be shown on the smartphone. When the user taps the notification, he/she will be directed to the current day's list of medications (the second interface). The detailed information on what time the user should take which medication(s) and how, as well as the unit measurement of doses, ensures the user's safety and completeness in following regimen. The medication names and figures (shown as Medication 1 and Medication 2 in Figure 12) would represent the real medications to help the user distinguish among all meds. The third interface shows the user's reward record. It includes the number of rewarded doses and the total amount of reward the user has earned so far. It also shows break-down information of reward according to different medication doses of the current week. Whether a dose's reward is in full or reduced amount is illustrated by the shade of colors. Lighter color represents a reduced amount.

The setting of reminder windows is shown in Figure 13.

If user A is an authorized person of user B to help user B monitor the medication-taking behavior, and user B does not follow the first reminder of a dose. One pushed notification of the situation of user B will be sent to user A to allow user A chooses to call or text user B as the second reminder. Figure 14 shows the interface of this condition, in which user A names Amber and user B names Robert. Figure 15 represents how notice of implementing negative reinforcement would be shown. This message will display on screen if the patient tries to access App Q when it is blocked. The number of the subsequent doses the patient should take to bring the MA to the desired level or higher and unblock the App is also displaying. This message can

also set to be shown constantly in the smartphone's notification center or set to pop-up temporarily with every reminder of doses.

Further, the system generates a consumption history report weekly and monthly. The user has easy access to review his/her overall MA and dose-taking behavior of each medication through the report. Also, the report can be transmitted to a healthcare professional who can determine if the intervention is working or not and can take suitable action if needed. Figure 16 represents the interface of the history report. If complying with the standards and specifications that are discussed previously, our system allows the users to access their EHR and integrate the generated data into the records. One interface example of Epic EHR access is demonstrated in Figure 17.

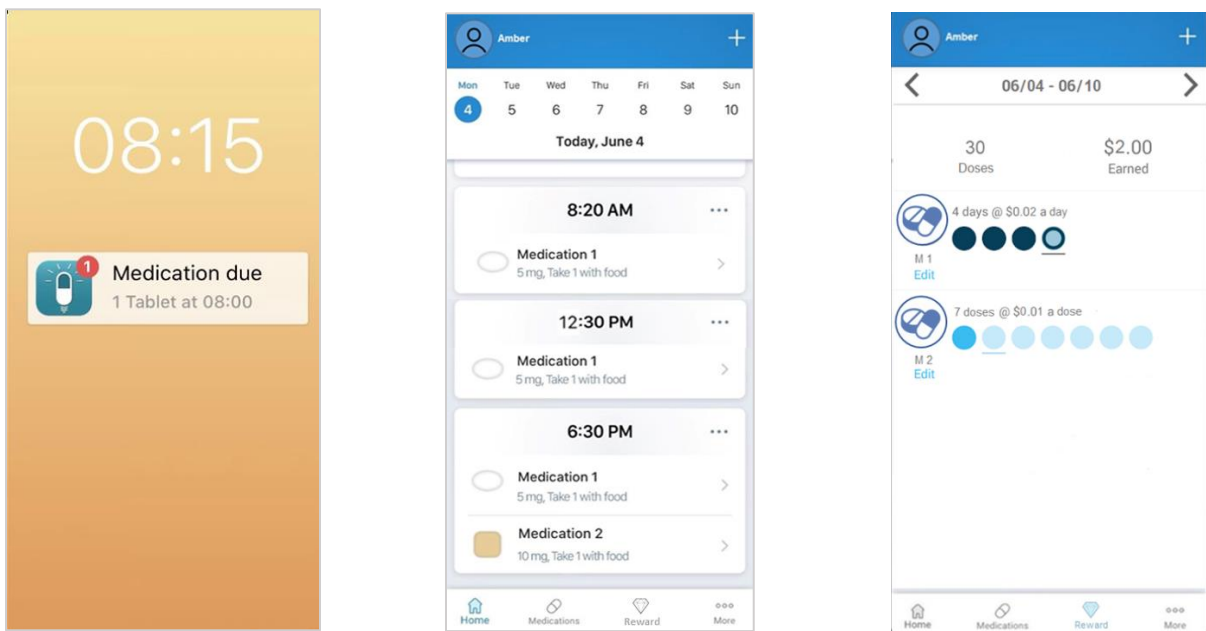


Figure 12. The Reminder, Daily Medication List, and Positive Reinforcement Interfaces

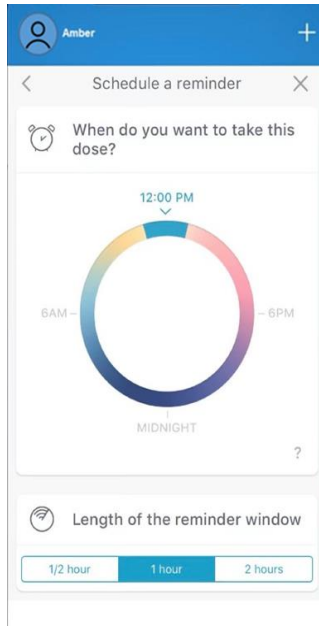


Figure 13. Reminder Windows Setting Interface

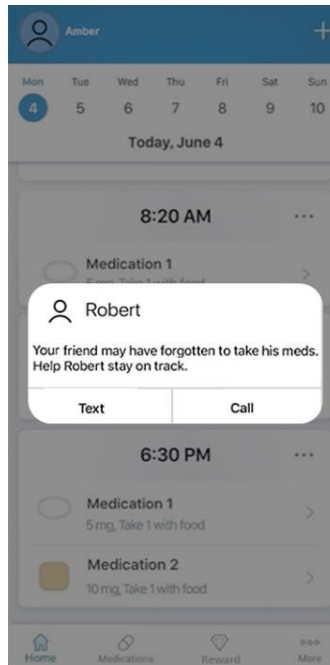


Figure 14. Notification Sent to Authorized Person

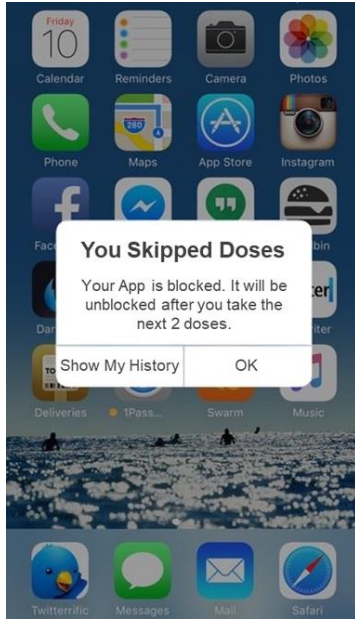


Figure 15. Notification of Negative Reinforcement

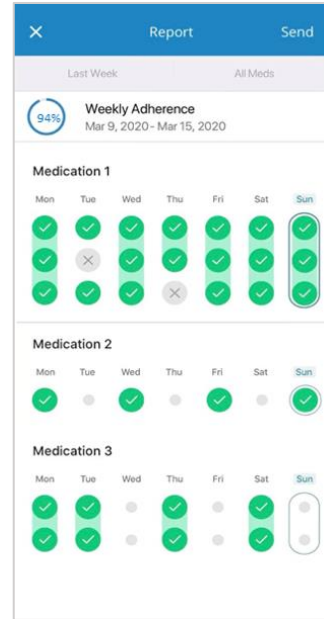


Figure 16. Consumption History

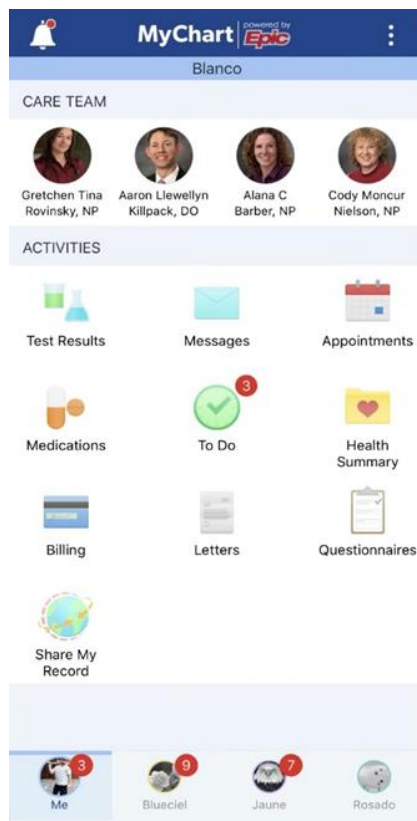


Figure 17. EHR Access Example

An example of dose consumption and the intervention is shown in Figure 18, which includes rewards based on when the dose was taken (FW: first reminder window or SW: second reminder window). If we set the desired MA goal as 80%, the first time when the patient misses a dose, it is not critical as the MA remains at/above 80%. However, when the patient misses the next dose, MA drops below 80% (67% if the patient misses the sixth dose), triggering the blocking of app Q (the most common app in use). The rewards are continued for future doses, and once the MA reaches 80% (8 out of 10 doses taken as instructed) again, the blocked app Q is unblocked again.

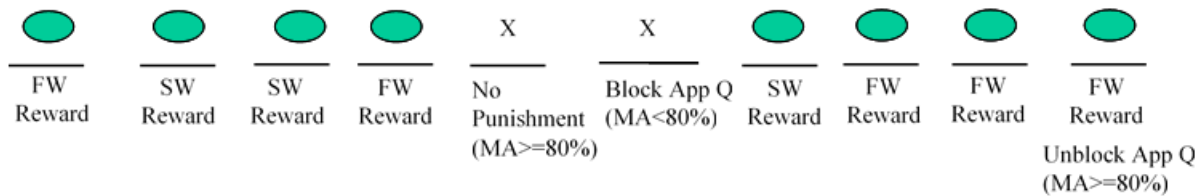


Figure 18. An Example of the Intervention

Section 5.5 Multiple Medications Condition

After describing the single medication scenario, we next describe a multi-medication condition, which is quite common for patients with chronic diseases or elderly patients.

For the multi-medication scenario, the positive and negative reinforcements are more complex. We have two different situations to consider depending on the patient's condition and the types of medications. One situation is that only overall MA of all medications matters to patients' health promotion, so the reward operations could be based on achieving overall adherence larger or equal to the desired value for all medications, and punishment operation could be implemented when the achieved adherence goes lower than the desired value. Under this situation, the implementation of positive and negative reinforcement could be similar to the

single medication condition since we don't need to set different rewards to ensure various medication-taking patterns among several medications. The only difference is that we calculate the average MA of multiple medications as the new MA. An example of two medications, MD1 and MD2, along with 80% average desired MA, is shown in Figure 19.

Another possibility is that different medications need different levels of adherence and have different levels of importance in health outcomes. Therefore, the rewards amount/type can be different for different medications to ensure the patient achieves a higher adherence rate for more important medications. Also, according to our design, patients are more prone to punishment when they miss their medication, which requires higher MA. An example of two medications, MD3 requires 90% MA, and MD4 requires 80% MA, is shown in Figure 20. We choose two different rewards, reward 3 for MD3 and reward 4 for MD4, to increase the possibility of reaching different MA. From Figure 20, if there is a medication requiring a rather high MA (90% in the example), a patient could easily have a blocked app because of a single missing dose, and it will take a long time to make up the effect of the missing dose to reverse the app.

The patient's history and medication-taking behavior are essential to decide whether the patient should follow the overall MA or various MA principles when he/she needs to take multiple medications. They are also the premise to design how to implement positive and negative reinforcement for the patient. If the patient needs to follow various MA principles, the Figure 16 interface could be adjusted to show MA of each medication instead of only displaying an overall MA of all medications.



Figure 19. An Example of Average MA Required Multi-Medication Intervention

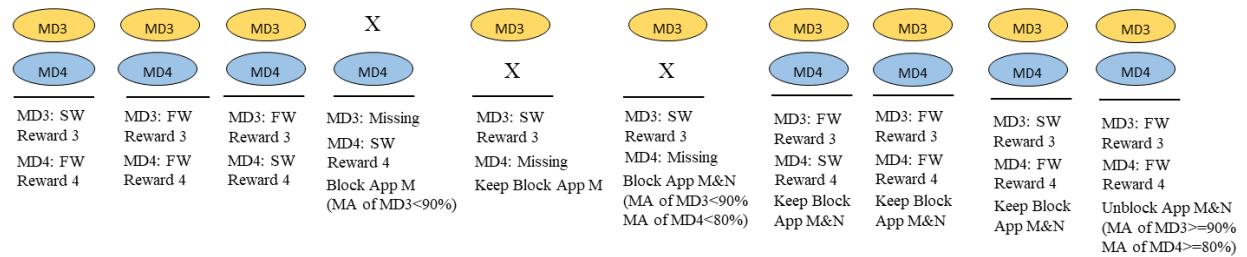


Figure 20. An Example of Various MA Required Multi-Medication Intervention

The proposed intervention is the first of its kind, which takes advantage of patients’ dependence on smartphones using the “Carrot and Stick” approach. To avoid confusion between scenarios involving “intentional blocking” and “app malfunction,” our intervention displays a message on the mobile phone that the App has been blocked and will be unblocked if the patient takes the next N doses (when due) as shown in Figure 15. The value of N is based on the target MA.

Section 5.6 Resources of Positive Reinforcements

In our design, no matter we use vouchers, gift cards, lottery, or any other kinds of financial incentives as our positive reinforcement, they all have monetary values. To initialize our intervention, the resources of positive reinforcements should be identified.

5.6.1 Insurance Companies

Several insurance companies have already involved in encouraging the uptake of health-related technology through incentive programs (see Table 7). These companies all offer health behavior tracking through mobile Apps or combined with wearables devices. They also encourage the use of remote patient data to improve patient self-management. The developed reward programs include health goals into point systems or insurance plans and offer incentives for customers if they achieve pre-established goals. The incentives include gift cards, electronic devices, and reductions in the cost of insurance coverage. The key health indicator which is tracked and rewarded is walking steps. Other indicators include healthy dietary, the participation of community events, and so on.

These rewards programs support the uptake of health technologies and expand the use of patient-generated data to improve patient health. There are limited reported information about how these programs are working because of their early stage of implementation. However, since medication nonadherence is also a burden to insurance companies, it is highly possible that they will sponsor the incentives to improve patients' MA as they are doing in rewarding users' walking steps.

5.6.2 Healthcare Providers

Besides the possible source from insurance companies, the physicians could also choose to provide incentives to patients. Based on what we discussed in the previous chapter, the payment reform correlates the physician's payment adjustments with their quality of care. The physicians could invest in improving their patients' MA to achieve a higher MIPS performance score, which represents higher payment adjustments. We will also evaluate the potential benefits that physicians could get from providing incentives to their patients in the Evaluation chapter.

Insurance Company	Program	Reward Type	Description
Oscar Health ⁵	Step-tracking rewards program	Amazon Gift Card	An app that tracks steps and synchronizes with Apple Health or Google Health. Insurance members who enable step tracking function can earn \$1 toward an Amazon Gift Card for every day that walking steps hit the step goal.
United Healthcare ⁶	Step-tracking rewards program	Deposit in out-of-pocket medical expenses	UnitedHealthcare Motion program which provide members financial rewards for out-of-pocket medical expenses if the member achieves walking goal measured by frequency, intensity, and tenacity. The app can sync with wearables using track steps. The reward earned is deposited quarterly.
Humana ⁷	Healthy actions rewards program	Gift Card	The Go365 program rewards members with points when they complete healthy actions such as prevention and workout activities, or when they engage in community events. The points can be redeemed as gift cards of varies vendors like Walmart, Amazon, and Shell.
John Hancock ⁸	Healthy actions rewards program	Gift card, discounts on health gear, savings of healthy food and fruits, savings on the cost of insurance coverage	Offers two different programs, Vitality GO and Vitality PLUS. Both programs provide points for members' everyday healthy activities, such as take a walk. The points can be used to redeem varies benefits. Vitality PLUS policyholders can save up to 15% on their annual cost of insurance coverage.

Table 7: Insurance Companies' Reward Programs

⁵ <https://www.hioscar.com/app>

⁶ <https://www.uhc.com/employer/programs-tools/unitedhealthcare-motion>

⁷ <https://www.go365.com/>

⁸ <https://www.johnhancockinsurance.com/vitality-program.html>

Chapter 6. Scenarios

Based on the theories we discussed, we have three segments of scenarios. The first one includes positive and negative reinforcements; the second segment considers goal-setting; the third one focuses on social connection. All scenario components details are listed in Table 8.

Section 6.1 Positive and Negative Reinforcement

Positive reinforcement (reward) has been used as an incentive to create desirable behavior in individuals. Some forms of rewards, such as money, lottery, and voucher, have been tested in clinical trials to examine their effect on patients' medication adherence behavior. Most of the studies have found that rewards are significantly effective in increasing the patient's adherence rate (Sen et al. 2014). While few of them found treatment group which receives rewards do have higher adherence rate, but the effect is insignificant (Barnett et al. 2009). Following the discussion in social exchange theory, the same reward would have a diminished effect in keeping people involved in an activity. Thus, the reward should have an increasing value over time. However, patients have distinctions in their sensitivity to the same repeated reward at the individual level. The reward amount is accumulated and calculated on a period's base. Thus, if the benefits of conducting specific health promotion behavior are reflected in perceived wellness improvement, the patient would lay less emphasis on the reward he/she could get. Or, if involving in the intervention provides the patient feelings of happiness, joy, or pleasure, the weight of diminished effect would be reduced. Under these circumstances, the diminishing utility of repeated reward would have little impact on the patient's subsequent behavior. Otherwise, the reward needs to have increased value over time to keep its effectiveness as an intervention. Thus, in the application of reward, it should be a fixed amount for some patients and an increasing amount for others to capture variations in patients.

Besides pursuing rewards, individuals can also adopt or give up specific behavior to avoid negative reinforcement. Sometimes, people tend to avoid losses to acquiring equivalent gains (Kahneman and Tversky 2013), and this is called loss aversion. In other words, people may think it is better not to lose \$5 than to gain \$5. Some studies have suggested that losses can be twice as powerful as gains psychologically (Tversky and Kahneman 1992). Thus, we can reasonably expect that negative reinforcement can also promote the patient's MA. However, unlike positive reinforcement, negative reinforcement can cause annoyances to individuals. In other words, fixed negative reinforcement may lead patients to stop receiving the intervention, let alone increasing negative reinforcement levels over time. On the other side, similar to reward, patients would have different sensitivity toward negative reinforcement so that we would have no or fixed negative reinforcement in our application scenario components. Thus, we have the following four different scenario components of reinforcements.

1. Fixed positive reinforcement and no negative reinforcement
2. Increasing positive reinforcement and no negative reinforcement
3. Fixed positive reinforcement and fixed negative reinforcement
4. Increasing positive reinforcement and fixed negative reinforcement

Section 6.2 Goal Setting

As we have discussed in the goal-setting theory, the comparison of effectiveness between the self-set goal and the counselor-assigned goal (in intervention design, it is the healthcare professional-assigned goal) on adopting health-promotion behaviors doesn't have a clear answer. Achieving a targeted goal can increase patients' confidence in managing their diseases and improve their self-efficacy critically. Some patients would have a deeper understanding of their capabilities and real-life difficulties than their physicians, so self-set goals would be more

appropriate for these patients. While some other patients would only set their goal to the minimum possible level, which might provide little help in improving their health, or they overestimate their capabilities to achieving their goal, causing frustration and discontinued involvement. The physician-assigned goal should be more suitable for these patients. Thus, we have two scenario components considering goal-setting:

5. Self-set goal
6. Physician-assigned goal

Section 6.3 Social Connection

The social support and reaction to an individual's behavior is an essential determinant in the behavior change process. However, in cultural research, individual-level variances have been found in valuing other people's opinion or judgment. For example, individualists would place more emphasis on autonomy and self-reliance (Grimm et al. 1999; Triandis 2001), while collectivists would be more comfortable with changing their opinions or behaviors by the impact of others (Cialdini et al. 1999; Triandis et al. 1985). To capture the differences in patients' social connection preference, we provide choices about sharing users' behavior information with other authorized user(s) in our designed application, referring to our discussion about the authorized user(s) in System Design chapter.

For those so-called "individualists" who emphasize autonomy and control of their life without other people's impact, personal information sharing about their medication-taking behavior and induced judgment could hinder their behavior change. While for those who like to be a member of a group and receive feedback from other people, information sharing could impact their behavior change positively.

Moreover, shared rewards or punishments information will induce different feedback sentiment; for example, rewards information could have positive feedback while punishments information could have negative feedback. In other words, patients in need of encouragement should share different information from patients who lack regulation. Thus, we have the following four scenario components of social connection.

7. Disable social connection
8. Enable social connection, but only sharing reward information
9. Enable social connection, but only sharing punishment information
10. Enable social connection, sharing both reward and punishment information

Indeed, these three segments of scenarios are not exclusive from each other. They cover different aspects to increase the intervention's effectiveness. One complete scenario of intervention application could include one or more segment's components. For example, a patient could set his own MA goal, receive a fixed reward for any dose he takes but no punishment if he does not reach his period's goal, and share only his reward information with others.

Scenario	Detail	Description
1	Fixed PR and no NR	In each intervention period, the patient will receive the same amount of reward. Also, the patient will not be punished if he/she doesn't achieve MA goal.
2	Increasing PR and no NR	The patient will receive an increasing reward in subsequent intervention periods. Also, the patient will not be punished if he/she doesn't achieve MA goal.
3	Fixed PR and fixed NR	In each intervention period, the patient will receive the same amount of reward. Also, the patient will be punished if he/she doesn't achieve MA goal.
4	Increasing PR and fixed NR	The patient will receive an increasing reward in subsequent intervention periods. Also, the patient will be punished if he/she doesn't achieve MA goal.
5	Self-set goal	The patient will set his/her period's goal.
6	Physician-assigned goal	The physician will set the patient's period's goal.
7	Disable social connection	No authorized user is added. The patient will not be able to share his/her medication-taking information with others.
8	Enable social connection, only sharing reward information	The patient will share his/her reward information with the authorized user(s).
9	Enable social connection, only sharing punishment information	The patient will share his/her punishment information with the authorized user(s).
10	Enable social connection, sharing both reward and punishment information	The patient will share his/her reward and punishment information with the authorized user(s).

Table 8. Scenario Components

Section 6.4 Comparison of Scenarios

Even though these ten different scenario components consider various intervention aspects, we can still have qualitative comparison within the three segments. We choose three angles to compare them. The first one is the possibility of quitting, which examines the level of obstacle that each component could cause to affect patients' continued engagement in the intervention. The second one is the suitable patient type, which compares the patients' characteristics that each component would be most effective for. Based on the assumption that each patient follows the most suitable scenario components, we consider the third angle, cost-effectiveness. Cost-

effectiveness compares the cost of the intervention to reach the same health outcome. The comparison details are listed in Table 9.

6.4.1 Possibility of Quitting

Segment 1 (scenario components 1 to 4): The existence of punishment could cause a higher probability of annoyance, frustration, and other negative emotions compare to no punishment when patients fail to reach their goal. These negative emotions would strongly associate with patients' dropping out behavior. However, if the rewards are calculated in an increasing pattern based on each period, the idea that "I will receive more if I continue engagement in the intervention process for the next period" will be a stronger incentive for patients compared to the incentive provided by a fixed reward. Thus, patients receiving fixed reward and fixed punishment will have a high possibility of quitting, while patients receiving increasing reward and fixed punishment will have the medium possibility of quitting because the increased reward would decrease the possibility of quitting. Also, patients receiving fixed reward and no punishment will have the medium possibility of dropping out because the exclusion of negative emotions caused by punishment would decrease the possibility. Patients receiving increasing reward and no punishment will experience both the incentive of increasing reward and elimination of negative sentiment caused by punishment, so these patients will have a low possibility of quitting.

Segment 2 (scenario components 5 and 6): goals do affect participants' persistence of activities in a way that hard goals prolong effort when participants are allowed to control the time they spend on a task (LaPorte and Nath 1976). However, we do not have enough evidence to compare the difficulty of self-set and physician-assigned goals, so we cannot examine the possibility of quitting in these two situations.

Segment 3 (scenario components 7 to 10): Sharing only the punishment information with others would lead to negative feedback to patients' behaviors as well as could damage their self-efficacy because the information represents that those patients cannot reach their preset goals. These adverse effects would cause a high possibility of patients to drop out. Compared with this situation, sharing both reward and punishment information will lead to positive feedback from others in addition to negative ones, balanced personal image, and stable self-efficacy level. Thus, the possibility of quitting would decrease from high to medium. In another situation, patients will not receive any outside judgments if they do not share information with others. Since people have a self-enhancement motive that involves a preference for positive over negative self-views (Sedikides and Gregg 2008), not sharing information with others will decrease the possibility of quitting from high to medium compared to the scenario of only sharing punishment information. When patients only share reward information with others, the positive feedback they get will further decrease the possibility of quitting to a low level.

6.4.2 Appropriate Patient Type

Savoli et al. (2020) conducted mixed-method research on patient types and self-management performance based on their reactions to and effective use of a web-based patient portal, which supports self-management of asthma patients. They categorized the patients as three types, autonomous patients, engaged patients, and reliant patients based on their causal attributions of self-management performances. Autonomous patients attributed the good performance to themselves and bad performance mainly to the portal and external impacts. Engaged patients believed the portal helped them reach good performance, and they had responsibilities when the performance is not good. Reliant patients attributed their good

performance entirely to the support of the portal and other external impacts, and they also attributed the bad performance to external effects.

When examining the patients' reactions to the portal, they found that autonomous patients view it as an "imposer" which forced them to engage in activities they did not want to and let them feel angry and frustrated. The engaged patients viewed the portal as a "facilitator," which made their self-management of the disease easier. The reliant patients saw the portal as a "protector," which provided them with help and took care of them (Savoli et al. 2020). We deploy the above three patient categories here to discuss our scenarios' suitable types.

Segment 1: Autonomous patients think they have enough disease-related knowledge and can manage their conditions well without external supports. Thus, NR could hurt their self-efficacy and cause bad emotions, while both fixed and increasing PR can add to their perceived usefulness of the intervention. Engaged patients can use self-management tools effectively with happiness, joy, and pleasure. So, no matter they receive either or both reinforcements, they can modify their behaviors accordingly. Reliant patients rely on others to take care of them. Increasing PR and NR forms a stronger connection between these patients' reactions and the incentive outcomes. In this way, they are more likely to participate effectively.

Segment 2: The suitability of these two goal-setting types is based on the accuracy of evaluation of patients' ability and real-life difficulties. Reliant patients do not have sufficient knowledge and motivation, so the physician-assigned goal should be suitable for them. While engaged patients understand their disease and life conditions well, they are eligible to set their own goals. The autonomous patients are challenging to accept the goal set by others, so they should set the goals.

Segment 3: Personality preference for social connection is the crucial factor in deciding information sharing styles. Patients who prefer a high level of autonomy and total control of their lifestyle, e.g., autonomous patients, are not suitable for enabling social connection. Because they believe they know what they should do and don't need external triggers for them to change behaviors, so no social connection should work well for them. If a patient is non-adherent to medication because he/she lacks self-regulation and rely on others to help them like reliant patients, sharing punishment information will be the right choice. Because there will be more people to help monitor and regulate his/her behavior in this way. For engaged patients, the sharing of reward information could be an encouragement for them to keep improving and keep or attain good performance. At the same time, the feedback from sharing NR information can also help them pursue better outcomes.

6.4.3 Cost-effectiveness

We conduct cost-effectiveness analysis under the assumption that all patients follow their most suitable scenario components, and they need the same time length of intervention to adopt a health-promoting behavior. Since the outcome is the same across all patients, so we only need to consider the cost of these scenario components to decide cost-effectiveness.

Segment 1: Implementing punishment will cost more than not implementing it in the application. Providing increasing rewards based on periods will also require more than providing fixed rewards over time. Therefore, scenario 1 will cost the least, scenario 2 will have an increased reward cost additionally, scenario 3 will have punishment implementation cost additionally, and scenario 4 will have both increased reward and punishment implementation cost additionally. The cost-effective level is a reversed cost sequence: scenario 1 has high cost-effectiveness, scenario 2 and 3 have a medium level, and scenario 4 has a low level.

Segment 2: The physician-assigned goal involves more interaction and efforts from both patient and physician side so that physician-assigned goal will cost more than a self-set goal. Therefore, the self-set goal has high cost-effectiveness, and the physician-assigned goal has low cost-effectiveness.

Segment 3: The cost of social connection will increase with increasing shared information amount due to storage and maintenance costs. In this way, scenario 7 will have high cost-effectiveness, scenario 8 and 9 will have medium cost-effectiveness, and scenario 10 will have low cost-effectiveness.

Scenario	Possibility of Quitting	Appropriate Patient Type	Cost-effectiveness
1	Medium	Autonomous patients, engaged patients	High
2	Low	Autonomous patients, engaged patients	Medium
3	High	Engaged patients	Medium
4	Medium	Engaged patients, reliant patients	Low
5	N/A	Autonomous patients, engaged patients	High
6	N/A	Reliant patients	Low
7	Medium	Autonomous patients	High
8	Low	Engaged patients	Medium
9	High	Reliant patients	Medium
10	Medium	Engaged patients, reliant patients	Low

Note: comparison levels are within scenario segments

Table 9. Scenario Comparison

Section 6.5 Multiple Medications Scenarios Comparison

Following our discussion in the System Design chapter, we compare multiple-medications scenarios under two situations, namely the overall required MA situation, and each medication requires a specific MA situation.

When a patient has multiple medications to take, but only an overall MA of them is required, all the scenarios process in similar ways as single medication scenarios besides the

increased complexity of medication schedule may cause a higher possibility of quitting. However, the patient could also get multiple rewards by following all medication prescriptions. Thus, the effect of rewards could counteract the impact of complexity, leading to little change in Table 9.

When a patient has multiple medications to take, and each of them has its own desired MA, both possibilities of quitting and cost-effectiveness of different scenarios are subject to change, especially when there is a medication requiring a high MA. Comparing Figure 19 and Figure 20, the probability of blocking more than one apps increases, and the time cost to unblock certain app lasts longer when a high required MA medication exists. The patient would be more likely to quit because of these impacts, even though various rewards are available. If we consider it from another aspect, we need to set and implement various rewards to fulfill the requirements of different medications and avoid patients' quitting. System operation costs will increase so that cost-effectiveness will drop because of the reward design.

We discuss and analyze scenario segments and compare each of them descriptively in this chapter. Next, we will evaluate our designed system using analytical models to illustrate the effectiveness of our system.

Chapter 7. Analytical Models

We evaluate the performance of interventions in the C&S system by using analytical models. Analytical models have been used as formal proofs for a long time in Computer Science, Design Science, and Engineering (Saaty and Vargas 2012) because they can express complex relationships among many variables of interest. They also provide intermediate and immediate results, which can help to improve the design of artifacts.

As our core dependent variable, we consider the percentage of prescribed medication taken by patients in this research as our calculated MA. We are aware that additional measurements of MA, such as the longest uninterrupted period of MA (the time period that a patient takes the prescribed medication according to schedule without even missing a single dose) and time expired before all prescribed doses are taken (the time period passed until a patient actually take all prescribed doses), can be useful supplementary outcome measures of our intervention (Noordraven et al. 2014). Nevertheless, in this research, we try to focus on the most critical outcome measurement, our defined MA.

Section 7.1 Patient's Model Assumptions

Several assumptions were made to keep the analytical model reasonably accurate. Some of these assumptions can be relaxed in future work to improve accuracy at additional complexity.

- Assumption 1: the model assumes the patients are able to self-medicate as prescribed.
- Assumption 2: the model assumes the patients are not fully non-compliant; in other words, patients take at least one medication dose within the observed period.
- Assumption 3: the model assumes the two conditions that the patient receives negative reinforcement are independent of each other. The two conditions are: (1) when the patient's MA drops below the expected MA for medication to be effective in treatment.

(2) when the patient has missed a certain number of doses consecutively even though his/her MA stays equal or higher to the expected MA.

Section 7.2 Validation of the Model

7.2.1 General Medication Adherence

The MA over the observed period is given by

$$\begin{aligned}
 MA &= (N_T / N_P) \times 100\% \\
 &= (N_T / (N_T + N_L)) \times 100\% \\
 &= (N_T / (N_T + (N_{un-missing} + N_{in-missing}))) \times 100\% \tag{1}
 \end{aligned}$$

where N_P is the number of prescribed doses for the observed period, N_T is the number of doses taken by the patient, and N_L is the number of doses left untaken by the patient.

Within doses left untaken by the patient, two types exist, the first one is the doses missed unintentionally by the patient due to forgetfulness or carelessness, the number of these unintentionally missed doses is represented by $N_{un-missing}$. The second type is the doses missed intentionally by the patient due to reasons such as patient characteristics, treatment factors, or patient-provider issues; the number of these doses is represented by $N_{in-missing}$.

To reduce unintentionally-missing-doses, we use two reminders with the time difference to inform the patient to take medication. Also, as mentioned in the System Design chapter, these two reminders can lower the possibility of overdose due to the patient's catch-up behavior to take doses at an inappropriate time to make up for their skipped or delayed doses.

The time interval between the beginning time of a dose's first reminder window and the end time of the next dose's second reminder window should not exceed the max-interdose-time for the dose to be effective. Thus,

$$T_{i+1,es} - T_{i,bf} \leq T_{max} \tag{2}$$

where T_{max} is the maximum interval time between two doses for them to remain medically effective and compliant, $T_{i,bf}$ is the beginning time of the first reminder window of dose i, and $T_{i+1,es}$ is the ending time of the second reminder window of dose i+1. Beside max-interdose-time, we also consider the min-interdose-time which prevents the patients from overdosing, that is to say

$$T_{i+1,bf} - T_{i,es} \geq T_{min} \quad (3)$$

where T_{min} is the minimum interval time between two doses for them to be compliant and safely consumed by the patient without causing any negative effects of overdosing, $T_{i,es}$ is the ending time of the second reminder window of dose i, and $T_{i+1,bf}$ is the beginning of the first reminder window of dose i+1. The illustration of reminder windows, max-iterdose-time and min-interdose-time is shown in Figure 21.

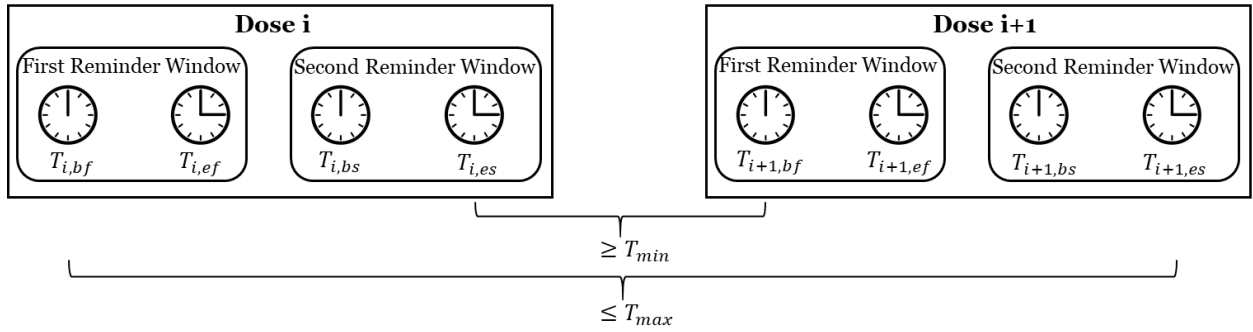


Figure 21. Illustration of Reminder Windows Design

7.2.2 Probability of reaching desired MA without interventions

Without intervention, the probability that the patient takes m doses among all prescribed doses for the observed period, N_p , is

$$P_{Ori} = \frac{\prod_{m=1}^{N_p} P_{Base}^m (1 - P_{Base})^{N_p - m}}{\prod_1^m m \times \prod_1^{N_p - m} m} \quad (4)$$

where P_{Base} is the inherent average probability of the patient takes a dose of medication. Thus, without intervention, the probability that a patient has MA equal or more than expected MA, represented using R_{ex} , is the sum of probability that a patient takes $[R_{ex}N_P]$ doses or more. This probability can be presented as

$$P_{without} = 1 - (N_P - [R_{ex}N_P]) \binom{N_P}{[R_{ex}N_P]} \int_0^{1-P_{Base}} t^{N_P-[R_{ex}N_P]-1} (1-t)^{[R_{ex}N_P]} dt \quad (5)$$

7.2.3 Probability of Reaching Desired MA with Reminders and Rewards

Interviews and surveys which examine the reasons for nonadherence indicate that forgetting is the reason offered by most patients for failing to take their medication (Khatib et al. 2014). Based on this fact, reminders have been tested to improve MA significantly in several studies. Since in our design, taking medication following reminders will induce the implementation of another type of intervention, rewards, we formulate the effects of these two intervention types together.

When we include rewards, the overall probability that a patient takes one dose through two reminder windows is

$$P_R = P_{st} + (1 - P_{st}) \times P_{nd} \quad (6)$$

where P_{st} is the probability that the patient takes the dose during the first reminder window, and P_{nd} is the probability that the patient takes the dose during the second reminder window.

Thus, the probability that the patient takes N_{st} out of N_P doses within the first reminder window is

$$P_F = \frac{\prod_{i=1}^{N_P} i \times P_{st}^{N_{st}} (1-P_{st})^{N_P-N_{st}}}{\prod_{i=1}^{N_{st}} i \times \prod_{i=1}^{N_P-N_{st}} i} \quad (7)$$

Based on the above, we express the probability that a patient takes total k dose(s) among N_P doses within either reminder windows as

$$P_{new} = \frac{\prod_{i=1}^{N_P} i \times P_{st}^{N_{st}} (1-P_{st})^{N_P-N_{st}}}{\prod_{i=1}^{N_{st}} i \times \prod_{i=1}^{N_P-N_{st}} i} \times \frac{\prod_{i=1}^{N_P-N_{st}} i \times P_{nd}^{k-N_{st}} (1-P_{nd})^{N_P-k}}{\prod_{i=1}^{k-N_{st}} i \times \prod_{i=1}^{N_P-k} i} \quad (8)$$

So, with reminders and rewards, the probability that a patient has MA equal or higher than expected MA is the sum of probability that a patient takes $[R_{ex}N_P]$ doses or more. Thus, the actual probability can be presented as

$$P_{withR} = [1 - (N_P - N_{st}) \binom{N_P}{N_{st}} \int_0^{1-P_{st}} t^{N_P-N_{st}-1} (1-t)^{N_{st}} dt] \times [1 - (N_P - N_{st} - N_{nd}) \binom{N_P-N_{st}}{N_{nd}} \int_0^{1-P_{nd}} t^{N_P-N_{st}-N_{nd}-1} (1-t)^{N_{nd}} dt] \quad (9)$$

where N_{nd} is the number of doses the patient takes during the second reminder window over the observed period, and it should be the number of $\max([R_{ex}N_P] - N_{st}, 1)$.

7.2.4 Probability of Implementing Negative Reinforcement

We discussed in the System Design chapter that NR would be implemented under two conditions. These are (1) when the patient's MA drops below expected MA and (2) when the patient has missed a certain number of consecutive doses.

To model the first condition, we realize it is the opposite situation of the patient always taking at least $[R_{ex}N_P]$ doses within N_P doses. So, based on equation 9, we have the probability of first NR condition as

$$P_{NR1} = 1 - P_{withR} \quad (10)$$

Following Feller (2008) study on consecutive missing trials, the probability of the patient receiving second condition NR can be expressed as:

$$P_{NR2} \sim 1 - \frac{1-P_R^x}{(N_m+1-N_m x)q} \times \frac{1}{x^{N_P+1}} \quad (11)$$

where N_m is the number of consecutive missing doses, P_R comes from equation 6, $q = 1 - P_R$, and x is the root near 1 of

$$1 - x + qP_R^{N_m} x^{N_m+1} = 0 \quad (12)$$

7.2.5 Fixed and Increasing Positive Reinforcement

RW is the amount of PR gained over the observed period. From the scenarios we discussed, RW for the fixed PR can be given as,

$$RW_F = R_{st} \times N_{st} + R_{nd} \times N_{nd} \quad (13)$$

where R_{st} is the constant PR amount the patient could receive when he/she takes the dose during the first reminder window, and R_{nd} is the constant PR amount the patient could receive when he/she takes the dose during the second reminder window. R_{st} should be larger than R_{nd} .

The other type of PR is increasing PR. Since we encourage the patient to take medication during the first reminder window, only the first reminder window reward increases over time. The RW for increasing PR can be given as,

$$RW_I = R_{st} \times (1 + \delta)^{t-1} N_{st} + R_{nd} \times N_{nd} \quad (t \geq 1) \quad (14)$$

where δ is the increase rate, and t is the number of observed periods.

7.2.6 Social Connection with Others

Social connection with other people, especially with family members, has shown to help the patient holding a more positive attitude towards medication. When the patient chooses to connect with other people, the feedback he/she receives could be an additive factor to improve MA, but not to exceed 100%. Therefore, the following expression can be developed:

$$P_{SC} = \text{Min}((P_{Base} + S \cdot M_{sc}), 1) \quad (15)$$

where S is the probability that the patient chooses to share personal MA information with other people, and M_{sc} represents the motivational factor the patient receives from social connections such as family support or better communication with healthcare professionals.

7.2.7 Impact of Goal-setting

Setting specific goals to achieve a task, in combination with performance feedback, has been found to result in better performance than does no goal setting or a vague goal setting (Latham and Locke 1991; Mento et al. 1987). The desire to fulfill a goal and the feedback provided to the patients after the goal gets reached are both additive factors to improve MA, but not to exceed 100%. Therefore, the following expression can be developed:

$$P_G = \min ((P_{Base} + M_G \cdot M_{FG}), 1) \quad (16)$$

where M_G represents the motivation that the patient has in reaching the goal, and M_{FG} represents the effect of feedback during the process to reach the goal.

7.2.8 Savings due to improved MA

The savings due to improved MA can be expressed as

$$S_{sav} = C_{OP} + C_{IP} + C_{OB} + C_{ER} + C_{PM} \quad (17)$$

The reduced healthcare expenditures attributed to increased MA, including outpatient expenditures (C_{OP}), inpatient expenditures (C_{IP}), office-based visits expenditures (C_{OB}), emergency room visits expenditures (C_{ER}), and medication prescription expenditures (C_{PM}).

7.2.8.1 Method and Data

In the analysis of how different MA would affect the total annual expenditures, we focus on patients who are diagnosed with diabetes. We conduct tests using data from the Medical Expenditure Panel Survey (MEPS) of 2016 and 2017. And then, we use the simulation method to capture the savings due to our intervention based on the results of our analysis of the MEPS data. Each panel gathers MEPS data last two years with five rounds of data collection. The data files contain personal information and related medical expenditures on the individual level for a nationally representative sample of the civilian noninstitutionalized population of the United

States. Figure 22 shows the data collection process. MEPS data have separate data files by their medical service types. The prescribed medicines file has information about how many days each prescription of medication supplies, as well as which year and which month the person started taking the medication. So, we can calculate MA as the proportion of days covered (PDC) using the available information and exclude individuals who are diagnosed with diabetes but has no prescribed oral medication records. The matched expenditure records of other medical services such as inpatient stays and outpatient visits allow us to capture the total expenditure of the year and analyze the impact of MA on it after controlling other effects. The data file details are listed in Table 10.

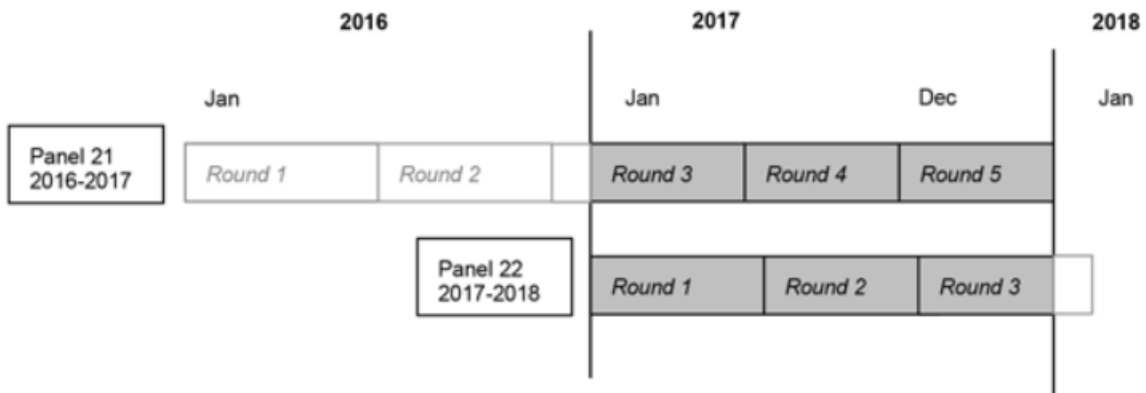


Figure 22: MEPS Collection Process

Information Type	Data Source
Personal Information	
Demographic Information	
2017 total income	
Whether diagnosed with diabetes	2017 Full Year Consolidated Data File
Which year the person has been diagnosed with diabetes	
Medication Adherence Information	
How many days each prescription of medication supplies	
which year the person started taking the medication	2017 Prescribed Medicines File
which month the person started taking the medication	
Expenditure Components	
2017 inpatient expenditures	2017 Hospital Inpatient Stays File
2017 outpatient expenditures	2017 Outpatient Visits File
2017 office-based visits expenditures	2017 Office-Based Medical Provider Visits File
Emergency Room Visits Expenditures	2017 Emergency Room Visits File
Prescribed Medication Expenditures	2017 Prescribed Medicines File

Table 10: Data Source Details

Since each MEPS panel lasts two years, we can estimate the natural change of annual MA from 2016 to 2017 at the individual level. Our test of the designed intervention’s impact on healthcare expenditure savings based on the increased probability for a patient to have a higher level of MA after receiving the intervention. Therefore, we assign utility weight of our intervention to the probabilities of all the transactions that are shown in Figure 23 and evaluate the savings using Simulation method to compare with natural changes without the intervention.

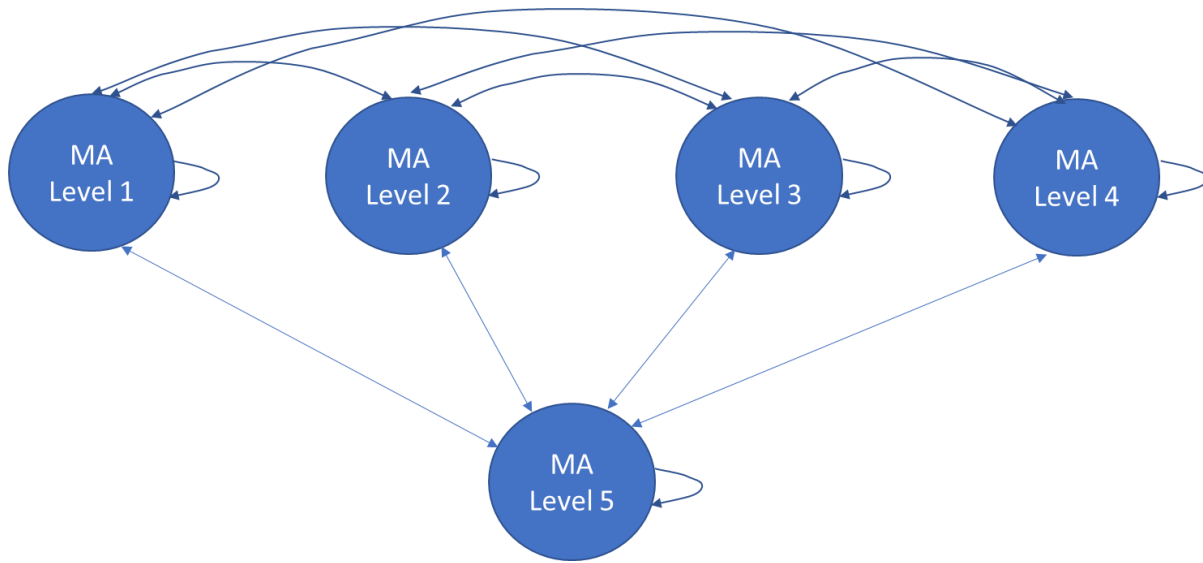


Figure 23: Simulation Model Base

Section 7.3 Healthcare Provider’s Participation

We have discussed in the previous chapter that the payment reform could encourage healthcare providers to invest in improving patients’ MA by providing positive reinforcement in our designed intervention. We develop models of the physician’s potential benefits following the setting of the current MIPS program.

Assign S_I as the physician’s MIPS score without intervening patients’ behavior. S_F is the score the physician could get if he/she provide incentives in our intervention to promote patients’ MA so to increase his/her treatment quality. We assume $S_F \geq S_I$. All other abbreviations are shown in Table 11. The relationship between MIPS performance score and payment adjustment rate is demonstrated in Figure 24.

Meaning	Notation
Physician's initial score	S_I
Physician's final score	S_F
Positive adjustment threshold score	S_B
Exceptional performance threshold Score	S_E
Maximum penalty threshold score	S_L
Maximum penalty rate (a negative number)	R_m
Maximum exceptional performance adjustment rate	R_{ex}
Physician's initial payment adjusted rate	$R_{I,i}$ ($i = 1,2,3,4,5$)
Physician's final payment adjusted rate	$R_{F,i}$ ($i = 1,2,3,4,5$)
Physician's Medicare Part B payment of year X	P_X
Physician's adjusted payment issued on year X+2	Ad_{Xi} ($i = 1,2,3,4,5$)
Amount change in adjusted payment if providing patients rewards	Ad_C
Scaling factor for positive adjustment	α
Scaling factor for exceptional adjustment	β
Annual discounting Factor	γ
Percentage of the clinician's anticipated adjusted payment used for incentives	p
Average additional work hours to support each patient	t
Average hourly wage of a registered nurse	w

Table 11. Model Notations

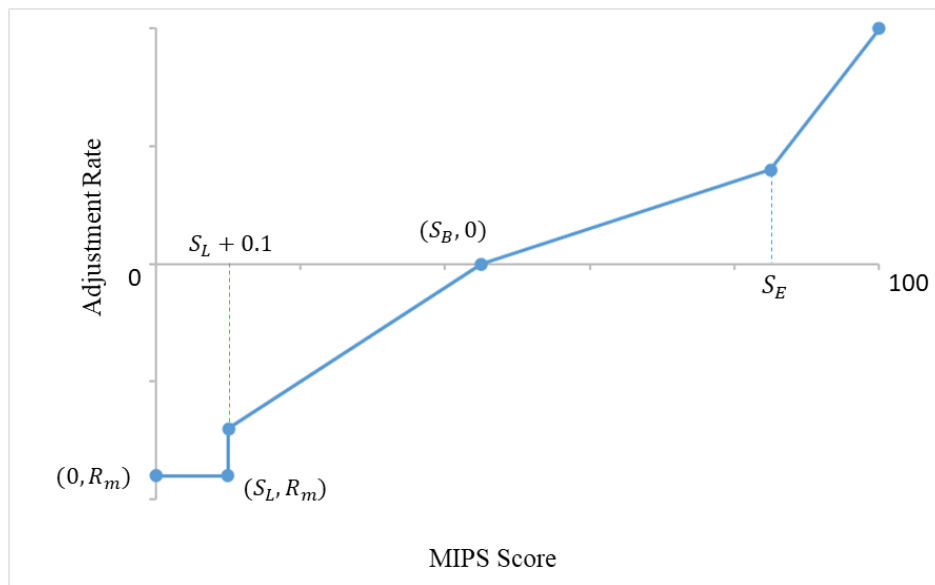


Figure 24: Payment Adjusted Rate

If S_I falls between 0 and S_L ($0 \leq S_I \leq S_L$), the physician will receive the maximum penalty rate.

$$R_{I1} = R_m \quad (18)$$

For the physician who has score larger than S_L but lower than S_B ($S_L < S_I < S_B$), he/she will receive a negative payment adjustment greater than the maximum negative rate and less than 0 percent on a linear sliding scale.

$$R_{I2} = (S_I - S_L) \times R_m / (S_B - S_L) \quad (19)$$

For the physician who has score equals to S_B ($S_I = S_B$), he/she will not receive any payment adjustment.

$$R_{I3} = 0 \quad (20)$$

For the physician who has score larger than S_B and lower than S_E ($S_B < S_I < S_E$), he/she will receive positive payment adjustment from greater than 0 percent to the absolute value of R_m ($|R_m|$) multiple a scaling factor α to preserve budget neutrality on a linear sliding scale.

$$R_{I4} = (S_I - S_B) \times \alpha |R_m| / (100 - S_B) \quad (21)$$

For the physician who has score greater or equal to S_E ($S_I \geq S_E$), he/she will receive additional payment adjustment for exceptional performance. The adjustment starting at 0.5% and increasing on a linear sliding scale to 10% multiplied by a scaling factor β .

$$R_{I5} = \alpha |R_m| + (S_I - S_E) \times \beta (10 - 0.5) / (100 - S_E) \quad (22)$$

The adjusted payment amount of year X is

$$Ad_{Xi} = P_X R_{Ii} \quad (i = 1,2,3,4,5) \quad (23)$$

When the physician provides the incentives to patients, the performance score will change to S_F . The adjusted rates of different conditions ($R_{F1} \sim R_{F5}$) according to S_F are similar to we have

in equation 18 to 22, so the change in the physician's performance score has the following fourteen conditions:

1. $0 \leq S_I \leq S_L$ and $0 \leq S_F \leq S_L$
2. $0 \leq S_I \leq S_L$ and $S_L < S_F < S_B$
3. $0 \leq S_I \leq S_L$ and $S_F = S_B$
4. $0 \leq S_I \leq S_L$ and $S_B < S_F < S_E$
5. $0 \leq S_I \leq S_L$ and $S_F \geq S_E$
6. $S_L < S_I < S_B$ and $S_L < S_F < S_B$
7. $S_L < S_I < S_B$ and $S_F = S_B$
8. $S_L < S_I < S_B$ and $S_B < S_F < S_E$
9. $S_L < S_I < S_B$ and $S_F \geq S_E$
10. $S_I = S_B$ and $S_B < S_F < S_E$
11. $S_I = S_B$ and $S_F \geq S_E$
12. $S_B < S_I < S_E$ and $S_B < S_F < S_E$
13. $S_B < S_I < S_E$ and $S_F \geq S_E$
14. $S_I \geq S_E$ and $S_F \geq S_E$

The changes in adjusted payment caused by the modified performance score according to these fourteen conditions are shown in Table 12 as equations 24 to 37.

Since the adjusted payment of year X will be issued in year X+2, the value of this payment at year X will be perceived discounted with factor γ^2 . A physician chooses to provide the incentives to the patients when the proportion of discounted adjusted payment the physician would like to invest exceeds the cost of enrollment:

$$\gamma^2 \times p \times Ad_C \geq C \quad (38)$$

The costs include the amount of rewards provided to patients and the extra time in monitoring the health status of patients and assisting them when needed. In a well-designed

chronic disease management team, the tasks of monitoring and follow-up with patients can be delegated to nurses, thus,

$$C = RW + ntw \quad (39)$$

Initial Score (S_I)	Final Score (S_F)	Changes in Adjusted Payment (Ad_C)	Equation #
$0 \leq S_I \leq S_L$	$0 \leq S_F \leq S_L$	0	(24)
$0 \leq S_I \leq S_L$	$S_L < S_F < S_B$	$(\frac{S_F - S_L}{S_B - S_L} - 1) \times R_m P_X$	(25)
$0 \leq S_I \leq S_L$	$S_F = S_B$	$- R_m P_X$	(26)
$0 \leq S_I \leq S_L$	$S_B < S_F < S_E$	$[\frac{(S_B - S_F) \times \alpha}{100 - S_B} - 1] R_m P_X$	(27)
$0 \leq S_I \leq S_L$	$S_F \geq S_E$	$[-(1 + \alpha) R_m + (S_F - S_E) \times \frac{9.5 \beta}{100 - S_E}] \times P_X$	(28)
$S_L < S_I < S_B$	$S_L < S_F < S_B$	$\frac{S_F - S_I}{S_B - S_L} \times R_m P_X$	(29)
$S_L < S_I < S_B$	$S_F = S_B$	$\frac{S_L - S_I}{S_B - S_L} \times R_m P_X$	(30)
$S_L < S_I < S_B$	$S_B < S_F < S_E$	$(\alpha \times \frac{S_B - S_F}{S_E - S_B} - \frac{S_I - S_L}{S_B - S_L}) R_m P_X$	(31)
$S_L < S_I < S_B$	$S_F \geq S_E$	$[-(\alpha + \frac{S_I - S_L}{S_B - S_L}) R_m + (S_F - S_E) \times \frac{9.5 \beta}{100 - S_E}] \times P_X$	(32)
$S_I = S_B$	$S_B < S_F < S_E$	$\alpha \times \frac{S_B - S_F}{S_E - S_B} \times R_m P_X$	(33)
$S_I = S_B$	$S_F \geq S_E$	$[-\alpha R_m + (S_F - S_E) \times \frac{9.5 \beta}{100 - S_E}] \times P_X$	(34)
$S_B < S_I < S_E$	$S_B < S_F < S_E$	$\alpha \times \frac{S_I - S_F}{S_E - S_B} \times R_m P_X$	(35)
$S_B < S_I < S_E$	$S_F \geq S_E$	$[\alpha R_m \times \frac{S_I - S_B}{S_E - S_B} + (S_F - S_E) \times \frac{9.5 \beta}{100 - S_E}] \times P_X$	(36)
$S_I \geq S_E$	$S_F \geq S_E$	$(S_F - S_I) \times \frac{9.5 \beta}{100 - S_E} \times P_X$	(37)

Table 12: Changes in Adjusted Payment

Chapter 8. Results and Discussion

Using the analytical models, we derived several results for the impact of the designed intervention on both patient's and healthcare provider's sides, including the impact of reminders and PR, the impact of NR, the savings by interventions, and the enrollment of healthcare providers.

Section 8.1 The Impact of Reminders and Positive Reinforcement

To evaluate the impact of reminders and PR, we utilize a real-life setting, which uses a prescription for 30 days with three doses/day. Thus the total doses are 90, and the expected MA is set as 80%. The probability of the patient reaching expected MA for different P_{Base} , the inherent average probability of the patient takes a dose of medication, P_{st} , and P_{nd} is shown in Figure 25. The line with $P_{nd} = 0$ represents the effect of different level of P_{Base} . Without reminders and PR, the higher the inherent average probability a patient takes each dose, the more likely he/she satisfies the expected MA. However, even when P_{Base} is relatively high (e.g., $P_{Base} = 0.8$), the probability that the patient reaches expected MA is relatively low (e.g., less than 60%). Also, with low P_{Base} (e.g. 0.2 ~0.4), it is almost impossible for the patient to meet the expected MA.

The situation is primarily changed by including reminders and PR as interventions. Even if the first reminder doesn't change the patient's behavior pattern, in other words, P_{st} is the same as P_{Base} , a low P_{nd} (e.g., $P_{nd} = 0.2$) could still improve the probability of the patient reaching expected MA significantly, from less than 60% to higher than 85%. If the first reminder and associating PR could lead to a small increase (e.g., 0.1, from 0.8 to 0.9), the change in the probability of the patient reaching expected MA will have a significant jump, from less than 60% to almost 100%.

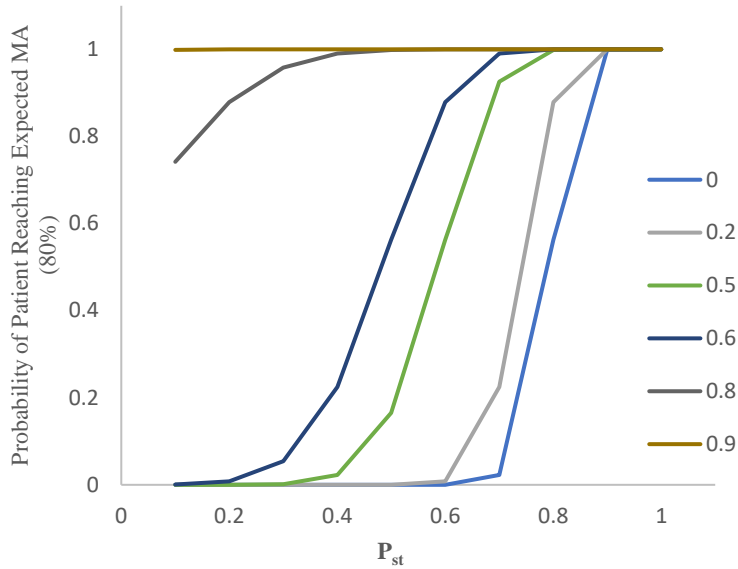


Figure 25. Probability of Reaching Expected MA

Section 8.2 Effectiveness of Reminders and Positive Reinforcement

We use \$1 reward (cash, voucher, lottery, or other types) as the financial value of R_{st} , and \$0.5 reward as the value of R_{nd} to analyze the effectiveness of reminders and reinforcement. The cost of delivering reminders is ignored as it can be done inexpensively on mobile phones. In Figure 26, we assume the increasing rate of reward is 5% ($\delta = 0.05$), and P_{st} and P_{nd} are both 0.5. The figure shows the difference in rewards the patient would get from taking each dose across twelve time periods. In Figure 27, we show the difference in rewards the patient would get from taking each dose with the same increasing rate ($\delta = 0.05$) but different P_{st} and P_{nd} . Increasing reward 1 captures the rewards based on $P_{st} = 0.5$, $P_{nd} = 0.5$, increasing reward 2 captures rewards based on $P_{st} = 0.7$, $P_{nd} = 0.5$, and increasing reward 3 captures rewards based on $P_{st} = 0.5$, $P_{nd} = 0.7$. This figure illustrates that P_{st} plays a bigger role than P_{nd} if the patient wants to get a higher reward in increasing PR scenarios.

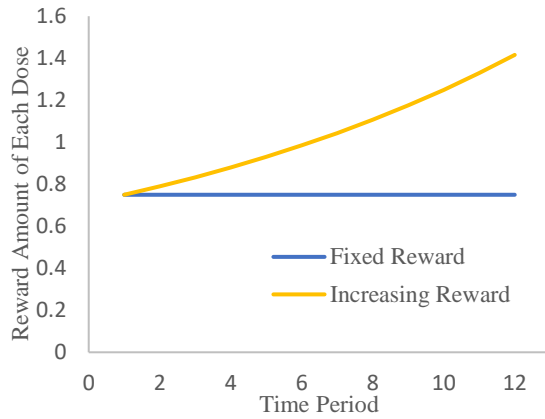


Figure 26: Difference in PR Amount with Fixed PR and Increasing PR

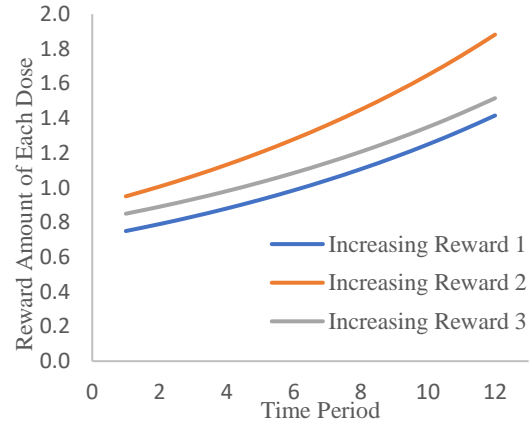


Figure 27: Difference in Increasing PR Amount with Different P_{st} and P_{nd}

The effectiveness of a fixed PR is shown in Table 13. The intervention reaches the highest effectiveness (0.99) when the probability that the patient takes his/her medication through the first reminder window is high (0.8 or 0.9) while the probability of taking his/her medication through second reminder window is low (0.1 or 0.2). Effectiveness decreases with decreasing first reminder-window probability and increasing second reminder window probability. If we set the adequate effectiveness level of the intervention to 0.9 or higher, then it is clear from Table 4 that we need to adjust the type of PR over time for different patients to ensure that their probability of taking medication during the first reminder-window is at least 0.3.

The effectiveness of increasing PR over time periods with different P_{st} and P_{nd} is shown in Figure 28. All parameters are the same as in Figure 27. Figure 28 demonstrates that the effectiveness of PR decreases over time since the amount of PR has to increase to keep the same P_{st} and P_{nd} . Comparing line 1 and line 3, it shows that with the same P_{st} , the effectiveness of PR which induces higher P_{nd} would have a slower decrease. Similarly, comparing line 1 and line 2, it shows that with the same P_{nd} , the effectiveness of PR which induces higher P_{st} would have a slower decrease.

		P_{nd}								
		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
P_{st}	0.1	0.76	0.68	0.64	0.61	0.59	0.58	0.57	0.56	0.55
	0.2	0.86	0.78	0.73	0.69	0.67	0.65	0.63	0.62	0.61
	0.3	0.91	0.84	0.79	0.76	0.73	0.71	0.69	0.67	0.66
	0.4	0.93	0.88	0.84	0.81	0.79	0.76	0.74	0.73	0.71
	0.5	0.95	0.92	0.88	0.86	0.83	0.81	0.79	0.78	0.76
	0.6	0.97	0.94	0.92	0.89	0.88	0.86	0.84	0.83	0.81
	0.7	0.98	0.96	0.94	0.93	0.91	0.9	0.88	0.87	0.86
	0.8	0.99	0.98	0.97	0.95	0.94	0.93	0.93	0.92	0.91
	0.9	0.99	0.99	0.98	0.98	0.97	0.97	0.96	0.96	0.95

Table 13. The Effectiveness of reminders and fixed PR

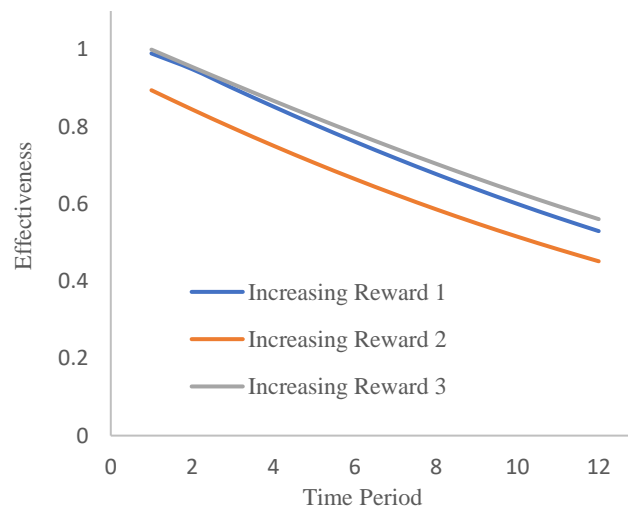


Figure 28: Effectiveness of Reminders and Increasing PR

Section 8.3 The Effectiveness of Negative Reinforcement

Now, we evaluate the two conditions of NR implementation using the same 90 doses in real-life settings. When NR is implemented as the patient's MA drops below expected MA, the NR receiving probability is shown in Figure 29. With the different levels of expected MA varying from 0.8 to 0.95, the patient needs to maintain a high P_R , the overall probability of taking a dose through two reminder windows with PR, to avoid receiving NR. For example, if the

expected MA is 0.8, the patient should have at least $P_R = 0.8$ to reduce his/her probability of favorite mobile app disconnection to less than 45%.

When the patient misses several consecutive doses, the probability of receiving NR is shown in Figure 30. With different limits of consecutive missing doses, the probability of the patient receiving NR varies. For example, comparing an allowance of two consecutive-missing-dose with an allowance of four consecutive-missing-dose, the patient would have a much lower P_R , 0.37, in four consecutive missing cases to avoid being disconnected from the favorite app, than the needed P_R , 0.7, for the two consecutive missing cases.

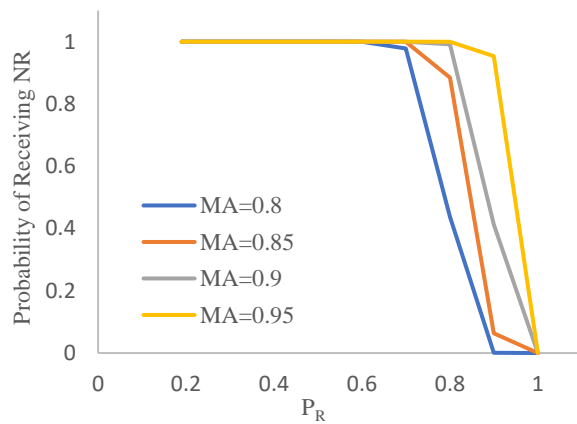


Figure 29. The Probability of Receiving NR due to MA lower than Expected

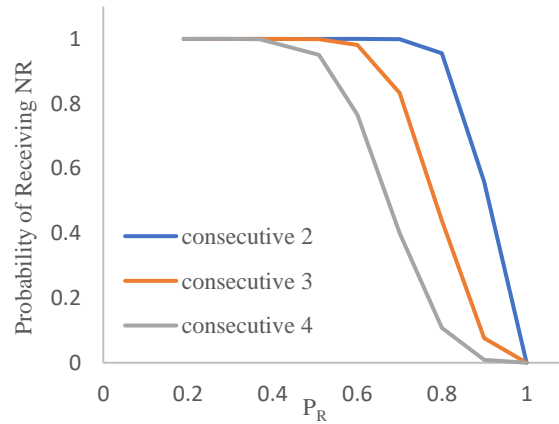


Figure 30. The Probability of Receiving NR due to Consecutive Dose Missing

Section 8.4 Savings from Reducing Healthcare Expenditures

From MEPS 2017 data, we retrieve records of 2843 individuals who are diagnosed with diabetes. Within them, 185 persons are of age < 18 , so we exclude them in our analysis. An additional 164 persons do not have prescribed medication records for treating diabetes, and we exclude them as well. Therefore, we have 2494 individuals included in our analysis. The medication list we use in filtering diabetes prescription is represented in Appendix C.

To set up our simulation model in R⁹, we follow five steps. First, we retrieve basic information from MEPS 2017 data, namely demographic information, MA information, and expenditures information. The MA is calculated using the proportion of days covered in a year. We set MA level 1 as $0\% < MA < 20\%$, MA level 2 as $20\% \leq MA < 40\%$, MA level 3 as $40\% \leq MA < 60\%$, MA level 4 as $60\% \leq MA < 80\%$, and MA level 5 as $MA \geq 80\%$. The desired MA level for diabetes treatment is level 5. The number of patients according to their MA levels to treatment for diabetes is shown in Figure 31, demographic information of the patients is shown in Table 14, and expenditures information is shown in Table 15. More than 1/3 of the patients reached the desired MA level, while the other 62% of patients' performance did not meet the expectation. The maximum office-based physician visits expenditures almost reached \$100,000, and the maximum inpatient stays expenditures exceeded \$100,000. The annual total healthcare expenditures were more than \$130,000.

In the second step, we analyze the impact of various MA levels on the healthcare expenditures after controlling the demographic variables. The result summary of logistic regression is shown in Table 16. We can interpret that low MA levels, namely level 1 and level 2, will significantly ($p = 0.039$, $p = 0.035$) increase healthcare expenditures comparing with the desired MA level. The average expenditures among patients in level 5 are \$6592. Keeping other indicators constant, the excess annual amount of patients in lower levels spend ranges from \$193.70 to \$1787.74. Also, the increase in the number of years diagnosed with diabetes will lead to higher healthcare expenditures significantly ($p = 0.005$). Holding all other variables constant, each additional year with diagnosed diabetes will cost \$180.31 more healthcare expenditures. The increase rate is 7.8% when compared to the mean of total healthcare expenditures.

⁹ The model is set up based on a GitHub project: <https://github.com/DARTH-git/Microsimulation-tutorial>

As described above, we matched records in MEPS 2017 data with MEPS 2016 data to capture the natural change of MA at the individual level and have 638 matched patients. The details of MA change rates are listed in Table 17. We transform the change rates into the probabilities of an individual's transition among MA levels as $probability = 1 - e^{-rate}$. The results of the transition probabilities are also listed in Table 17.

In the last step, we estimate the utility of our intervention as the times it increases the probabilities that a patient change from lower levels of MA to higher levels or decreases the probabilities of changing from higher levels to lower levels. We assign the utility that ranges from 1.2 to 1.5 for patients in level 4 to level 1, respectively. We also include an intervention effect modifier, a uniform distribution *Uniform (0.9, 1.1)*, to capture the differences in the real impact of intervention utility at the individual level. In addition, we assume the decremental utility rate is 3% each year.

In the simulation, we discount all future years' estimated healthcare expenditures to the current year with a discount factor. The discount factor is represented using the average inflation rate from 2010 to 2019 Bureau of Labor Statistics' records¹⁰, and the number is 1.8%. The detailed parameters of our simulation model are listed in Appendix D.

¹⁰ <https://www.bls.gov/cpi/>

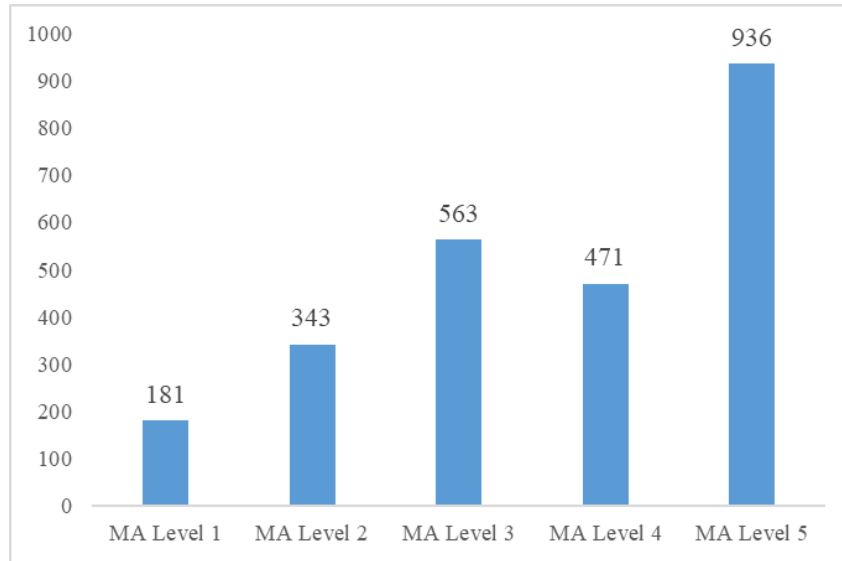


Figure 31. Patients of Different MA Levels

		n	%
Age group (years)	18 - 34	43	2%
	35 - 44	201	8%
	45 - 54	405	16%
	55 - 61	737	30%
	≥ 65	1106	44%
Gender	Male	1200	48%
	Female	1294	52%
Race	White	1076	42%
	Black	517	21%
	Hispanic	688	28%
	Asian	141	6%
	Other races or multiple races	72	3%
Income	Less than \$20,000	1226	49%
	\$20,000 - \$44,999	761	31%
	\$45,000 - \$139,999	461	18%
	\$140,000 - \$199,999	30	1%
	≥ \$200,000	16	0.7%
	Average	Min - Max	
Number of years diagnosed with diabetes	12	0 - 58	

Table 14. Characteristics of Individuals Included in Analysis (n = 2494)

	Min	Max	Mean
Prescribed Medication Expenditures	\$0.00	\$15,658.00	\$849.29
Outpatient Visits Expenditures	\$0.00	\$28,544.90	\$652.00
Inpatient Stays Expenditures	\$0.00	\$101,935.00	\$2,985.00
Emergency Room Visits Expenditures	\$0.00	\$11,320.80	\$321.20
Office-based Physician Visits Expenditures	\$0.00	\$97,256.00	\$2,683.00
Total Healthcare Expenditures	\$5.43	\$131,164.31	\$2,304.59

Table 15. Healthcare Expenditures Details

	<i>Estimate</i>	<i>Std. Error</i>	<i>P-value</i>
Age	79.54	45.30	0.079
Gender	1517.18	1059.39	0.152
Hispanic	-1983.34	1303.20	0.128
Black	-2599.29	1401.01	0.064
Asian	-3575.38	2307.92	0.122
Other races	-4380.64	3144.98	0.164
lg(Income)	-1.80	1.64	0.260
Number of years diagnosed with diabetes	180.31	64.26	0.005 **
MA1	1787.74	1092.86	0.039 *
MA2	1529.09	733.15	0.035 *
MA3	595.81	372.24	0.166
MA4	193.70	464.52	0.189
R²		0.0874	

Note: * p < 0.05, ** p < 0.01

Table 16. Regression Result

MA level in 2016	MA level in 2017	n	%	Probability of transition between levels
Level 1	Level 1	20	32%	
	Level 2	11	17%	0.16
	Level 3	8	13%	0.12
	Level 4	13	20%	0.18
	Level 5	11	18%	0.16
Level 2	Level 1	10	11%	0.10
	Level 2	32	37%	
	Level 3	13	15%	0.14
	Level 4	18	21%	0.19
	Level 5	14	16%	0.15
Level 3	Level 1	8	6%	0.06
	Level 2	4	3%	0.03
	Level 3	66	49%	
	Level 4	19	14%	0.13
	Level 5	38	28%	0.24
Level 4	Level 1	7	5%	0.05
	Level 2	23	17%	0.16
	Level 3	29	22%	0.20
	Level 4	40	30%	
	Level 5	35	26%	0.23
Level 5	Level 1	2	1%	0.01
	Level 2	17	8%	0.08
	Level 3	30	14%	0.13
	Level 4	63	29%	0.25
	Level 5	104	48%	

Table 17: MA Change Between 2016 and 2017

Table 18 shows our simulation results for the patients' annual savings for five years. The simulated population is 10,000 or 100,000. On average, a patient with diabetes can save more than \$600 per year in his/her healthcare expenditures when he/she engages in receiving our intervention.

Strategy	Expenditures (\$)	Total savings (\$)	Savings per person (\$)
n = 10,000 and seed =123			
No intervention	78,862,305 (750,174)	--	
With intervention	72,674,988 (645,231)	6,187,317	618
n = 100,000 and seed =123			
No intervention	793,751,136 (7,418,335)	--	
With intervention	731,366,975 (6,785,612)	62,384,161	623

Table 18. Simulation Result

From the above model and results, the following observations can be made:

- The combined intervention of two reminders and PR can increase the probability of the patient achieving the expected MA.
- Reminders and fixed PR intervention can be highly effective even when the patient's probability of taking the dose in the first reminder window is moderately low.
- The type or amount of PR should be adjusted over time to compensate for the diminishing effects of the same stimulus.
- If the patient wants to absolutely avoid NR (probability of receiving NR to 0), he/she must maintain a very high level of the overall probability of taking doses. This overall probability is higher than the outcome increased by only delivering reminders and PR, especially when the expected MA is high, or the limit for consecutive-missing-dose is small.
- The composite intervention provides better performance in assisting the patient in attaining his/her health goal than only reminders and PR or only NR.
- The savings in healthcare expenditures are estimated to be more than \$600 per year per patient in the five years simulated period.

Section 8.5 Healthcare Provider’s Enrollment

To estimate the enrollment of healthcare providers, we deploy information from multiple sources (Table 19) to test our model.

Parameter	Value	Data Source
S_B	45	2020 QPP Final Rule ¹¹
S_E	85	2020 QPP Final Rule
S_L	10	2020 QPP Final Rule
R_m	-9%	2020 QPP Final Rule
R_{ex}	10%	2020 QPP Final Rule
α	0.14	2020 QPP Final Rule
β	0.499	2020 QPP Final Rule
P_x	$\geq 90,000$	MIPS Eligibility
W	\$37.24	Bureau of Labor Statistics ¹²
γ	1.8%	Bureau of Labor Statistics

Table 19. Parameters, Values, and Sources

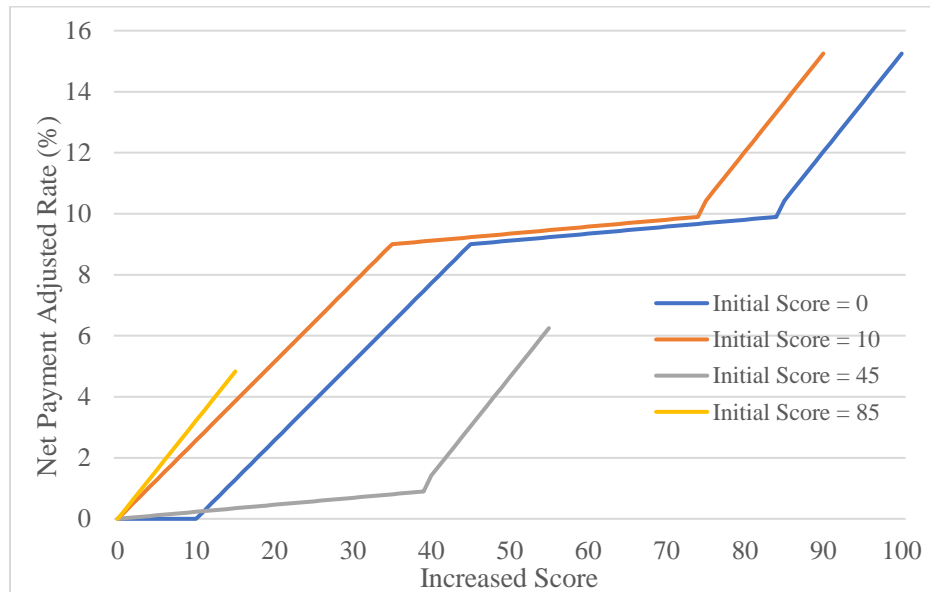


Figure 32: Net Payment Adjusted Rate for Different Increased Score

¹¹ 2020 QPP Final Rule: <https://www.federalregister.gov/documents/2019/11/15/2019-24086/medicare-program-cy-2020-revisions-to-payment-policies-under-the-physician-fee-schedule-and-other>

¹² <https://www.bls.gov/oes/current/oes291141.htm>

Calculating based on equations 18 to 22, Figure 32 illustrates the payment adjusted net rate according to different increased score points with the initial point at each performance threshold score. From the figure, the highest net adjusted rate is 15.25%, which is from -9% to 6.25%, representing the score increases from the maximum penalty range (0 to 10) to 100. The rate increases slowest when the score changes between 45 and 85, and it increases fastest when the score changes between 85 and 100. If the physician falls into the penalty range (10 to 45) initially, an investment in the intervention to increase performance score is also a good choice to avoid or reduce the penalty. Because the increment in adjustment rate of every additional point in penalty score range (0.26%) is only slightly lower than the change in exceptional performance range due to each single point (0.32%).

Besides increasing within the maximum penalty range, the adjusted rate according to 5 points increase ranges from 0.12% to 1.61%, the adjusted rate according to 10 points ranges from 0.23% to 3.22%, and ranges from 0.28% to 4.83% for 15 points increment. We consider the potential influence of the adjusted payments on the physician's participation in providing reinforcements to the patients under these 5 points, 10 points, and 15 points increase conditions.

Referring to the eligibility of a physician to participate in the MIPS 2020, the minimum Medicare Part B payment is \$90,000. And we use the same discount factor as we used in the patients' healthcare expenditures' savings estimation, 1.8%, to calculate the present value of the adjusted payment. Figure 33 shows the adjusted payment value in the present year with a \$90,000 payment, and according to the three conditions which are mentioned above.

Combining the present value of the adjusted payment and possible proportions that the physician could likely to invest in incentives, Figure 34 shows the minimum and maximum total incentives of the three conditions.

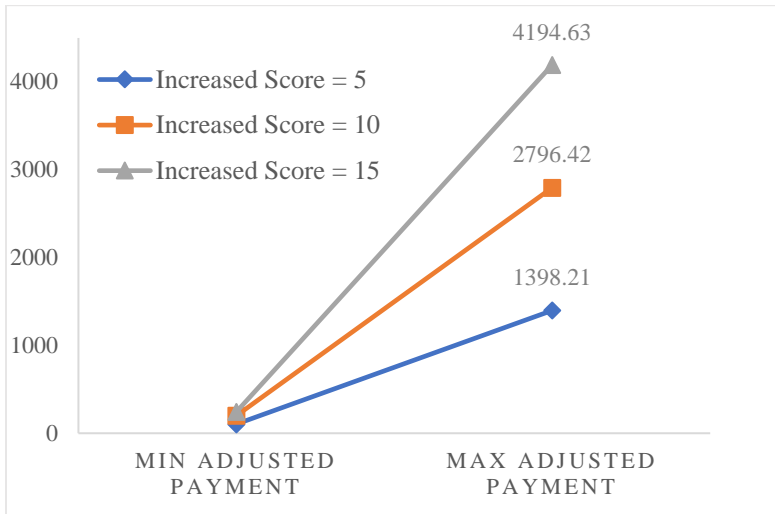


Figure 33. Present Value of Adjusted Payment (\$)

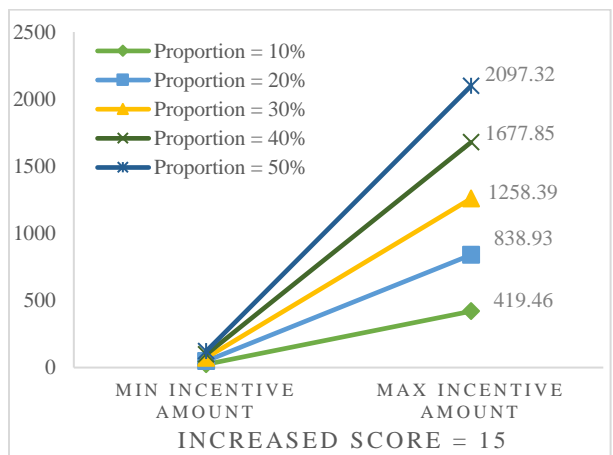
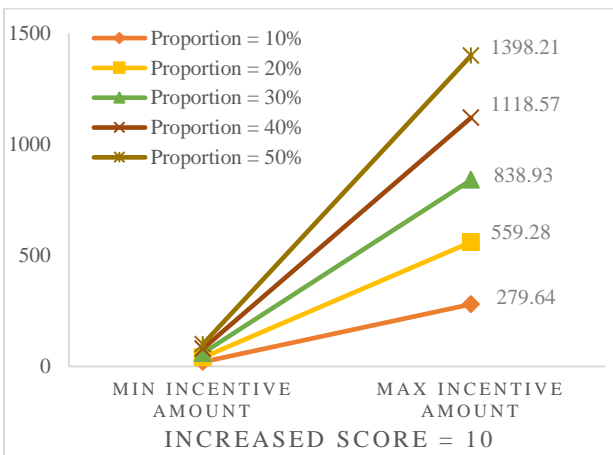
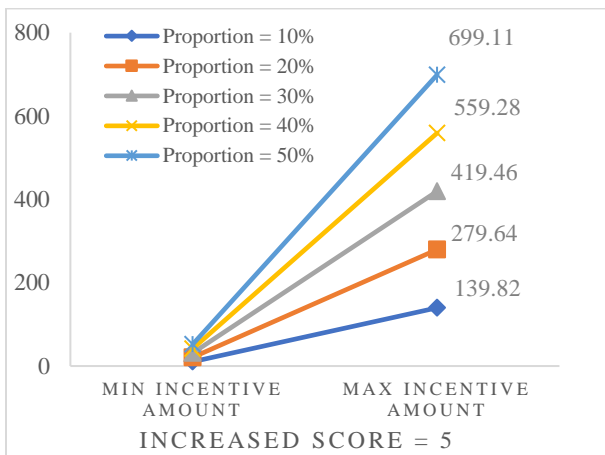


Figure 34. Incentives Range (\$)

When assessing the cost of the physician's enrollment, we estimate the rewards patients can get from achieving level 5 MA because it is our desired outcome with intervention. We vary the number of doses a patient should take within a day from 1 to 3. Following the estimation of the effectiveness of PR, we assign full reward as \$0.1 per dose and reduced reward as \$0.05 per dose in our evaluation. We use the mean hourly wage of a registered nurse to calculate the cost of extra work hours, and assume each patient adds ½ hour extra work per month to the nurse. The cost of rewards and extra work per patient according to different intervention period is listed in Table 20.

Comparing the cost and discounted adjusted payment, we can estimate the number of patients that the physician could support (Table 21). If the physician's initial performance score lies in the positive adjustment range (45 to 84.99), the earned adjusted payment will be low, and it will not be enough to use as incentives for patients if the intervention period lasts from 3 months to 1 year. Therefore, the physician is unlikely to adopt the intervention to assist the treatments for patients. However, if the physician's initial performance score lies in the exceptional adjustment range (≥ 85), the amount earned in adjusted payment could at least support one patient even if the increased score is 5 points, and only 20% of the payment is used.

Align with our analysis of patients with diabetes, the most recent physician payment data of 2017 from CMS's Medicare Provider Utilization and Payment Data¹³ shows among the average number of Medicare Part B beneficiaries identified with diabetes is 211 for each endocrinologist. The adjusted payment of 15 points increase can cover the cost for up to ½ of those patients in one-month intervention period if 50% of it is used, and it may support all the patients if we only provide incentives to patients with low MA, such as level 1 and level 2.

¹³ Data access: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Physician-and-Other-Supplier2017>

From these models and results, we can conclude that:

- Physicians who have an initial score lies in positive adjustment range are unlikely to support the intervention.
- Physicians who have an initial score lies in exceptional adjustment range are likely to support the intervention.
- Physicians who want to avoid or reduce penalties are likely to support the intervention.
- More resources should be utilized in addition to the physician’s input to ensure the intervention can work for a full year.

Intervention period	Extra work cost	# of doses per day	Min reward amount for level 5 MA	Max reward amount for level 5 MA
1 year	\$223.44	1	\$14.60	\$36.50
		2	\$29.20	\$73.00
		3	\$43.80	\$109.50
½ year	\$111.72	1	\$7.20	\$18.00
		2	\$14.40	\$36.00
		3	\$21.60	\$54.00
3 months	\$55.86	1	\$3.60	\$9.00
		2	\$7.20	\$18.00
		3	\$10.80	\$27.00
1 month	\$18.62	1	\$1.20	\$3.00
		2	\$2.40	\$6.00
		3	\$3.60	\$9.00

Table 20. Cost of Intervention from Healthcare Provider’s Side

Increased score	Proportion of adjusted payment	Intervention period							
		1 year		½ year		3 months		1 month	
		Min # of patients can be sponsored	Max # of patients can be sponsored	Min # of patients can be sponsored	Max # of patients can be sponsored	Min # of patients can be sponsored	Max # of patients can be sponsored	Min # of patients can be sponsored	Max # of patients can be sponsored
5	10%	0	0	0	1	0	2	0	7
	20%	0	1	0	2	0	4	0	14
	30%	0	1	0	3	0	7	1	21
	40%	0	2	0	4	0	9	1	28
	50%	0	3	0	5	0	11	1	35
10	10%	0	1	0	2	0	4	0	14
	20%	0	2	0	4	0	9	1	28
	30%	0	3	0	7	0	14	2	42
	40%	0	4	0	9	0	18	2	56
	50%	0	5	0	11	1	23	3	70
15	10%	0	1	0	3	0	7	0	21
	20%	0	3	0	7	0	14	1	42
	30%	0	5	0	10	0	21	2	63
	40%	0	7	0	14	1	28	3	84
	50%	0	8	0	17	1	35	4	105

Table 21. Number of Sponsored Patients

Chapter 9. Conclusion

The prevalence of chronic diseases leads to a great financial burden on the US healthcare system. Despite significant efforts and investments, the quality of chronic disease management has been less than satisfactory. The management of chronic diseases requires effective and efficient interactions from multiple components. The Chronic Care Model illustrates how the six components, communities of resources and policies, healthcare organization, self-management support, decision support, delivery system design, and clinical information system, should be implemented to facilitate high-quality chronic disease management (Wagner 1998). Providing sufficient self-management support lies in the center of the model. Self-management emphasizes the active role of patients themselves and their family members in making disease-related decisions. It has been identified to be critical to achieving better outcomes.

One component which influences the engagement of healthcare providers in supporting patients' self-management is currently under major transformation. The payment structure of clinicians is changing from rewarding the number of services they provide into rewarding the quality of service outcomes. Physicians can receive positively adjusted reimbursement if their performance is beyond the threshold and will receive the negative adjustment if their performance is below the threshold. Also, with the rapid development of related technologies and devices, and the improvements in data transmission standards and specifications, m-health has facilitated patients' self-management as well as collecting patient-generated data and integrate them into EHRs.

As a critical task in patients' self-management, there is a need to keep MA beyond 80% with higher rates for certain diseases or conditions (Osterberg and Blaschke 2005). How to attain the level has received researchers and healthcare professionals' attention for years. Various

formats of intervention have been developed and examined for their effectiveness and cost-effectiveness. M-health is one of the practical and inexpensive solutions to help track and promote patients' medication intake behaviors. However, reinforcements delivered through m-health were less studied in previous research, let alone the characteristic of users' dependency on mobile phones that provides a natural way to implement negative reinforcement by cutting the accessibility to the social media or entertainment Apps. Also, the lack of theoretical support in design, and short-term tests both decrease the evaluation results' reliability. In addition, the choices from healthcare providers in supporting the interventions were seldomly discussed.

Thus, in this paper, we present, evaluate, and validate a novel mobile health intervention, Carrot & Stick (C&S), to support patients' decisions to take medication doses and to reinforce behavior changes. Our design of C&S is innovative in several ways:

- 1) It integrates PR and NR with previously validated reminders and social connection elements into a composite intervention. The NR provides the opportunity to influence the behaviors of the patients who understand they should follow the prescription instructions but choose not to.
- 2) Every functionality in our design is based on theories. It increases the reliability of results on the effectiveness of our design using the analytical model.
- 3) The ten scenario components illustrate different applications of the intervention, and the identified suitable patient type and the cost-effectiveness of those components provide decision support for both patients and healthcare professionals.
- 4) The use of two reminder windows, as well as association to the wireless electronic medication container, leads to the maximum avoidance of forgetting, overdosing, and taking doses at the wrong time.

Section 9.1 Research Contributions

We contribute with the above innovations as well as through the results of our analysis. From the results of the analytical model, the patient's probability of achieving expected MA is significantly increased after utilizing the composite intervention. Even reminders and PR alone can be effective in promoting MA, but NR can still assist. Patients adopt better medication intake habits when they engage to avoid NR compare to the situation that they only pursue to accumulate PR. Also, according to our simulation model, whose input was based on analyzing healthcare expenditures data, healthcare savings due to higher MA are significant. Our intervention can assist patients in saving more than \$600 per year per person.

For healthcare providers' involvement in the intervention, we examined their choices based on the current large scale pay-for-performance program. We find that if the physicians are doing exceptional in the performance measures, they are more likely to invest in promoting patients' outcomes to receive even higher payment adjustment. Moreover, if the physicians are currently below the performance threshold, they are likely to invest in order to reduce or fully avoid the negative adjustment. However, if the physicians are doing moderate well, they are less likely to enroll actively because the increase in adjusted payment is shown to be lower than the cost.

Section 9.2 Limitations

We note several limitations of the present study. First, we choose the average MA as our primary and single outcome measurement. This measurement has its weakness in reflecting the patterns of patients' medication intake behavior, which is also an important factor affecting medications' efficacy. Future work can use alternative measurements, including the longest uninterrupted period of medication adherence, to examine the effectiveness of C&S. Second, in our estimation of savings due to our intervention, we only include the savings in the direct

healthcare expenditures but not the indirect expenditures such as the reduction of work productivities and the absent workdays. This is because of the low response rate of related questions in our dataset. Also, the absence of controlling insurance coverage status of the patients is due to the same reason. More supplement data can be included in the future to form a more robust estimation. The third limitation pertains to the application and comparison of scenarios. We follow pre-established patient types and compare those scenarios within segments, while more work can be done to explore patient categories according to their reactions to our intervention and develop the comparisons across different segments. The final limitation is that even though the design of our model leverages the intelligence from well-established theories, we have not contributed to extending them. Further support from empirical data could be added to develop or extend concrete theories in future work.

In summary, as an intervention with functionalities designed based on theories and the first one which integrates both positive and negative reinforcements with reminders and social support, our work can lead to the implementation of different intervention types and their combinations to improve MA among both willing and unwilling patients with chronic diseases.

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Appendix A. Promoting Interoperability Category of MIPS

Measurement	Measurement Description
Clinical Data Registry Reporting	The MIPS eligible clinician is in active engagement to submit data to a clinical data registry.
e-Prescribing	At least one permissible prescription written by the MIPS eligible clinician is queried for a drug formulary and transmitted electronically using certified electronic health record technology (CEHRT).
Electronic Case Reporting	The MIPS eligible clinician is in active engagement with a public health agency to electronically submit case reporting of reportable conditions.
Immunization Registry Reporting	The MIPS eligible clinician is in active engagement with a public health agency to submit immunization data and receive immunization forecasts and histories from the public health immunization registry/immunization information system (IIS).
Provide Patients Electronic Access to Their Health Information	For at least one unique patient seen by the MIPS eligible clinician: (1) The patient (or the patient-authorized representative) is provided timely access to view online, download, and transmit his or her health information; and (2) The MIPS eligible clinician ensures the patient's health information is available for the patient (or patient-authorized representative) to access using any application of their choice that is configured to meet the technical specifications of the API in the MIPS eligible clinician's CEHRT.
Public Health Registry Reporting	The MIPS eligible clinician is in active engagement with a public health agency to submit data to public health registries.
Query of the Prescription Drug Monitoring Program (PDMP)	For at least one Schedule II opioid electronically prescribed using CEHRT during the performance period, the MIPS eligible clinician uses data from CEHRT to conduct a query of a Prescription Drug Monitoring Program (PDMP) for prescription drug history, except where prohibited and in accordance with applicable law.
Support Electronic Referral Loops by Receiving and Incorporating Health Information	For at least one electronic summary of care record received for patient encounters during the performance period for which a MIPS eligible clinician was the receiving party of a transition of care or referral, or for patient encounters during the performance period in which the MIPS eligible clinician has never before encountered the patient, the MIPS eligible clinician conducts clinical information reconciliation for medication, medication allergy, and current problem list.

Syndromic Surveillance Reporting	The MIPS eligible clinician is in active engagement with a public health agency to submit syndromic surveillance data from an urgent care setting.
Verify Opioid Treatment Agreement	For at least one unique patient for whom a Schedule II opioid was electronically prescribed by the MIPS eligible clinician using CEHRT during the performance period, if the total duration of the patient's Schedule II opioid prescriptions is at least 30 cumulative days within a 6-month look-back period, the MIPS eligible clinician seeks to identify the existence of a signed opioid treatment agreement and incorporates it into the patient's electronic health record using CEHRT.

Note: Table is organized based on the Promoting Interoperability category of MIPS 2020 measures

Appendix B. Included Articles in Literature Review

Article	Disease Type	Type of Study	Key Findings	Intervention Type
(Strandbygaard et al. 2010)	Asthma	Randomized controlled trail for 12 weeks. Intervention group (n = 13) received SMS reminder daily to follow the regimen of anti-asthmatic. Control group (n = 13) does not receive messages.	Adherence rate in treatment group was significantly higher than control group. But no significant differences were observed between the two groups for the clinical outcomes, such as lung function and airway responsiveness .	SMS
(Shetty et al. 2011)	Diabetes	Randomized controlled trail for 12 months. Intervention group (n = 78) received SMS once every 3 days as a reminder to strictly follow the regimen of dietary modification, physical activity, and medication schedules. Control group (n = 66) does not receive messages.	Adherence rate to diet prescription did not change significantly in either group during trail period, and post 12 months. Adherence to physical activity improved, but the change was statistically nonsignificant.	SMS
(Vervloet et al. 2012)	Diabetes	Random controlled trail for 6 months. Intervention group (n = 56). receives medications in the real time medication monitoring (RTMM) dispenser and receives SMS reminder if medication intake was not registered within the agreed time period. Control group (n = 48) receives RTMM but no SMS.	Groups did not differ significantly in the average number of days without dosing. Intervention group patients missed 5% fewer doses than patients in control group, but the difference is not significant. Patients in intervention group took significantly more doses within the agreed time period compared to control group.	SMS and electronic medication monitoring device
(Zolfaghari et al. 2012)	Diabetes	Random controlled trail for 3 months. Intervention group (n = 38) receives around 6 SMS messages per week with information on diet, exercise, medication intake, BG monitoring, and stress management. Control group (n = 39) receives telephone follow up.	There was no significant difference in diet, physical exercise, and medication intake adherence in either group.	SMS
(Khonsari et al. 2015)	Coronary heart disease	Random controlled trail for 8 weeks. Intervention group (n = 31) receives automated SMS reminders before every intake of cardiac medications. Control group (n = 31) receives usual care.	Intervention group has significantly higher medication adherence level than the control group. Risk of being low adherent among the control group was significantly greater than the intervention group.	SMS
(Park et al. 2015)	Coronary heart disease	Random controlled trail for 30 days. Two intervention groups, one receives (n = 30) SMS of educational messages only, the other one (n = 30) receives SMS of medication reminders and educational messages. Control group (n = 30) receives no SMS.	Medication self-efficacy improved over 30 trial in the intervention groups, but there was no significant difference between the two intervention groups in this improvement. Less depression and higher social support significantly predict higher medication adherence	SMS and electronic medication monitoring device.

			after controlling for other variables (e.g. age, education).	
(Park et al. 2014)	Coronary heart disease	Random controlled trail for 30 days. Two intervention groups, one receives (n = 30) SMS of educational messages only, the other one (n = 30) receives SMS of medication reminders and educational messages. Control group (n = 30) receives no SMS.	Self-reported adherence revealed no significant differences among groups but patients in intervention group had significant higher rate of correct doses taken and significant higher proportion of doses taken on time.	SMS and electronic medication monitoring device.
(Quilici et al. 2013)	Coronary heart disease	Random controlled trail for 1 month. Intervention group (n = 250) receives standard care and daily personalized SMS. Control group (n = 249) receives standard care and educational sessions highlighting the importance of adherence to recommendations.	Intervention group had significant higher medication adherence than control group.	SMS
(Brath et al. 2013)	Diabetes, hypertension	Randomized crossover study for 40 weeks. Two test groups: one group (n = 25) starts with intervention phase and then non-intervention phase, another group (n = 28) enrolls in reverse sequence.	M-health-based adherence management is feasible and well accepted by patients. It helps to increase adherence and lead to improved control of indicators including blood pressure and cholesterol concentrations.	Mobile App associates with electronic medication monitoring device
(Cook et al. 2015)	HIV	Randomized crossover study for 4 weeks. The group (n = 37) receives tailored text messages during intervention period, and receives untailored text messages during control period.	No difference on adherence rate whether messages are personalized or not.	SMS and electronic medication monitoring device
(Arora et al. 2014)	Diabetes	Random controlled trail for 6 months. Intervention group (n=64) receives 2 daily text messages. Control group (n=64) receives usual care.	Self-reported medication adherence improved significantly in the intervention group compared with a net decrease in the control group.	SMS
(Yu et al. 2015)	Chronic diseases	Pretest and posttest about the intervention of social prompting system, which combines ubiquitous sensors in the smart home and mobile social networks.	Elderly people show more stable medication intake behavior after social prompting intervention. They are willing to share their profile but not their medication loggers with others in the same community.	Mobile App enabled ubiquitous sensors and social network interactions
(McGillicuddy et al. 2015)	Hypertension	Follow up study on 3, 6, and 12 months after the complete of 3-months intervention. Intervention group (n = 9) involves in using a mobile app for self-management. Control group (n = 9) receives usual care.	Short term intervention shows significant improvement on medication adherence while it is lasting. Also, it shows significant difference between two groups at the 12-month post-intervention clinic visits.	Mobile App

(Singh and Varshney 2014)	Chronic diseases	Evaluation and comparison of different kinds of wireless interventions	Two main findings: (1) reminders can improve the pattern and average value of medication adherence but may lead to undesirable drug events; (2) context-aware reminders can improve both the pattern and average value of adherence without increasing the undesirable drug events.	SMS
(Bobrow et al. 2016)	Hypertension	Randomized controlled trail for 5 months. Two intervention groups, one group (n=457) receives information-only SMS, the other one (n=458) receives interactive SMS. Control group (n=457) receives usual care.	Two intervention groups both showed average lower blood pressure after 12 months of the beginning of trail than control group. Group received information only messages showed lower average blood pressure than group received interactive messages.	SMS
(Mertens et al. 2016a)	Coronary heart disease	Crossover study for 56 days. 24 patients use tablet app during interventional phase for 28 days and use paper diary during control phase for 28 days.	Using app to track medication adherence can induce higher medication adherence rate among elderly patients undergoing rehabilitation than using diary.	Mobile App
(Yeung et al. 2017)	Diabetes, coronary heart disease, and hypertension	Quasi-experiment with 34 patients receiving intervention and examined medication adherence after 180 days of intervention. The intervention is educational message.	Patients in intervention group have significant higher medication adherence compared with their matched controls.	Disease specific flashcards and QR-coded prescription bottles for disease and medication education
(Myoungsuk 2019)	Hypertension	Randomized controlled trail for 3 months. The study has three intervention groups and one control group. The control group (n = 31) receives usual care. One intervention group (n = 30) receives coach phone call, one intervention group (n = 32) receives educational text messages, the other one intervention group (n = 31) receives coaching phone call and text messages.	Phone-based health-coaching with text messages was effective in improving medication adherence and self-management behavior as compared to text messages only. There were also improvements in medication adherence and self-management behavior in the text messages group as compared to the control group.	SMS and health coaching call
(Chandler et al. 2019)	Hypertension	Randomized controlled trail for 9 months. The study focuses on Hispanic adults. Intervention group (n = 26) uses mobile app for self-monitoring. Control group (n = 28) receives educational text messages.	At 1, 3, 6, and 9-month points, the group uses self-monitoring mobile app has significant higher MA as well as significant lower controlled systolic blood pressure than the group which receives educational text messages.	SMS, mobile App that associated with electronic medication monitoring device
(Márquez Contreras et al. 2019)	Hypertension	Randomized controlled trail for 12 months. Treatment group (n = 77) uses a mobile app to promote health education and reminder of	At 6 and 12 month-month points, the treatment group has significant higher daily MA and	Mobile App

		appointments. Control group (n = 77) receives usual care.	significant higher percentage of controlled blood pressure patients.	
(Kamal et al. 2018)	Coronary heart disease	Randomized controlled trail for 3 months. The intervention group (n = 99) receives daily interactive voice call, daily tailored medication reminders, and weekly lifestyle modification messages. Control group (n = 98) receives usual care.	There is no significant improvement in MA has been found between intervention group and control group after 3 months intervention.	Interactive voice call, SMS
(Mohan et al. 2018)	Asthma	Randomized controlled trail. The study assesses and compares the effectiveness of reminder cards and a reminder mobile application to improve the MA of asthma patients. Both groups have 50 patients.	Both reminder card system and reminder mobile app increase patients' MA significantly. But the mobile app makes more significant difference.	Mobile App
(Schnall et al. 2018)	HIV	Randomized controlled trail for 12 weeks. Test sample is low income persons with HIV. The intervention group (n = 40) uses mobile app on improving MA and symptom management. Control group (n = 40) receives usual care.	Participants in the intervention group showed greater improvement in adherence to their antiretroviral medications as compared to those in the control group in the 12-week trial.	Mobile App, monetary incentive.
(Mayberry et al. 2019)	Diabetes	Pretest and posttest study. The study assesses the effects of out-of-home social support on type 2 diabetes patients' (n = 313) medication adherence, diabetes distress, and HbA1c.	Greater emotional closeness with out-of-home social connections was associated with a higher medication adherence and lower diabetes distress. More frequent contacts with out-of-home social supporter was associated with better HbA1c among patients with a family supporter but with worse HbA1c among patients without family supporter.	Mobile App.
(Serlachius et al. 2019)	Gout	Randomized controlled trial for 2 weeks. Treatment group (n = 36) uses a mobile app which targets on gout patients to facilitate self-management. Control group (n = 36) uses a dietary app.	Participants engaged more in using gout app for self-management, while no significant difference was found between two groups' self-care behaviors such as medication adherence within the two-weeks trial and two-weeks follow up.	Mobile App.

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Appendix C. Prescribed Medication List

Medication Class	Multum Medication Name	Whether Have Records (Y/N)
Sulfonylureas	Glipizide	Y
	Glyburide	Y
	Gliclazide	N
	Glimepiride	Y
	Tolbutamide	N
Meglitinides	Repaglinide	N
	Nateglinide	N
Biguanides	Metformin	Y
Thiazolidinediones	Rosiglitazone	N
	Pioglitazone	Y
α-Glucosidase inhibitors	Acarbose	N
	Miglitol	N
	Voglibose	N
GLP-1 analogs	Exenatide	Y
	Liraglutide	Y
	Albiglutide	N
	Dulaglutide	Y
DPP-4 inhibitors	sitagliptin	Y
	Saxagliptin	Y
	vildagliptin	N
	Linagliptin	Y
	Alogliptin	N
SGLT2 inhibitors	Dapagliflozin	Y
	Canagliflozin	Y
	Empagliflozin	N

Appendix D. Simulation Input Parameters

Parameter	R name	Value
<i>Time horizon</i>	n.t	5 y
<i>Cycle length</i>	cl	1 y
<i>Number of simulated individuals</i>	n.i	10,000 or 100,000
<i>Names of health states</i>	v.N	L1, L2, L3, L4, L5
<i>Annual cost discount rate</i>	i.c	0.018
<i>Annual transition probabilities</i>		
Level 1 to level 2 MA	p.L1L2	0.16
Level 1 to level 3 MA	p.L1L3	0.12
Level 1 to level 4 MA	p.L1L4	0.18
Level 1 to level 5 MA	p.L1L5	0.16
Level 2 to level 1 MA	p.L2L1	0.10
Level 2 to level 3 MA	p.L2L3	0.14
Level 2 to level 4 MA	p.L2L4	0.19
Level 2 to level 5 MA	p.L2L5	0.15
Level 3 to level 1 MA	p.L3L1	0.06
Level 3 to level 2 MA	p.L3L2	0.03
Level 3 to level 4 MA	p.L3L4	0.13
Level 3 to level 5 MA	p.L3L5	0.24
Level 4 to level 1 MA	p.L4L1	0.05
Level 4 to level 2 MA	p.L4L2	0.16
Level 4 to level 3 MA	p.L4L3	0.20
Level 4 to level 5 MA	p.L4L5	0.23
Level 5 to level 1 MA	p.L5L1	0.01
Level 5 to level 2 MA	p.L5L2	0.08
Level 5 to level 3 MA	p.L5L3	0.13
Level 5 to level 4 MA	p.L5L4	0.25
<i>Annual healthcare expenditures</i>		
Individuals in L1 MA	c.L1	8380
Individuals in L2 MA	c.L2	8121
Individuals in L3 MA	c.L3	7188
Individuals in L4 MA	c.L4	6786
Individuals in L5 MA	c.L5	6592
Annual increase with each additional cycle year	c.ad	180
<i>Utility of intervention</i>		
Utility for individuals in L1	u.In1	1.5
Utility for individuals in L2	u.In2	1.4
Utility for individuals in L3	u.In3	1.3
Utility for individuals in L4	u.In4	1.2
<i>Time varying extension</i>		
Intervention effect modifier at baseline	v.x	<i>Uniform (0.9,1.1)</i>
Utility decrement of individuals with every additional year	ru	0.03