Psychosocial Determinants of Statin Medication Adherence

by

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DEDICATION

To Jesus and my Parents.

Thank you for your sacrificial love.

This work is a tribute to the three of you.

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ABSTRACT

While the effectiveness and benefits of statin medications have been demonstrated in numerous studies, adherence to statin therapy is still less than optimal. Psychosocial factors are attributed to a variety of health behaviors, but the study of their impact on statin medication adherence is limited. This study aimed to (1) investigate the effect of self-regulatory mechanisms impacting patients' adherence to statin medications, (2) assess the effect of a regulatory fit intervention on the behavior, and (3) investigate how optimism may play a role in adhering to statin medications.

Adults taking a statin medication were recruited from a Midwestern University health system and were randomized into two study groups. Each study group was primed with messages that were framed either as promotion or prevention; another randomization followed into three groups for each. Patients were primed with implementation intentions framed as promotion or prevention and one group served as the control receiving no implementation intentions. The Regulatory Focus and Fit Theories were used to design the intervention. The behavior of statin medication adherence and patient psychosocial factors were assessed via a series of questions delivered in two questionnaires two weeks apart. Conditional indirect processing models were designed to test the relationships between the psychosocial factors and the behavior of statin medication adherence.

A total of 326 patients completed both surveys. Patients' prevention compared to promotion orientation positively and significantly impacted the behavior of statin medication adherence directly and indirectly via behavioral intentions and motivational intensity. At weak

patient psychosocial factors, the Fit intervention resulted in higher statin medication adherence levels compared to the non-fit or control groups. Patients' optimism levels positively impacted the behavior of statin medication adherence by significantly influencing behavioral intentions and motivational intensity, when levels of self-efficacy and outcome expectations were low or moderate.

Patient psychosocial factors present an area of opportunity to explain the behavior of medication adherence and design interventions that will motivate patients to successfully engage in medication adherence. Future studies are needed to further investigate the effect of these and other psychosocial factors in a variety of medications and populations.

Chapter 1 - **LITERATURE REVIEW AND BACKGROUND**

Introduction

Medications are one pathway by which the health of individuals and populations at large could be improved. From the Hippocrates' times to the invention of penicillin to the discovery of DNA to today - the development and use of new medicines to ameliorate and/or cure various diseases is promising. Along with these positive promises come many challenges.

One challenge is the complex biological system of the body unique to each individual. Another challenge is the complex psychosocial system, again unique for each individual. A person's biological makeup interacting with the psychosocial environment subsequently influences the decisions and lifestyle a person engages in on a daily basis.

In the pursuit of health, many individuals affected by either an acute or chronic condition will choose to take one or more medications during their lifetime. This decision may or may not be coupled with choosing to engage in other behaviors that could improve one's health; a decision that is impacted again by a multitude of factors. Although many medications are being prescribed by health care providers to their patients, a decline in taking the prescribed medication as recommended is seen over time. This is called medication non-adherence, and this behavior serves as the focus of this study.

In the next sections of this chapter the focus is on unwrapping the challenge of medication adherence. Specifically, medication adherence is being investigated in cardiovascular

patients who have been prescribed statin medications. This chapter begins with providing an overview of medication adherence followed by discussing the issue of statin medication adherence among cardiovascular patients. Next, it examines contributing factors and interventions focused on improving statin medication adherence followed by examining theories used to improve other health behaviors. Gaps and opportunities to improve medication adherence are identified and a theoretical framework for this study is created with the goal to potentially bridge the existing gaps. This chapter ends with an outline of the aims and hypotheses for the study.

Medication Adherence

The World Health Organization (WHO) reports that medication adherence in the developed world among patients with chronic diseases averages to 50%.[1] Investing millions of dollars in developing new drugs will help only if patients adhere to their medications. As C. Everett Koop simply stated "drugs don't work in patients who don't take them".[2] This section will present how medication adherence is defined, why it is important, how it is measured, and describe the challenges associated with the behavior of adhering to medications.

Medication adherence is defined as the extent to which a patient takes a prescribed medication according to the prescribed schedule by their health care provider.[2-5] The terms adherence and compliance are often used interchangeably. Some studies differentiate adherence as primary or secondary.[1] Primary adherence refers to the behavior of filling new prescription medications while secondary adherence refers to the behavior of taking the medication as prescribed once the prescription has already been filled. The term medication persistance refers to whether or not a patient stays on the prescribed therapy. Both, adherence and persistence to a

prescribed treatment, are complex behavioral processes influenced by the patient, providers, and their internal and external environments.

Understanding medication adherence accross conditions in various populations is important for several reasons. One, there are negative conequences associated with medication non-adherence. Examples of consequences of medication non-adherence are: worsening of the disease, poor clinical outcomes, poor quality of health, high morbidity and mortality rates, and a heavy economic burden on the health care system.[1,2,4,6-8] Specifically for the US health care system, non-adherence translates to a $290 billion of annual health care expenditures.[6] It is also known that low adherence to placebo is linked to increased risk of death.[8] Therefore, adherence to medications leads to improved patient outcomes via the effect of the medications or via the overall healthy adherer effect. This leads to the second reason why medication adherence is important. The positive outcomes of improved medication adherence are better health and quality of life for the patients, lower mortality rates across various conditions, and reduced health care costs. Hence, improving medication adherence across conditions and in various populations is a worthwhile goal.

The need to improve medication adherence is clear. The strategies used to measure the behavior of medication adherence vary. There are more than 12 types of tools to measure medication adherence, ranging from specific statistical tools used in secondary analyses to pill counts to various questionnaires/scales and direct patient interviews.[1]The tool of choice used to measure medication adherence for each study varies depending on how medication adherence is defined and the scope of the project.

Measures of medication adherence, can be simplified in two categories: subjective and objetive measures.[1] Subjective measures involve evaluation of medication-taking behavior either at the patient or provider level usually in the form of self-report. Objective measures are biochemical measures of the drug in the body, pill counts, electronic monitoring, and secondary database analyses. Other studies clasify the measures as either direct or indirect; biochemical measures representing the direct measures and the self-report measures representing the indirect ones.[1,3,5] Strenghts and limitations are found in each measure. For example, the direct measures of medication adherence are usually costly with the potential bias of the white coat adherence and not feasible to be performed in large numbers. The indirect measures of medication adherence present recall and social desirability biases and in some cases communication challenges between the patient and the health care providers. Because perfect adherence where patients adhere to the treatment regimen 100% of the time is difficult and unrealistic, adherence to medications 80% of the prescribed doses or higher is often used as a benchmark when measuring medication adherence.[5,8] However, the best strategy to measure medication adherence is to use a combination of methods, as not one tool is considered the gold standard.

Among the multitude of medication adherence measures, some are utilized more commonly than others. Andrade et al., summarized in a review all the current known methods used to assess medication adherence and persistence. Among the multitude of choices of medication adherence measurements, the most common measure reported in this study is the medication possession ratio (MPR).[3] MPR is a tool used to investigate medication adherence in secondary database analyses and can be defined generally in two ways. It may be defined as the proportion of days supply obtained during a specified time period or over a period of refill intervals.[1,3]

In terms of questionnaires, with a 93% sensitivity and 53% specificity, the eight-item Morisky Medication Adherence Scale (MMAS-8) seems to be the most accepted self-report measure of medication adherence to medications. Its shorter version, the four-item Morisky Medication Adherence Scale (MMAS-4), is the most widely used scale for research as it is quick to administer and score.[1]

Another valid and reliable measure of medication adherence is the single-item visual analogue rating scale (VAS). VAS asks individuals to estimate along a continuum from 0 to 100% the percentage of medication dosages taken as prescribed during a specified period of time. It demonstrated similar adherence estimates to unannounced pill counts, electronic medication monitoring, and self-reported recall.[9,10] This tool may serve best when medication adherence is investigated and measured among other factors.

Challenges to ideal medication adherence involve medication, patient, provider, and health system factors.[4] Medication factors include a complex regimen, side effects, and high out-of-pocket costs. Patient factors may include a patient's demographic characteristics such as race, marital status, ethnicity, socio-economic status; a patient's health literacy; psychological and/or social challenges; perceived benefit of the medication; beliefs about the medication; patient's motivation; and others. Provider factors may include poor communication, empathy, and compassion strategies offered to the patient. And lastly, health system factors may include insurance coverage and access to a health care facility.

Addressing these challenges at all points of care: medication, patient, provider, and health system is important towards the improvement of medication adherence. Suggested by the WHO, medication adherence is based on three main pillars: patient information, motivation, and

behavioral skills, out of which motivation is considered to be most important.[4] Patient's motivation to engage in a behavior along with patient-provider communication and relationship are considered by other researchers, as well, as two key factors to consider when improving the quality of medication use.[2,11]

Therefore, this study focuses on investigating a variety of patient-related factors, including motivation, affecting medication adherence. Specifically, the study focuses on statin medication adherence. The next section describes statin medications and their aid in cardiovascular health.

Cardiovascular Health

Since 1900, cardiovascular diseases (CVDs) have posed a public health challenge every year since except for 1918 and have accounted for more deaths in the United States than any other cause.[5] A total of 83 million American adults are affected by CVDs.[12] The total annual costs for CVDs and stroke are reported to be $316.6 billion, out of which $193.1 billion represent direct costs and $123.5 billion represent indirect costs.[13] In 2010 the American Heart Association (AHA) stated its goal to improve the cardiovascular health of Americans by reducing deaths from cardiovascular diseases and strokes by 20% by 2020.[13,14] To achieve this goal, various efforts are needed for cardiovascular health promotion and disease prevention, spanning from patient behaviors, to basic clinical research, to public policy programs.

For an individual to achieve ideal cardiovascular health, one must engage in ideal health behaviors and attain ideal health factors.[13,14] The considered ideal health behaviors are: nonsmoking, a body mass index of <25kg/m2, physical activity at goal levels, and a diet consistent with guideline recommendations. The ideal health factors to be attained are: total

cholesterol levels of <200 mg/dL, blood pressure levels of <120/80 mmHg, and fasting glucose of <100 mg/Dl in the absence of drug treatment.[13,14] If any of the health factors are less than optimal, health care providers recommend an appropriate treatment guideline tailored for each patient. For example, if one's cholesterol levels are too high, and ideally after all other tried health behaviors have failed, a patient is prescribed a cholesterol lowering medication.

Lowering the cholesterol levels has been shown to reduce the incidence of Coronary Heart Disease (CHD).[5] CHD is one type of Cardiovascular Disease (CVD), and it is described as atherosclerotic disease of the arteries. It is the leading cause of heart disease caused by plaque buildup in the arteries that supply blood to the heart. It is also named as coronary artery disease (CAD).[5] Therefore, using various strategies to lower cholesterol levels and reduce the incidence of CHD via various health behaviors, including statin medications, is essential.

Statin Medication Adherence

To achieve cardiovascular health, one of the health behaviors individuals engage in is taking cholesterol lowering medications with the focus on reaching one of the ideal health factors of total cholesterol levels of <200 mg/dL. Cholesterol lowering medications have proven to prevent and reverse the progression of high cholesterol, known as hypercholesterolemia.[15] Statins are one class of cholesterol lowering medications and are currently the most commonly prescribed medications used to manage cholesterol levels.

Statins play a critical role in the treatment (secondary) and prevention (primary) of heart disease and reduction of cardiovascular mortality.[5,16,18] They have been shown to effectively lower cholesterol levels, have been proven to reduce cardiovascular mortality, and to substantially reduce plaque in coronary arteries. Although considered safe and effective, statin

non-adherence is documented in numerous studies.[16-18] Specifically, taking statin medications as prescribed is known to be as low as 25% for primary prevention, 36% for coronary heart disease and 40% for acute coronary syndrome. The current statin medication adherence of 25-40% is suboptimal in view of the general targeted medication adherence goal of 80% or greater. Therefore, finding ways to better understand and increase statin medication adherence is of vital importance to decreasing cardiovascular events and disease.

Contributing Factors

There are four main categories of factors contributing to statin medication adherence: health system factors, health care provider, patient, and medication factors. Interactions between these factors influence patients' adherence to statin therapy. Variability exists among research when identifying predictors for statin non-adherence in each of these categories. This variability may be due to various designs of research studies, different patient population, and diverse methodologies used. In the next four sub-sections, factors affecting statin medication adherence in each category are examined utilizing synthetized information from review and individual studies.

Health System factors. Health system factors most often include the feasibility of access to care and costs.[5] Although the cost of statin medications has been made more patient friendly over the years, studies still report that unfavorable co-payment structures to the patient and high out-of-pocket costs to be associated with lower adherence to statin therapy.[16,18,19] Interestingly, increased lipid testing has been associated with better statin medication adherence.[16] This may be due to patient's being more educated and knowledgeable of potential risks of high cholesterol thus leading to better adherence.

Health care provider factors. Within the health care system, health care providers play an essential role contributing to statin medication adherence. The specialty of the health care provider influences patients' behavior of adherence to statin therapy. It is found that certain types of physicians: cardiologist, primary care physician, and US medical graduate are associated with higher statin medication adherence.[20] This may be due to the degree of trust the patient has in their health care provider and the strength of the patient-physician relationship developed. This trust has the potential to be strengthened at the patient and provider level. Patient reluctance to freely express his/her thoughts in regards to statin therapy during the patient-physician interaction may be due to views of the physician as the authority figure.[18] Empowering patients with confidence in shared decision making in regards to their therapy may improve the patient-physician relationship. This of importance as Chee et al. specifically reported that a poor physician-patient relationship was found to negatively affect adherence to statin therapy.[21] This poor patient-physician relationship was expressed via patient dissatisfaction with the physician's explanation in regards to disease, therapy, and potential adverse events and limited amount of time spent with the patient during consultation.[18,21] Patient dissatisfaction with the physician's explanation may be a perceived lack of effective communication. This is noteworthy as healthcare professionals have an opportunity to improve and tailor communication strategies with their patients according to their needs in regards to their behavior of taking statin medications.

Patient factors. There are a multitude of patient factors that may influence the behavior of statin medication adherence, either in a positive or negative way. Specifically, for statin medication adherence, the most common predictors are: age, gender, race, income, health-literacy, comorbidities, perception/beliefs, and lifestyle factors.[5,16,18,20-23]

Older patients of >70 years or greater and youngest patients of <50 years are found to have lower adherence to statin therapy compared to patients with ages between 50 to 69 years of age.[16,20,21] Women are more likely to be more non-adherent to statin therapy than men.[16,20,22,24] Minorities are less likely to be adherent to statins compared to Caucasians.[16,20,22,24] Higher income is associated with higher statin medication adherence[16,20,21] while low health-literacy is associated with lower statin adherence.[18,21] Lower educational attainment and high poverty levels are associated with statin non-adherence.[24]

When it comes to comorbidities, there is a mix of findings on how they affect statin adherence.[16,21] For example, patients with a history of cardiovascular disease and hypertension are more likely to be adherent to statin therapy. Conversely, patients with depression are found to be less adherent to statin therapy. And patients who have a history of diabetes present conflicting results when it comes to statin medication adherence; some studies report better adherence while others worse.[16,21] It is also known, that first time statin users are less likely to be adherent compared to experienced statin users.[16]

Lack of perceived benefits that statin therapy offers, low perceived need for statin therapy, perceived side-effects, overestimation of the effectiveness of the dietary change, previous negative experiences with pharmacological treatments, psychological challenges, and cognitive impairment - all were found to be a hindrance to adherence to statin therapy.[18,21] For example, some concerns expressed by patients about statins were being uncertain about benefits or about statin importance, being inconvenienced by taking the a medication, being restricted to not drinking grapefruit juice, while other concerns were related to information of statin adverse events patients likely gathered from the internet.[18] Based on the Theory of Planned Behavior, side-effects associated with statins are one of the perceived barriers to statin therapy, with

approximately 20% of patients discontinuing therapy due to myalgia.[21] Other perceived barriers are costs of statin - increase in copayment for statin results in a 7% decrease in adherence, dissatisfaction with relationship between patient and physician – due to poor treatment explanation and short consultations, and reliance on diet control alone – many patients have the perception that it is sufficient for managing dyslipidemia.[21]

Additionally, lifestyle factors were found to influence statin medication adherence.[23] Specifically, being overweight or obese and former smoking were found to be associated with better statin medication adherence, while risky drinking behaviors and a cluster of lifestyle risk factors were found to be associated with statin nonadherence. The cluster of lifestyle risk factors may include a high BMI, low physical activity, high alcohol consumption, and current smoking.

Medication factors. In regards to regiment complexity, a pattern of high number of medications that are non-cardiovascular is linked to low statin adherence while a high number of cardiovascular medications is associated with statin adherence.[16] Switching to generic statins lead to improved adherence to statin therapy.[19] Statin medication adherence over time could drop significantly from 50% at 6 months to 30-40% at 12 months and cost for statin therapy may be a barrier to optimal adherence.[16,25-27]

To conclude, all factors affecting statin medication adherence are important. Addressing all factors for all patients is neither feasible nor applicable, as some factors are relevant to some patients and not for others. Therefore, finding which factors influence statin medication adherence for a patient or a group of patients may be best in regards to finding interventions and solutions to helping patients improve their adherence to statin therapy.

For this study, we chose to focus on patient-related factors. Specifically, we chose to investigate how patients' psychosocial factors such as patients' motivation, intentions, optimism, self-efficacy beliefs, outcome expectations affect the behavior of statin medication adherence. Motivation is considered by WHO as a main pillars of medication adherence WHO.[4] Hence, understanding patients' motivational factors to engage in the behavior of statin medication adherence is important as it will bring insights on how to improve the patient-provider communication in future studies. Therefore, the findings of this study have the potential to help the patient, provider, and by improving outcomes the health care system as a whole.

Interventions

Interventions to improve statin medication adherence have been tested in various studies.[27-35] Methods and result varied. Table 1.1 provides an overview of these studies and this section highlights findings as well as suggestions to moving forward.

The studies reviewed tested interventions aimed at improving statin medication adherence focusing either on the entire class of statins, a single statin, and in some cases a combination therapy consisting of a statin and other medications. The duration of interventions and follow-up ranged from 4 months to 2 years. The majority of studies used usual care as the control group, with one study using data from a national pharmacy claims database to assess statin adherence as the control group. The most common measure for statin medication adherence in these studies was MPR; other measures included pill and packet counts, refill records, MEMS records, and self-report questionnaires.

Interventions included patient-pharmacist counseling, patient-physician counseling, telephone counseling and reminders, and mailing of educational materials. The majority of

interventions, except two, resulted in better adherence to statin therapy.[27-35] The ones resulting in better statin therapy all involved counseling with a health care professional, either a pharmacist or physician, in person or via the telephone. One intervention that resulted in no significant increase in statin medication adherence consisted of mailing video educational materials.[34] Furthermore, one study that included both telephone and postal reminders, in addition to physician counseling, resulted only in significant association between statin medication adherence and adopting other coronary-risk reduction health behaviors.[32]

Table 1-1. Interventions to Improve Statin Medication Adherence

Author, Year	Study Population	Length	Intervention	Control	Effect on Adherence	Limitations
Taitel, 2012	Patients new to statin therapy in the Midwest (N=1102)	2 months and followed for 12 months	Two face-to-face patient counseling sessions with a pharmacist	Standard of care (no face-to-face pharmacist consultation)	Greater statin adherence and persistence	Potential uncontrolled bias – patients self-selected the group
Faulkner, 2000	Post cardiac surgery patients with high LDL (N=30)	12 weeks 2 year follow-up	Pharmacist telephoned patients every week	Usual care	Adherence (compliance) and LDL profile significantly better	Hawthorne effect
Stuurman-Bieze, 2013	Patients initiating statin therapy at 9 Dutch pharmacies (N=1002)	1 year	Monitoring adherence and counseling for nonadherent patients	Usual care	Better adherence and less discontinuation of therapy	Generalizability
Casula, 2016	Physicians treating statin users in Lombardy, Italy (N=705)	1 year	Information about statin use and adherence sent to physicians	Pre and post information data was analyzed	Adherence and persistence increased in post-i significantly compared to pre-i	Lack of control group
Eussen, 2010	New statin users in Netherlands (N=899)	1 year	Five pharmacist counseling sessions	Usual care	Better adherence at 6months	
Guthrie, 2001	Patients at high risk for a first MI identified by physicians (N=13100)	6 months	Postal and telephone reminders, and physician counseling	Usual care	Intervention did not result in better drug compliance (adherence). Statin medication adherence was significantly associated with adopting other behaviors.	Self-reported adherence, recall and social desirability bias

Casebeer, 2009	Patients new to statin therapy (N=355)	120 days	Brief in-office physician counseling and mailings	Data from national pharmacy claims to assess adherence to statin was used as comparison	Increased statin adherence	Short study period, recall and social desirability bias, no direct control group
Powell, 1995	Patients from pharmacy claim taking simvastatin and 3 other medications (N=4256)	6 months	Mailed videotape programs	Usual care	No significant increase and difference in adherence	No intervention follow-up, recall bias
Vrijens, 2006	Patients on atorvastatin >3 months (N=392)	12 months	Pharmacist counseling to patient and educational reminders	Usual care	Increased adherence to atorvastatin therapy	Selection bias, generalizability

*adherence and compliance terms are used interchangeable in studies

These studies suggest that patient contact by a health-care professional in regards to statin therapy is essential in improving adherence. Pharmacists serving as health-care professionals with direct contact with the patients are prime candidates for these interventions and have proven to serve effectively in this cause. Future studies are needed to investigate best approaches to counseling tailored to patients' needs and motivation to improve the behavior of statin medication adherence. This study focuses on investigating patient motivational factors that affect statin adherence. In the next section theories addressing patient-related factors and various health behaviors are discussed.

Theories and Concepts Addressing Patient Psychosocial Factors and Health Behaviors

The focus of this study is to understand how patient related factors affect the behavior of statin medication adherence. Specifically, patient-related factors related to motivation, such as a patient's regulatory orientation, intentions, self-efficacy, outcome expectations, and optimism were investigated in this study. Some of these factors have been studied in the context of medication adherence while others have been extensively studied and applied in other health behaviors. Next, theories and concepts related to these patient factors are described followed by their importance in studying the behavior of statin medication adherence.

Regulatory Focus and Fit Theories

Regulatory Focus Theory. The first patient related factor described is patient's regulatory focus, also called regulatory orientation. The concept of regulatory focus originates from the regulatory focus theory proposing that all goal-directed behaviors are regulated by two independent motivational systems, namely promotion (self-regulation to strong ideals) and prevention (self-regulation to strong oughts).[36-39] Higgins generated the concept while exploring how and why individuals are able to manage themselves in pursuit of a goal. More specifically,

he was interested to better understand how a person's orientation affects perceptions, judgments, decisions, and behavior.

The regulatory focus theory proposes that the promotion and prevention self-regulatory motivational systems operate differently according to specific human need.[36-39] The human promotion motivational system operates to meet the survival need of nurturance (nourishment) and is characterized by ideals including hopes, wishes, and aspirations as maximal goals to be reached. Ideal self-regulation then is concerned with the presence or absence of positive outcomes and involves promotion-focus concerns, such as advancement, aspirations, and accomplishments. The human prevention motivational system operates to meet the survival need of obtaining security and is characterized by oughts including duties, obligations, and responsibilities as minimal goals to be met. Ought self-regulation is concerned with the presence or absence of negative outcomes and involves prevention-focus concerns, such as protection, safety, and responsibilities. Additionally, situations involving gain-nongain induce a promotion focus while situations with loss-nonloss induce a prevention focus.[36] Higgins explains gain and loss originating from the child-caretaker relationship. For example, nongain would be withdrawing love from a child by the caretaker to communicate an undesired state of the child's actions, such as lack of advancement or accomplishment.[40] The prospect theory suggests that individuals respond differently to messages that are framed as gain or loss.[41] For example, in the context of smoking and dental health, gain-framed messages resulted in increased interest in plaque-fighting mouth rinse and in increased abstinence from smoking compared to loss-framed messages.[41,42] The regulatory focus theory consists of message framing as well, with promotion focus characterized by maximizing gains and with prevention focus characterized by minimizing losses.

Higgins suggests via the regulatory focus theory that the two systems, promotion and prevention, have distinct strategic means of regulating behavior towards desired end-states or end-goals.[36,37,39] Promotion focused individuals use approach-eagerness strategic means and prevention focused individuals use an avoidance-vigilant strategic means to achieve a goal. Approach strategic means are described by strategically approaching matches to desired end-states and ensuring hits and against errors of omission. Avoidance strategic means are described by strategically avoiding mis-matches to desired end-states, ensuring correct rejections and against errors of commission.

A person's regulatory focus may be chronic or situational and it can be induced.[36,38] Individuals with a chronic or situationally induced regulatory focus are inclined to utilize that approach's (promotion or prevention) strategic means in order to achieve a goal. The chronic regulatory focus is measured with the Regulatory Focus Questionnaire (RFQ) and is associated with styles of child-caretaker interaction and socialization processes.[43] The chronic orientations are not bipolar constructs; a patient may be high or low in both.[39] The situational regulatory focus is experimentally manipulated using a priming technique. The priming technique involves framing worded statements as either promotion or prevention. For example, priming for promotion focus would include ideals, such as dreams, hopes and aspirations a patient may have in regards to their goal of cardiovascular health and priming for prevention focus would include oughts, such as duties, obligations, and responsibilities a patient may have in regards to their goal of cardiovascular health.

In the context of the behavior of medication adherence, a patient that is at high risk for cardiovascular disease and has a promotion focus will have a goal to have great cardiovascular health and will engage in nutrition, exercise, and medication behaviors including taking their

statin medication as indicated by their health care provider that will lead to reducing risks and achieving the goal of cardiovascular health. A patient with a prevention focus with the same goal will be careful to fulfill and know the required information about cardiovascular disease and avoid anything that will hinder achieving this goal, including not taking their statin medication as directed by the health care provider. Taking the statin medication as directed and engaging in additional behaviors leading to cardiovascular health represent promotion orientation while fulfilling requirements and avoiding any potential hindrances represent prevention orientation. The promotion-prevention orientations co-exist within every person and when activated via priming tend to alter perception and behavior.[43]

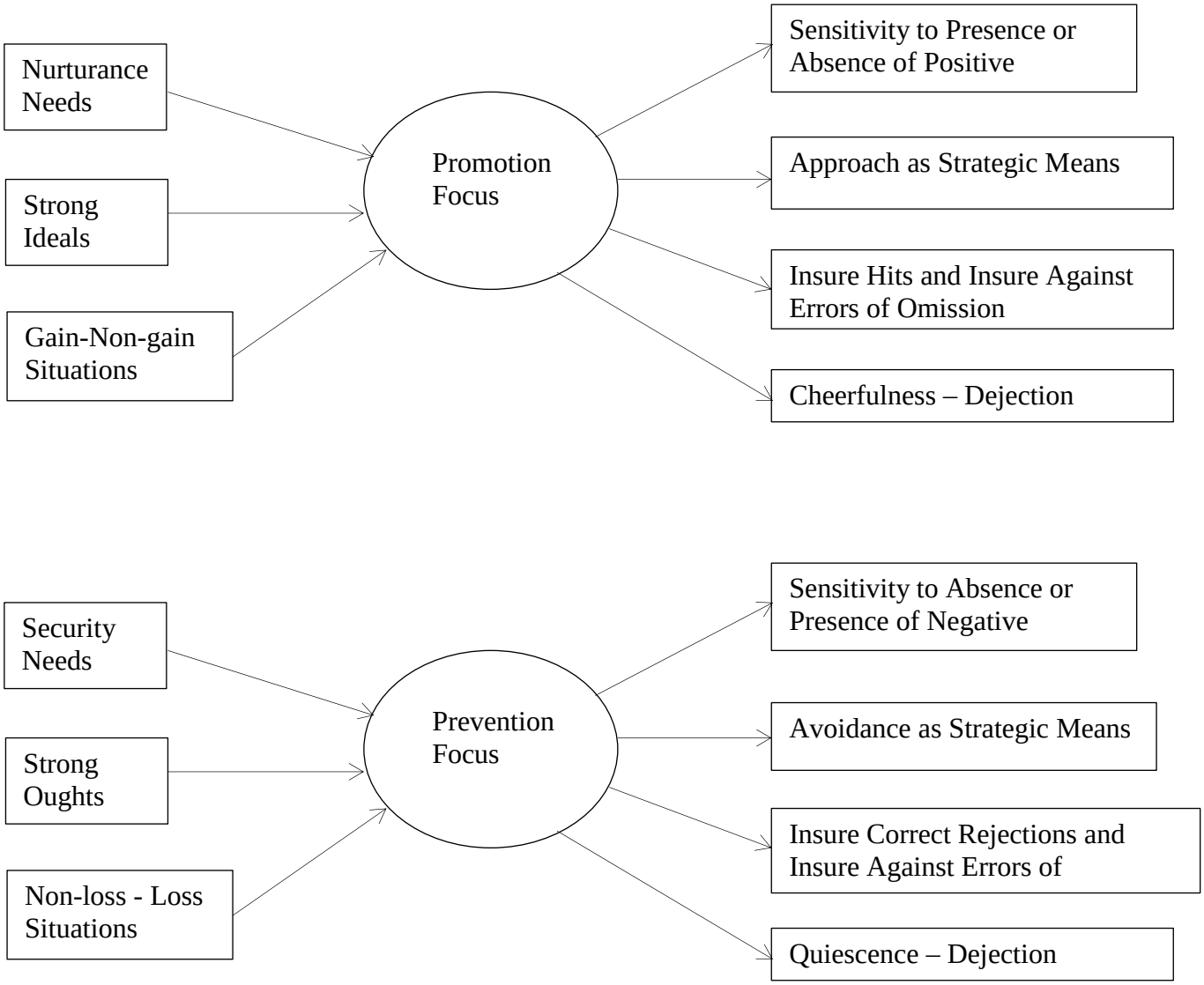
The Regulatory Focus Questionnaire (RFQ) that measures chronic orientation was developed by Higgins. It consists of eleven items, six of which are promotion scale items and five of which are prevention scale items. It exhibits good internal reliability (alpha=0.73 for promotion and 0.80 for prevention) and excellent fit (0.95). There was no correlation found between the promotion and prevention scales.[38]

Studies on regulatory focus investigated the effect of orientation on decision-making.[36,37,39] Specifically, the value derived from various outcomes and from fit was determined. For the value from outcomes studies, findings indicate that decision makers in a promotion focus treat promotion relevant outcome dimensions, such as emotional appraisal and object evaluation, as more important than prevention relevant outcome dimensions, and vice-versa. For example, one study demonstrated that promotion individuals value the dimensions of luxury and innovation of a car product while prevention individuals value the dimensions of protection and reliability of the same car product.[39] The value of fit studies focus on how the match between individual's orientations and strategic means affect emotions or object

evaluation. Findings indicate that a match, defined as fit, results in better feelings about a choice or decision and higher value assigned to a product.[36,39]

This study focuses on how regulatory focus as a motivational system drives the behavior of adhering to one's prescribed medication. Specifically, we are interested whether promotion or prevention will affect statin medication adherence similarly or different. Understanding under which regulatory orientation system a patient operates will equip us to tailor medication adherence messages and communication according to each patient's orientation in future research. The next section examines the Regulatory Fit Theory to explain how a match between a person's orientation towards a goal and the means used to achieve the goal affect the end results.

Figure 1-1. Promotion and Prevention Focus[36]



Regulatory Fit Theory. The regulatory fit principle encompasses and goes beyond the regulatory focus theory proposing that motivational strength to obtain a goal is enhanced when the strategy used sustains the current regulatory orientation.[37,44,45] In other words, a match between a person's orientation (promotion/prevention) towards a goal and the means (approach-eagerness/avoidance-vigilance) that a person uses to achieve the goal produces a state of regulatory fit, which in turn creates a feeling of rightness. This feeling of rightness increases the person's engagement in the task necessary to accomplish the goal. Regulatory fit operates independently of one's expectancies and value assigned to a goal and leads to not only higher motivation in goal pursuit, but also to feeling better and more alert about a decision, and to enjoying goal pursuit more.[37]

To demonstrate the applicability of the regulatory fit theory, an example of students working towards the goal of attaining an A in a course is considered.[37] All students in the course if achieve the goal of receiving an A will have outcome benefits; however the means to achieve the goal may be different for different students. Some students in the course may have a promotion orientation and see the goal of obtaining the A as an accomplishment, while others may have a prevention orientation and see the goal of obtaining the A as a responsibility. Hence, the promotion oriented students may read material beyond the assigned readings as the means to attain the A and the prevention students may be careful to fulfill all course requirements as the means to attain the A. The fit here exists between students' regulatory orientations and goal pursuit means. Reading extra material fits an accomplishment orientation. Fulfilling course requirements fits a responsibility orientation. Independent of the value from the worth of obtaining the A in the course, students will experience a regulatory fit when they use goal pursuit means that fit their regulatory orientation. This regulatory fit increases the value of what they are

doing and increases their motivation to accomplish the goal. Higgins reports that goal performance is best when a fit is experienced between the means and the chronic or induced regulatory orientation.[37]

Considering goals in the context of improving health behaviors, health care providers can be trained via different strategies to enhance communication. For example, considering the health behavior of interest in this study, medication adherence, pharmacists can frame health messages as promotion or prevention according to each patient's regulatory orientation, and/or prime a patient's regulatory orientation to match the strategic means to achieve better medication adherence and ultimately better health outcomes. By tailoring communication to create regulatory fit, patients' motivation to engage in pursuits towards accomplishing the goal will be increased. Testing and applying the regulatory fit theory in communication strategies utilized by health care providers when interacting with their patients to improve medication adherence is a future research goal to be pursued. Understanding how to tailor communication is an important first step. Thus, the ramifications of this study are to better understand and enhance the effectiveness of tailored messages targeting medication adherence using the regulatory fit theory. The next section will examine how the regulatory fit theory has been studied in the context of tailored messages and human behaviors thus far.

Regulatory Fit in Human Behaviors

Regulatory focus theory and the regulatory fit principle can be used to increase the effectiveness of health messages and health behavior. The behaviors studied in the context of the regulatory fit theory include physical activity, fruit and vegetable consumption, writing,

smoking, unhealthy snacking habits, supplementing with omega-3 products, and cancer detection.[44,46-50]

Findings indicate that tailored messages that fit individuals' regulatory focus lead to greater physical activity participation and more positive feelings than non-fit messages.[46] Regulatory focus studies on fruit and vegetable consumption show that participants who experienced fit (promotion/benefits and prevention/costs) ate about 20% more fruits and vegetables compared to participants experiencing non-fit (promotion/costs and prevention/benefits participants).[44] Furthermore, tailored messages targeting increase of fruit and vegetable consumption at the 4th month follow-up were more efficacious when congruent with participants' regulatory focus.[47] Similarly, promotion/eagerness and prevention/vigilance participants are found to be 50% more likely to turn in their written reports during their leisure time than promotion/vigilance and prevention/eagerness participants.[44] Regulatory fit increases an individual's motivational intensity to engage in changing strong unhealthy snacking habits.[48] Prevention regulatory fit with worry leads to engagement in cancer detecting behaviors while a promotion regulatory fit leads to use of stimulants in order to achieve academic goals.[50] When supplementing with omega-3 products, findings indicate that prevention outcome expectations are strengthened at high levels of self-efficacy.[49]

Examples of a promotion and prevention-focused messages in the context of physical activity are:" Scientists say to accumulate physical activity throughout the day to stay healthy or improve your health" and" Scientists say failing to accumulate enough physical activity throughout the day can lead to poor health".[46] Examples of promotion and prevention-focused messages in the context of fruits and vegetable consumption are: "Optimize your health: eat 5 to 9 fruits and vegetables every day; add chopped green peppers, mushrooms, and onions to your

scrambled eggs or omelet – they add fiber, which promotes optimal colon function; so, achieve the 5 to 9 goal every day to look and feel your best; promote your health: eat more fruits and vegetables today" and "Protect your health: eat 5 to 9 fruits and vegetables every day; add chopped green peppers, mushrooms, and onions to your scrambled eggs or omelet – they add fiber, which helps to prevent colon cancer; meet the 5 to 9 guideline every day to protect your health; prevent disease: eat more fruits and vegetables today".[47]

Next, in order to better understand the methodology used in these studies, a detailed description is provided for each study investigating regulatory focus/fit in the context of the specific behavior studied.

Specific Example of Behaviors Examined via Regulatory Fit: Turning in Reports and Eating more Fruits and Vegetables. Spiegel et al. examined via two experiments how regulatory fit enhances motivational strength during goal pursuit.[44] The first experiment examined whether students with a chronic promotion or prevention focus who used strategic means that fit their regulatory state would be more likely than those who used non-fitting strategic means to write and turn in a report. The second experiment examined whether students who read a promotion or a prevention framed message that encouraged eating more fruits and vegetables would eat more over the course of a week if they imagined the benefits they might get by complying or the costs they might incur via non-compliance. These two tasks are common in life and considered to have a practical value in addition to the theoretical significance.

For the first experiment, a total of 71 Columbia undergraduate students participated. They received $5 for the first part completing a Self-Guide Strength measuring people's ideal (promotion) and ought (prevention) selves and $7 when turning the report of minimum 100

words. The ‘ideal’ self was defined as the type of person they ideally would like to be. The ‘ought’ self was defined as the type of person they believed they ought to be. Participants were asked to list in a random order, 3 ideals and 3 oughts. They were asked to rate from 1-4 (slightly, moderately, a great deal, extremely) the extent to which they ideally like for their ideals or the extent they ought for their oughts. They were also asked to rate the extent to which they actually possessed the attribute on the same scale. A total ideal strength score and ought strength score were calculated by summing the ideal/ought attribute and the extent reaction times.

The strategic means in this experiment refer to implementation intentions. Participants were asked to imagine certain steps that they might take in writing the report: when, where, and how participants planned to write. For the when/eagerness manipulation, participants were asked to imagine a good convenient time when they would be able to write their reports while for the when/vigilance manipulations, participants were asked to imagine times that were bad or inconvenient for writing their reports, such as when they were busy, so that they could avoid those times. For the where/eagerness manipulation, participants were asked to imagine a comfortable, quiet place where they might write their reports while for the where/vigilance manipulation, participants were asked to imagine places that were uncomfortable or with lots of distractions so that these places could be avoided when writing their reports. For the how/eagerness manipulation, participants were asked to imagine capturing as many details as they could and creating their reports as vivid and interesting as possible while the how/vigilance manipulation, participants were asked to imagine not forgetting to leave any details out and being very careful not to make their reports bland or boring.

A 3-way chi-square with dominant regulatory focus (promotion/prevention), strategic means (eagerness/vigilance) and whether participants turned in their report (yes/no) revealed that

74% of participants who experienced a fit turned in their reports compared to 54% in promotion/vigilance and 46% in prevention/eagerness groups ($p<0.05$). This result indicates that the presence of regulatory fit between students' chronic regulatory orientation and the type of plans they mentally stimulated was found to have a significant impact on the likelihood that they would complete the goal of writing and turning in a report. No main effects were found between regulatory focus or implementation intentions on participants turning in their reports; only the fit between regulatory focus and implementation intentions exerted an influence on students' behavior.

The second experiment extended the test by manipulating participants' regulatory focus instead of measuring the chronic state. Additionally, rather than varying the plans of mental stimulations, participants were asked to imagine possible outcomes (the benefits of compliance or costs of non-compliance). The explanation of this design is based on the idea that a recipient's behavioral response to a health message may be a function of both the strategic framing of the outcomes to be imagined and the pre-existing psychological perception of the health issue. Specifically, this experiment investigated how the fit between regulatory focus and strategic outcome framing influences the effectiveness of health messages in changing the behavior of eating more fruits and vegetables.

Participants consisted of 150 Columbia undergraduate students. The experiment consisted of two sessions. In session 1, participants were given a booklet that had a cover letter, the food habits questionnaire, a health message, and an item measuring their confidence level "if you wanted to change your current diet by including more fruits and vegetables, how confident are you that you could make such a change?" (1=not at all to 7=extremely). This last measure was included as a way to rule out the possibility that the effect of regulatory fit on the behavior is

mediated by students' beliefs. Session 2 consisted of students completing a daily nutrition log booklet for 7 days.

Regulatory focus was manipulated by imagining either the benefit or the cost of eating or not eating the right amounts of fruits and vegetables consumed daily. Examples of promotion regulatory focus framing: 'If you eat the right amount of fruits and vegetables daily, you can experience an overall sense of feeling good about yourself' and "If you eat the right amount of fruits and vegetables, you can actively help keep yourself safe from illness and obtain overall good health". Examples of prevention regulatory focus framing: 'If you do not eat the right amount of fruits and vegetables, you cannot experience an overall sense of feeling good about yourself' and "If you do not eat the right amount of fruits and vegetables, you cannot actively help keep yourself safe from illness and facilitate overall good health". The health message was 150 words in length and was either promotion or prevention focused. The promotion message emphasized accomplishments while the prevention one emphasized safety. The health message outcome framings were expected to interact with regulatory focus to predict behavioral change.

Results of a 2x2 ANOVA with regulatory focus and outcome framing indicated no significant effects on participants' confidence that they could change their eating habits. Therefore, confidence was not a mediator of the fit effects on fruits and vegetable consumption. The main findings of the second session were that participants with regulatory fit between their regulatory focus and outcome framing ate 21% more servings of fruits and vegetables during that one week. This behavior change occurred only as a function of the fit between the strategic direction of outcome framing and the regulatory orientation of the participants. This finding can be utilized to improve effectiveness of health messages.[44]

Other Behaviors Examined via Regulatory Fit. The behavior of physical activity, snacking habits, supplementing with omega-3 products, and that of health care-taking were studied in the context of regulatory fit as well.[46,48-50] Another study examined whether tailored messages to individual's regulatory focus increased the persuasiveness of messages encouraging greater fruit and vegetable intake.[47] In this study tailored messages as promotion or prevention were mailed to participants who were randomly assigned to promotion and prevention groups. The first study on fruit and vegetable consumption manipulated regulatory focus as well, the approach being with framing the health message outcomes as either benefits or costs while this study framed the goal and the means to achieve the goal. The behavior was measured via self-report over the telephone at 1month and 4month after the study. Findings of this study indicate that at 4 months individuals with a fit between their orientation and framed messages resulted in increased likelihood of adhering to the fruit and vegetable intake guideline compared to non-fit.

Similar findings were found for the behavior of physical activity.[47] The intervention consisted in tailored messages delivered via the telephone that fit an individual's regulatory focus resulted in greater physical activity participation and more positive feelings than non-fit messages. This is true for both promotion and prevention messages; promotion group was the only one with statistical significance. The behavior was assessed two weeks after the delivery of the intervention via a telephone interview. Tam et al. examined whether matching implementation intentions to people's regulatory orientation affected the effectiveness of changing unhealthy habits in undergraduate students.[48] Results showed that participants with weak unhealthy snacking habits consumed more healthy snacks when forming implementation intentions that matched or mismatched with their regulatory orientation compared to no implementation intentions formed. Participants with strong unhealthy habits, however, consumed

more healthy snacks only when forming implementation intentions that fit their regulatory orientation: promotion-focused participants with promotion implementation intentions or prevention-focused participants with prevention implementation intentions.[48]

Tudoran et al. investigated how regulatory focus, self-efficacy, and outcome expectations serve as drivers of motivation to consume omega-3 supplements and omega-3-enriched food products.[49] The researchers of this study assessed how self-efficacy interacted with promotion and prevention outcome expectations to determine an individual's motivation to engage in the behavior of adopting health food products. Findings indicated that the relationship between prevention outcome expectations impacted intentions directly and interacted with self-efficacy beliefs, while promotion outcome expectations had a significant main effect on intentions independently of self-efficacy. This study suggests that consumers' motivation to adopt healthy food products needs to be encouraged by stimulating promotion outcome expectations. When a prevention frame is chosen, consumers' motivation needs to be enhanced by self-efficacy beliefs.[49]

Uskul et al., investigated the fit between prevention regulatory focus and tendency to worry about ill health and fit between promotion regulatory focus and tendency to perceive thrilling activities as pleasurable.[50] The health-related behaviors investigated were: vigilant health care-taking such as cancer detection vs eager disregard of health in pursuit of academic goals. Main findings from this study indicate that prevention individuals that are high in worry or who have had worry about health triggered in the moment were more likely to engage in health care-taking behaviors, such as cancer detection. Conversely, promotion individuals were more likely to use stimulants (caffeine, cold remedies) to overcome physical weakness in pursuit of academic goals. This suggest that regulatory fit can result in both, positive and negative

behavioral outcomes, such as cancer detection and a tendency to engage in negative detrimental behavior of using stimulants to control the body that may compromise health.

Table 1-2. Regulatory Fit/Focus Studies

Author, Year	Study Population	Length	Behavior	Intervention	Groups	RFit defined	Effect on Behavior
Spiegel, 2004	Students (N=71)	4 weeks	Writing and turning in reports	Self-guide strength measure of RF; manipulation of ii (strategic means)	Pro vs Pre	RFit = RFc (pro/pre) and strategic means (eagerness or vigilance)	RFit increases the likelihood of writing and turning in reports (50% increase)
Spiegel, 2004	Students (N=150)	7 days	FV intake	RF(pro/pre); Health message framed (pro/pre)	Pro vs Pre	RFit = RFm (pro/pre) and health outcome frame (pro/pre)	RFit results in a 21% increase of FV intake
Latimer, 2008	Participants from a National Cancer database (N=206)	2 weeks	Physical activity	Physical activity guide and telephone messages, both tailored pro and pre	Pro vs Pre	RFit = RFm (pro/pre) and tailored messages (pro/pre)	RFit results in greater physical activity
Latimer, 2008	Participants from a National Cancer database (N=518)	3months	FV intake according to guideline	Mailed tailored messages	Pro vs Pre	RFit = RFc (pro/pre) and tailored messages (pro/pre)	RFit increased the likelihood to meeting the guideline of FV intake

Tam, 2010	Students (N=559)	Same day online reports	Unhealthy snacking habits	Manipulation of RF and ii	ii: pro vs pre vs control	RFit = RFc&m (pro or pre) and ii (pro or pre)	RFit increased motivational intensity; strong unhealthy habits are influenced by fit
Tudoran, 2012	Participants from phone book listing and volunteers (N=959 and 2400)	Not reported	Health supplements	OE framed (pro or pre)	Pro vs pre	Relationship b/w OE (pro/pre), SE, and intentions	OE (pre) and intention is strengthened at high levels of SE; OE (pro) directly affected behavior independent of SE
Uskul, 2007	Study 1: students (N=90) Study 2: students (N=70)	Completed paper questionnaire at one time	Cancer detection and use of stimulants	RFm and studied in two health-related behaviors; Health message leaflets (worry/thrill)	Pro vs pre	RFit = RFm (pro/pre) and behaviors (thrill seeking/worry about health); RF (pro/pre) and leaflets (thrill/fear)	RFit(pre) led to engaging in cancer detection behaviors; RFit(pro) led to use of stimulants to help with physical weakness; PreFit with worry increased

							readiness to engage in behavior

In summary, these studies suggest that the motivational regulatory fit theory applied to various health related behaviors results in positive outcomes. Specifically, when applying the principle of regulatory fit, positive outcomes were identified in behaviors such as: improved writing and turning academic reports, increase of physical activity, more fruit and vegetable consumption, changing in unhealthy snacking habits, engagement in cancer detection behaviors, and the use of stimulants (caffeine, cold remedies) to achieve academic goals.[44,46-50] The definition of regulatory fit varied across studies. Regulatory fit was defined as the fit or non-fit between regulatory focus and strategic means used to affect a behavior, between regulatory focus and tailored messages/outcome message framing, between regulatory focus and implementation intentions, and between regulatory focus and thrill seeking or worry about health behaviors. The majority of studies manipulated regulatory focus,[44,46,48,50] others measured an individual's chronic regulatory focus,[44,47] and one study measured both the chronic and manipulated regulatory focus with similar findings among the two.[48] Additionally, in one study the relationship between three factors including outcome expectations, self-efficacy, and intentions, where outcome expectations were manipulated (promotion and prevention), indicated that self-efficacy affects one orientation (prevention) to impact intentions and not the other; promotion outcome expectations impact intentions independently of self-efficacy.[49]

The effect of regulatory focus and fit has not yet been studied to our knowledge in the behavior of medication adherence. Using a similar strategy described in some previous studies, the effect of regulatory fit on the behavior of statin medication adherence was investigated. Regulatory fit in this study was defined as patients' regulatory focus matched with implementation intentions. Furthermore, this study sought to better understand how this effect is

influenced by a patient's motivation and behavioral intention (mediators) to engage in the behavior of adherence, and the concepts of self-efficacy and outcome expectations were tested as potential moderators affecting the behavioral outcome.

Next, a description of the mediators and moderators used in the study along with theories behind them is provided.

Behavioral Intentions

Behavioral intentions served as a mediator in this study. Behavioral intentions are derived from The Theory of Reasoned Action and The Theory of Planned Behavior, both designed by Ajzen to predict and explain human behavior in specific contexts.[51] They capture a person's motivational factors that influence behavior and are an indication of how hard a person will try in order to achieve the behavior.

Theory of Reasoned Action.[51] In social psychology, the majority of human behavior is thought to be goal-directed. To achieve a goal, action must be taken. Actions, in turn, are controlled by intentions. However, not all intentions are transformed into action. The Theory of Reasoned Action explains causal links of intentions and behavior. The theory suggests that a person's intention is determined by personal and social factors. The personal factor is the attitude towards the behavior defined as the positive or negative evaluation of performing the behavior. The social factor is one's perceived perception of social pressures to perform or not the behavior, termed subjective norm. The intention to perform a behavior is determined by the positive evaluation and the salient beliefs that important others think.

Why people hold certain attitudes and subjective norms is important to understand. Attitude towards a behavior is determined by a person's salient beliefs, which in turn link the

behavior with a valued outcome. A person's attitude is determined by the evaluation of outcomes. If one believes that performing the behavior will lead to positive outcomes, the attitude towards performing the behavior will be favorable; conversely, a belief of the behavior being linked to negative outcomes will produce an unfavorable attitude. These beliefs are termed behavioral beliefs. Subjective norms are associated with one's beliefs of what others think; these are termed normative beliefs. Therefore, behavior is determined by intentions, intentions are determined by attitude towards the behavior and subjective norms, and attitude and subjective norm are determined by behavioral and normative beliefs. Beliefs represent information one holds, whether correct or incorrect, about their world. Hence one's behavior is determined by this information.

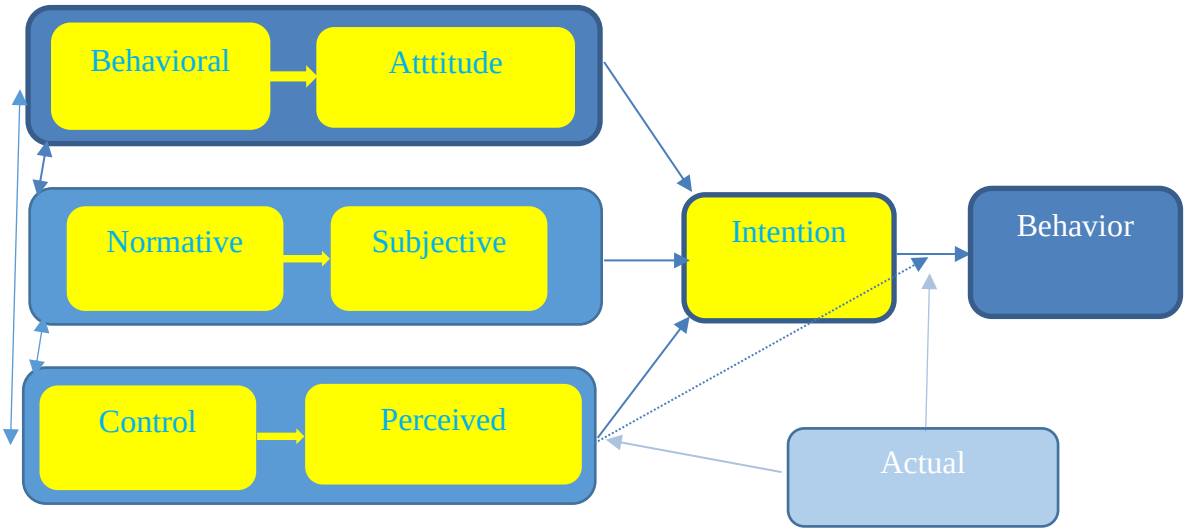
The theory is applicable to a variety of behavioral domains. Generally, people act in accordance to their intentions. There are many factors and anticipated events that can influence intentions. For example, events such as sudden illness, death in the family, loss of a job, effects of time, new information, confidence and commitment, individual differences, and long-range prediction can change one's intention to engage in a specific behavior. One way to ensure the stability of intentions is to measure intentions immediately prior to the observation of the behavior. The stability of intentions influences the accuracy of behavioral predictions.

A person's volitional control influences the behavior towards a goal. Volitional control considers one's perception of their ability to control events in their lives, as opposed to environmental factors. Beliefs in personal control over behaviors are related to internal factors such as individual differences, information, skills, abilities, will power (strength of character), emotions and compulsions, and to external factors such as time and opportunity, and dependence on other people.

The Theory of Planned Behavior (TPB)[51] (Figure 1.2). Based on the Theory of Reasoned Action, behavioral intention is best defined as the intention to attempt to perform a certain behavior, given all the internal and external factors influencing the behavior. If an intention predicts attempts to perform a behavior and fails to predict the attainment of the behavioral goal, then factors that are outside one's control (nonvolitional factors) block one in carrying out the intention. Control is related to developing a plan to achieve a behavioral goal. A plan may consist of intentions and possible alternatives, considering successes versus failures in achieving the goal.

When the behavior is under complete volitional control, the theory of reasoned action applies. However, when internal and/or external factors influence successful performance of behavior and the possibility of failure is a consideration, its necessary to go beyond the theory of reasoned action to the theory of planned behavior. The theory of planned behavior allows study of behaviors influenced by internal and/or external factors when volitional control is limited. The difference between the theory of reasoned action and the theory of planned behavior is the introduction of the concept of perceived behavioral control. The concept of perceived behavioral control is determined by control beliefs and facilitates the implementation of behavioral intentions into action and predicts behavior directly.

Figure 1-2. Theory of Planned Behavior (Copyright ©2006 Icek Ajzen)



Attitudes, subjective norm, and perceived behavioral control, predict intentions differently across behaviors and situations.[52] Examples of behaviors that have been studied in the context of The Theory of Planned Behavior are parenting,[53] nutrition,[54] weight control,[55] physical activity,[56] and medication use.[57,58]

Application of the TPB to different behaviors resulted in insights into what influences parents' feeding behaviors.[53] Findings indicate that peers have more influence than dietary guidelines in parents' decision on what to feed their children. In an attempt to improve nutrition, the TPB was applied to explain dietitians' intentions to promote whole-grain foods.[54] Findings indicate that dietitians are overall positive about the health benefits associated with whole-grain foods, however many were found to have low levels of knowledge and self-efficacy in helping clients eat more whole-grain products. When investigating weight control, TPB was found to have a modest explanation between variables and as a model as a whole to explain only 11% of the variation in weight control.[55] For physical activity, perceived behavior control strongly predicted physical activity and a person's attitude was influenced by one's intention to engage in exercise.[56] Subjective norms were most influential when individuals had no intention to engage in exercise. In the context of medication adherence, subjective norms were found to be associated with increased adherence to antipsychotic medications in a sample of schizophrenic patients of Mexican American origin; attitudes and perceived control were not.[57] The TPB was found to be effective in identifying factors that influence intentions to adhere to treatment among HIV-positive immigrant Latinos in a specific program.[57] These studies indicate that the TPB and its concepts are useful when investigating human behaviors.

This study utilized the concept of behavioral intentions from the TPB to better understand the behavior of medication adherence. The specific behavior is adherence to statin medications in

American adults who have been prescribed a statin medication. The uniqueness is that the concept in this study is examined as a mediator between patients' regulatory focus and their actual behavior of adhering to statin medications.

Although the theory of planned behavior is effective in identifying factors that lead to certain behaviors, often intentions may not be carried out. Development of plans to implement intentions can help transform the intention into actual behavior. Next, formation of implementation intentions is discussed.

Implementation Intentions

Implementation intentions are simple plans that help a person translate their goal into action.[56] They are most helpful when people encounter challenges in their goal-intention such as failing getting started, becoming distracted, or falling into bad habits. Behavioral intentions by themselves, although found to predict behaviors, do so at a modest level. Only 20 to 30% of the variance in behavior is accounted to intentions.[59] Therefore, formation of plans to implement an intention may serve as an effective self-regulatory tool for people who are motivated to overcome challenges and achieve their goal-directed behaviors.

The purpose of implementation intentions is to promote attainment of a goal, specified in goal intention. They do so by automatizing action initiation, linking goal-directed responses to situational cues that elicit responses when encountered.[59] When the pursuit of a goal is planned ahead of time, goal-directed behaviors can be more easily initiated once a situation is encountered. For example, a person will think of a situation X and link it to behavior Y by thinking *when X occurs, I will perform response Y*. Making specific decisions of *when, where,* and *how* will help in taking action to perform the *Y* behavior.[59-61]A specific example in the

context of medication adherence: people with the goal intention to adhere to their medications can form implementation intentions specifying when, where, and how they will take their medications; thus making behavior be under direct control of situational cues rather than it being under conscious and effortful control.

Implementation intentions have proven to be effective in completing personal goals and in taking immediate action. The mechanism suggested by which implementation intentions do so is by heightened mental representation of a potential situation which leads to easier recognition, recall, and engagement in that situation when it comes.[59-61] Initiation and engagement of action in that situation suggests that implementation intentions help resist temptation, fight bad habits, and create instant potentially good habits.[59,60]

In the context of health promotion and health prevention behaviors, implementation intentions are found to be effective in a variety of behaviors. Examples of such behaviors are: promoting the inclusion of healthy food items, such as eating more fruits in one's diet,[62] increasing physical activity,[63-65] weight loss for overweight and obese women,[66] reducing dietary fat intake,[67] reducing smoking,[68,69] reduction in drinking among undergraduate students,[70] increase in cervical screening,[71] and self-monitoring of blood glucose.[72]

Findings indicate that implementation intentions are an effective tool for promoting the inclusion of healthy foods, such as more fruits, in one's diet, but less so for reducing unhealthy snacks in one's diet.[62] Implementation intentions are also effective in increasing physical activity in children.[63] Moreover, when combining implementation intentions and a motivational theory based intervention, such as a decision balance sheet, a dramatic effect on exercise behavior was seen.[64,65] Motivational intervention on itself produced significant effects on intentions only, not

on the exercise behavior itself.[64] Simply forming implementation intention plans has proven to be effective in reducing dietary fat intake during a period of one month, to achieving greater weight loss among obese women, and to reducing of drinking and smoking.[66-70] Furthermore, implementation intentions led to increased attendance for cervical screening for those forming implementation intentions compared to control, despite equivalent motivation to attend.[71]

Interestingly, some studies tested implementation intentions on their own compared to a control group while other studies tested implementation intentions coupled with other motivational interventions. In both cases implementation intentions were found to have a positive effect on behavior either when tested on their own or coupled with a motivational strategy. In the case of self-monitoring blood glucose, implementation intentions together with implementation desire were tested as mediators between goal intentions and the behavior.[72] Both were found to mediate this relationship.

In one study, the role of implementation intentions was examined on healthy snacking behavior when the presence of fit or non-fit exists, where the fit condition was a match between regulatory orientation (promotion/prevention) and formed implementation intentions (promotion/prevention).[48] Findings indicated that people who formed implementation intentions that matched their regulatory orientation experienced regulatory fit, which in turn heightened motivational intensity to attain a specific goal. To better understand the mechanisms of the behavior of statin medication adherence, similar approaches have been implemented. This study specifically investigated the role implementation intentions play when a match versus a mismatch is formed with regulatory focus on the behavior of medication adherence.

Additionally, this study considered the effect of one's self-efficacy and outcome expectations on this relationship between regulatory fit/non-fit and statin medication adherence. These concepts are discussed next.

Self-Efficacy and Outcome Expectations

The concept of self-efficacy and that of outcome expectations originates from Bandura's Social Learning Theory.[73,74] Bandura defined the role of self-efficacy in the context of a person engaging in a behavior with a consequent outcome. The outcome, such as behavior change, is a function of one's expectations about the outcome and one's ability to engage in behavior (Figure1.3).

Outcome expectations is defined as the belief about the likelihood of the behavior leading to certain outcomes.[73,75] Self-efficacy is defined as one's belief about his/her ability to successfully perform specific behaviors in particular situations to produce the outcomes.[73,75] The two concepts operate independently of each other. One may believe that a specific action to produce a certain outcome, however if doubt about performing the behavior is included, then the belief will not be strong enough to influence the behavior. Furthermore, Maddux et al., determined that when a behavior is challenging to perform, if individuals believe that the behavior will result in favorable outcomes, they express greater confidence in their ability to perform the behavior.[75] Conversely, individuals who have a weak relationship in their belief that the behavior will result in favorable outcomes, they express less confidence in their ability to perform.

Self-efficacy is a major determinant of one's choice of activities, effort, and persistence when stressful situations arise.[73] Moreover, self-efficacy is found to be an accurate predictor of

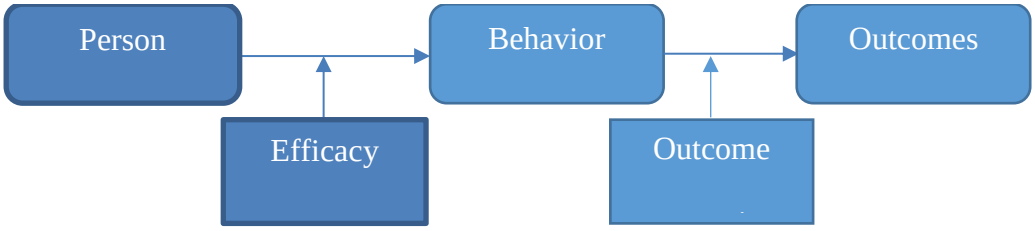
performance on tasks of varying difficulty and an important determinant of health behavior change.[74,76,77] Both self-efficacy and outcome expectations are found to be predictors of behavioral intentions.[78] In a review of the effect of self-efficacy and outcome expectations on health practices, such as cigarette smoking, weight control, contraception, alcohol abuse, and exercise, findings indicate relationships between health behavior change with one or both concepts is strong.[74]

In the context of regulatory focus, one specific study investigated how self-efficacy beliefs interact with different types of outcome expectations (prevention or promotion) to affect an individual's behavior of adopting an omega-3 supplement or an omega-3 enriched food product.[49] Findings indicate that outcome expectations and intention to engage in behavior were significantly enhanced by high levels self-efficacy beliefs only when a prevention frame was used. In this case only intentions and not the behavior itself were investigated.

This study advances research of the two concepts, self-efficacy and outcome expectancies, by examining how the two moderate the relationship between behavioral intentions and the behavior itself, where behavioral intentions act in turn as a mediator between regulatory focus and the measured behavior of statin medication adherence.

Next, the concept of optimism is described in this study. We examined whether patients' optimism is mediated by intentions and motivation, and moderated by self-efficacy and outcome expectancies.

Figure 1-3. Effect of Self-efficacy and Outcome Expectations on Outcomes



Optimism

The concept of optimism refers to a person's generalized favorable expectations for the future.[79] Optimists expect good outcomes, even when things are hard. Pessimists expect the opposite. These expectations affect how optimists and pessimists approach the world and influence their behaviors. Individuals range from being very optimistic to very pessimistic. The theoretical basis for the concept of optimism comes from the expectancy-value theories of motivation,[79] suggesting that in pursuit of goals, the more important the goal, the greater its value and likelihood of engaging in a behavior that would result in the desired end state or action. Optimism is a trait-like concept pertaining to life in general, rather to a specific context.

The concept of optimism was measured in a multitude of studies and is found to be associated with multiple favorable behavioral outcomes. It is associated with better emotional well-being, more effective coping strategies, with better outcomes in physical health, with persistence in educational efforts, with higher income, and with better relationships.[79] It is also linked to higher levels of engagement coping, better subjective well-being in times of difficulty, and greater likelihood that an individual will take proactive steps to protect one's health.[79]

In the context of behavioral and cardiovascular health, optimists tend to know more about risk factors related to heart attack.[79] Optimism has also proven to have a protective effect on all-cause cardiovascular mortality in old age,[80] was found to be associated with a lower risk of stroke in older adults,[81] and is associated with lower rates of rehospitalization after coronary artery bypass graft surgery.[82] Furthermore, individuals who are optimistic were found to have a faster rate of physical recovery after coronary artery bypass surgery during the period of rehospitalization and faster rate of return to normal life activities once discharged from the hospital.[83] Optimistic patients participating in a cardiac rehabilitation program have greater

success in achieving lower levels of saturated fat and body fat and overall coronary risk.[84] Among post-CABG treatment, optimists responded at higher rates to depression treatment.[85] Optimistic women are less likely to develop coronary heart disease, to die from coronary heart disease related causes, and have lower mortality due to all causes.[86]

As demonstrated, optimism, as a trait-like concept, has favorable outcomes for cardiovascular patients. Many cardiovascular patients, to protect their heart health engage in the behavior of taking medications, including statins. Patients' general expectations for the future (optimistic or pessimistic) may influence their intention or motivation to engage in the behavior of taking their statin medication as prescribed. This study examined whether optimism influences the behavior of statin medication adherence. Specifically, optimism levels of an individual were measured and determined whether it influenced one's behavioral intentions or motivation leading to the behavior of statin medication adherence, considering a person's self-efficacy and outcome expectancies. This is also the first study to our knowledge thus far where optimism is examined in the context of statin medication adherence.

To measure optimism, the Life Orientation Test Revised (LOT-R) tool was used in this study.[87,88] This is the most widely used and validated optimism measure thus far. The LOT-R is a 10-item scale that was adapted from the LOT instrument developed to asses individual differences in generalized optimism versus pessimism. The LOT-R scale was constructed by eliminating two items dealing with coping style rather than with positive expectations for future outcomes. The items in the LOT-R consist of 3 positive worded items, 3 negative worded items, and 4 filler items. The higher the value implies higher optimism; scores ranging from 0-13 indicate low optimism, 14-18 moderate optimism, and 19-24 high optimism. The LOT-R has

good internal consistency with a Cronbach's α=0.78 and its test-retest reliability is 0.68 at 4 months and 0.79 at 28 months.

Concluding Remarks

In summary, patient related factors are important in the context of human behavior. Regulatory focus, behavioral intentions, implementation intentions, self-efficacy, outcome expectations, and optimism have all been studied in the context of different behaviors and determined that each plays a role in behavioral goal decision-making. The review of this literature leads to the conclusion that identifying an individual's regulatory focus and using means or tools, such as implementation intentions, that fit that individual's orientation leads to increased motivation to engage in a behavior and ultimately to improved or changed behaviors. Furthermore, intentions to engage in a behavior have proven to be a significant predictor of behavior. In this study, the effect of intentions on behavior was examined. Specifically, intentions were chosen to be tested as mediators between an individual's orientation and behavior. Beliefs about the likelihood of the behavior leading to certain outcomes (outcome expectancies) and beliefs in ability to successfully perform specific behavior (self-efficacy) are all linked to positive behavioral intentions or behavioral outcomes. In this study, it was tested whether the concepts of self-efficacy and outcome expectancy influenced a person's behavioral intentions to engage in the actual behavior of taking statin medications as prescribed. Favorable outcomes of one's generalized favorable expectations for the future, termed as optimism, were tested as a predictor of statin medication adherence for the first time in research's history. Based on these theories and concepts, a conceptual model was developed and is described in the next section pictorially and in words.

Next Steps

Gaps and Opportunities

The needs to improve medication adherence across conditions and to improve the cardiovascular health of patients across the nation are well established. Even though a multitude of studies focused to better understand factors contributing to medication nonadherence and interventions to improve both adherence and cardiovascular health exist, no one study or intervention can possibly explain all causes for these two needs. This is due to the multifactorial complexity of what constitutes health and that of medication adherence.

The commonality across diseases and the challenge of medication adherence is the interaction of the patient seeking to improve their health with their health care professional. One health care professional of particular relevance to medication adherence is the pharmacist. The pharmacist serves as an ideal candidate to be an agent of positive change in improving medication adherence and help patients achieve their health goals. With tailored communication addressing the specific needs of each patient, this interaction can result in increased patient motivation to engage in the behavior of adherence. This study presents an innovative approach in better understanding patient motivational factors affecting the behavior of medication adherence. The patient motivational factors examined are derived from theories successfully used in the social-psychology literature to investigate other behaviors.

The regulatory focus and fit theories provide a strong foundation in better understanding human motivation and strategies used to engage in goal-directed behaviors. The promotion and prevention self-regulatory motivational systems provide an explanation of how different individuals self-regulate either with ideals or oughts to meet specific needs. When individuals' motivational system match their strategic means used to engage in a specific goal-directed

behavior, regulatory fit results. The fit effect results in greater motivation to engage in a task needed to accomplish a goal and has been proven effective in a variety of health behaviors. To our knowledge, the two theories have not yet been applied to the behavior of medication adherence. This study focuses on a unique opportunity of applying the two theories to the behavior of medication adherence, specifically on the behavior of adhering to statin medications prescribed to cardiovascular patients. This represents an important milestone in the field of medication adherence, as this study will present a better understanding of patient motivational factors to engage or not engage in the behavior of taking medications as prescribed. Furthermore, understanding under which regulatory orientation system a patient operates will equip us to tailor medication adherence messages and communication according to each patient's orientation in future research.

Before a patient engages in the behavior of adhering to statin medications, an intention to engage in the behavior is formed. Referred to as behavioral intentions, this concept captures a person's motivation and indicates the degree of effort one will exert to achieve a behavior. Intentions originate from the Theory of Planned Behavior and have been applied to a variety of behaviors. Only a small percentage of the variance in behavior is accounted to intentions. Therefore, this study presents a unique approach to investigating how a person's intentions mediate the relationship between one's motivational orientation and the actual behavior of adhering to statin medications. This relationship is further tested to identify whether other patient psychosocial and medication-related factors, such as a patient's self-efficacy, outcome expectations, insurance for drug therapy, duration of therapy, and others influence intentions to engage in the behavior. Self-efficacy and outcome expectations both are determinants of health behavior change and are found to be predictors of behavioral intentions. Examining whether the

two influence this relationship between intentions and the behavior statin medication adherence is important, as this will provide a better understanding on the specific patient psychosocial related factors that influenced medication adherence. Furthermore, the moderating effect of self-efficacy and outcome expectations on behavioral intentions and motivational intensity was tested on the relationship between optimism and statin medication adherence.

In order to achieve a behavioral goal, plans must be formed that will help one achieve the goal. These plans are often termed as implementation intentions and have been utilized as a helpful tool in goal attainment. In this study implementation intentions are coupled with a person's motivational orientation in order to create fit or non-fit. Previously, this concept was tested in the behavior of healthy vs unhealthy snacking. Implementation intentions will be applied in this study to the behavior of statin medication adherence for the first time.

In summary, this study is innovative and unique in combining concepts and theories across the social-psychology and health-pharmacy fields to better understand the behavior of statin medication adherence. Utilizing the motivational self-regulatory and fit principles as well as potential patient-related factors, such as their beliefs, expectations, and optimism levels, with the application of the tools of implementation intention, this study presents a novel way of studying medication adherence and understanding patient psychosocial factors influencing the behavior of adherence. This study is important in helping to better understand the behavior of statin medication adherence, with the hope to designing more effective interventions in future studies.

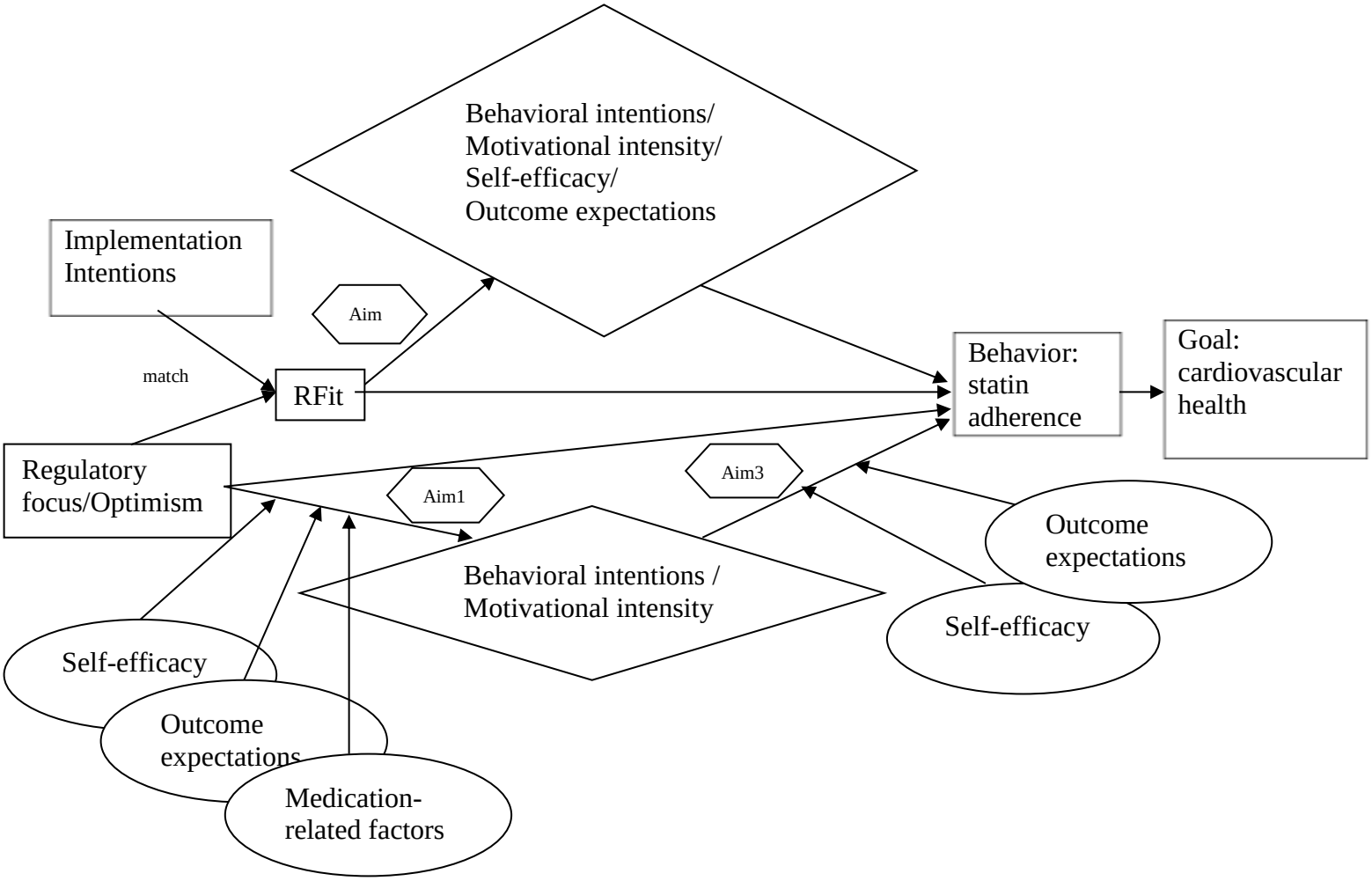
Proposed Theoretical Framework

The theoretical framework used in this study combines the concepts of regulatory focus, regulatory fit (regulatory focus and implementation intentions), optimism, motivational intensity, behavioral intentions, self-efficacy and outcome expectations from the theories described in previous sections and medication-related factors to better understand the complexity of the health behavior of medication adherence (Figure 1.4).

In this conceptual model the effect of regulatory focus, regulatory fit, and optimism on statin medication adherence was tested. In the first aim, the effect of Regulatory Focus (promotion/prevention) on statin medication adherence was tested with Motivational Intensity or Behavioral Intentions serving as the mediator and the concepts of Self-Efficacy, Outcome Expectations, or a Medication-related factor serving as the moderator. In the second aim, the effect of a Regulatory Fit intervention on statin medication adherence was tested. Specifically, interaction effects of Regulatory Fit, Non-fit, and Control were tested between high (strong) and low (weak) behavioral intentions, motivational intensity, self-efficacy, and outcome expectations. In the third aim, the effect of Optimism on statin medication adherence was tested with Motivational Intensity or Behavioral Intentions serving as the mediator and the concepts of Self-Efficacy or Outcome Expectations serving as the moderator.

Figure 1.4 shows the conceptual framework used in the study. The squares/rectangles designate primary predictors and outcomes, including regulatory focus, regulatory fit (regulatory focus and implementation intentions), optimism, and statin medication adherence. The lines indicate causal pathways. The diamonds represent mediating variables or alternatively causal pathways between the predictor and behavior. The circles indicate the potential moderators of the causal relationships. Next, the overall objective, aims, and hypotheses for the study are presented.

Figure 1-4. Conceptual Framework



Overall Objective and Central Hypothesis

The overall objective of this study was to test the effect of patient psychosocial factors on the behavior of statin medication adherence. The central hypothesis was that patient psychosocial factors will predict the behavior of statin medication adherence via a conditional indirect effect and that a Fit intervention will result in greater statin medication adherence compared to non-fit and control groups.

Study Aims and Hypotheses

Aim 1 (Regulatory focus): To test the conditional indirect effect of patients' regulatory focus on statin medication adherence with behavioral intentions/motivational intensity as the mediator and patients' self-efficacy/outcome expectations/ medication-related factors (time on statin, insurance coverage, and the number of non-prescription medications) as the moderator.

Aim 2 (Regulatory fit): To test the effect of fit versus non-fit versus control on the behavior of statin medication adherence at weak versus strong behavioral intentions, motivational intensity, self-efficacy, and outcome expectations.

Aim 3 (Optimism): To test the conditional indirect effect of patients' optimism on statin medication adherence with behavioral intentions/motivational intensity as the mediator and with self-efficacy/outcome expectations as the moderator.

Hypotheses for aim 1: Regulatory focus

H1a: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the self-efficacy.

H1b: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the outcome expectations.

H1c: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the longer the statin therapy.

H1d: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence if insurance is present.

H1e: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the number of non-prescription medications present.

H2: The stronger the behavioral intentions the greater the statin medication adherence levels.

H3a: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the higher the self-efficacy.

H3b: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the higher the outcome expectations.

H3c: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the longer the statin therapy.

H3d: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence if insurance is present.

H3e: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the greater the number of non-prescription medications.

H4: The stronger the motivational intensity the greater the statin medication adherence levels.

Hypotheses for aim 2: Regulatory fit

H1: There is no difference between regulatory fit, non-fit, and control groups when it comes to statin medication adherence. This hypothesis was tested with four different independent variables: motivational intensity, behavioral intentions, self-efficacy, and outcome expectations.

H2: There is no difference between the weak and strong independent variable groups when it comes to statin medication adherence. This hypothesis was tested within each regulatory fit group (fit, non-fit, control).

H2a1: There is no difference in statin medication adherence levels between the motivational intensity groups (weak vs strong) within the fit group.

H2a2: There is no difference in statin medication adherence levels between the motivational intensity groups (weak vs strong) within the non-fit group.

H2a3: There is no difference in statin medication adherence levels between the motivational intensity groups (weak vs strong) within the control group.

H2b1: There is no difference in statin medication adherence levels between the behavioral intention groups (weak vs strong) within the fit group.

H2b2: There is no difference in statin medication adherence levels between the behavioral intention groups (weak vs strong) within the non-fit group.

H2b3: There is no difference in statin medication adherence levels between the behavioral intention groups (weak vs strong) within the control group.

H2c1: There is no difference in statin medication adherence levels between the self-efficacy groups (weak vs strong) within the fit group.

H2c2: There is no difference in statin medication adherence levels between the self-efficacy groups (weak vs strong) within the non-fit group.

H2c3: There is no difference in statin medication adherence levels between the self-efficacy groups (weak vs strong) within the control group.

H2d1: There is no difference in statin medication adherence levels between the outcome expectations groups (weak vs strong) within the fit group.

H2d2: There is no difference in statin medication adherence levels between the outcome expectations groups (weak vs strong) within the non-fit group.

H2d3: There is no difference in statin medication adherence levels between the outcome expectations groups (weak vs strong) within the control group.

Hypotheses for aim 3: Optimism

H1: The greater the optimism the greater the intentions to engage in the behavior.

H2a: Behavioral intentions will influence the behavior of statin medication adherence the greater the self-efficacy.

H2b: Behavioral intentions will influence the behavior of statin medication adherence the greater the outcome expectations.

H3: Optimism affects statin medication adherence directly.

H4: The greater the optimism the greater the motivational intensity to engage in the behavior.

H5a: Motivational intensity will influence the behavior of statin medication adherence the greater the self-efficacy.

H5b: Motivational intensity will influence the behavior of statin medication adherence the greater the outcome expectations.

H6: Optimism affects statin medication adherence directly.

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Chapter 2 - **PAPER 1: REGULATORY FOCUS' EFFECT ON STATIN MEDICATION ADHERENCE**

Abstract

Background: Medications are one effective tool used to improve health. Despite their effectiveness, medication adherence in the developed world among patients with chronic diseases is reported to be less than optimal, and efforts to improve statin medication adherence have been moderately successful. Regulatory focus, as a human motivational system, has been studied in various health-behaviors; however, its effect on the behavior of statin medication adherence has not been investigated. Understanding how regulatory focus affects statin medication adherence may provide important insights into designing new interventions to improve adherence.

Aim: The aim of this study was to investigate the conditional indirect effect of regulatory focus on statin medication adherence.

Methods: Patients were recruited from a large university health system to participate in the study. Data were collected from patients via two online questionnaires. Questionnaire one assessed the psychological and environmental variables and questionnaire two, sent two weeks later, medication adherence. The conditional indirect effect between regulatory focus and statin medication adherence was analyzed via the PROCESS macro tool.

Results: The conditional indirect effect of regulatory focus on statin medication adherence was established when time on statin and insurance coverage were the moderators and behavioral

intention was the mediator. Furthermore, the conditional indirect effect of regulatory focus on statin medication adherence was seen when self-efficacy and the number of non-prescription medications served as moderators and motivational intensity as the mediator.

Conclusion: Regulatory focus was a significant predictor of statin medication adherence, influencing the behavior directly and indirectly via several patient and medication-related factors.

Introduction

As the saying goes 'Health is wealth'. Viewed as a resource for everyday life, health is pursued by people across all nations and cultures. In the pursuit of this valuable resource, individuals chose to engage in various health-promising behaviors, one of which is the behavior of taking medications. Medications serve as an effective tool in preventing, treating, or curing diseases. Despite the positive outcomes associated with the behavior of taking medications, challenges in taking medications as prescribed (adherence) or staying on the prescribed therapy (persistence) arise.[1-4] These challenges are complex multifactorial behavioral processes.

The challenges can present themselves at various levels including factors related to the medication, patient, health care provider, and health care system.[3] Examples are: complex regimen and side effects; demographic, psychological, social characteristics and beliefs; communication and empathy with and towards the patient; insurance coverage and access to a health care facility; for each level. Addressing challenges at all levels is desirable, yet impractical. Therefore, for this study we focused on patient and medication-related factors. Specifically, we chose to investigate how certain patient and medication-related factors affect the behavior of statin medication adherence. In the next sections we describe the challenges with

medication adherence, in general and statin specific in the context of cardiovascular diseases. Then, we describe patient motivational factors and intentions to engage in goal behaviors and medication factors influencing the behavior of statin medication adherence, ending with the aims and hypotheses of the study.

Medication adherence among patients with chronic diseases is reported by the World Health Organization (WHO) to be on average 50% in the developed world.[5] The low adherence levels pose consequences, such as worsening of disease, poor clinical outcomes, poor quality of health, mortality, and an economic burden of $290 billion USD in annual health expenditures.[1,3,5-8] Therefore, efforts to improve medication adherence are worthwhile.

Medications are an essential tool in managing chronic diseases, including cardiovascular diseases (CVDs). CVDs are the leading cause of morbidity and mortality in developed nations; by year 2030 they are projected to be the leading cause of death globaly.[9-11] To improve the cardiovascular health of Americans, the American Heart Association aims at reducing CVDs and strokes by 20% by the year of 2020.[12] To attain cardiovascular health one must seek to engage in health behaviors and to attain ideal health factors. One of the factors is a cholesterol level of <200 mg/dL. Attaining this cholesterol level can be done via one or more behavioral tools including diet, exercise, and taking medications. We are focusing on the behavior of taking medications. Specifically, our focus is on the most commonly prescribed medications used to lower cholesterol levels, statins.

Statins have proven to be effective and safe. A systematic review over a 10year period of statin adherence and persistance reported that reduction in CVD and mortality are a result of adherence and persistance to statin therapy.[13] Despite their benefits, statin medication adherence

levels have been reported to be between 25 to 48%.[14-17] The most recent review documents statin medication adherence levels between 18.3% to 91.9% represented as percentage of patients achieving MPR ≥80%.[13] Factors contributing to statin medication non-adherence present themselves at the medication, patient, patient-health care provider, and health system levels. Interventions to improve statin medication adherence thus far have included patient-pharmacist counseling, patient-physician counseling, telephone counseling and reminders, and mailing educational materials.[18-26] The results of these interventions suggest that statin medication adherence improves for patients who are counseled by a health-care professional, a pharmacist or physician, in person and/or over the telephone. Developing best practices for counseling to improve statin medication adherence is the next step. In order to do that, we must first identify and understand the factors that affect patient motivation and intention to engage in the behavior of medication adherence.

Patient motivation is considered by the World Health Organization (WHO) to be the most important pillar of medication adherence.[3] Other research similarly suggests that patient motivation and patient-provider relationship serve as two key factors to improve the medication experience for patients.[1,27] These research findings reinforce the need to develop best counseling strategies for patients. Our strategy to do so is by focusing first on better understanding patient motivational factors in the context of medication use. Next, we describe human motivation, intentions, and other factors potentially affecting our behavior of interest.

Human motivational factors have been studied in a variety of health behaviors. Regulatory focus (RF) theory explains two self-regulatory motivational systems under which individuals operate to achieve a goal-directed behavior. The two motivational systems are: promotion (self-regulation to strong ideals) and prevention (self-regulation to strong oughts).[28-31]

The two motivational systems are independent of one another and meet different human needs. The promotion motivational system meets the need of nurturance and is characterized by ideals (hopes, wishes, and aspirations). The prevention motivational system meets the need of security and is characterized by oughts (duties, obligations, and responsibilities). The mechanisms of promotion and prevention self-regulation differ in the presence and absence of positive versus negative outcomes, respectively.

A person's regulatory focus may be chronic or situational and it can be induced.[28,30] For the chronic regulatory focus, a patient may be high or low in both promotion and prevention regulatory focus, as the two chronic orientations are not bipolar constructs.[31] Chronic regulatory focus is associated with styles of child-caretaker interaction and socialization processes[32,33] and is measured with the Regulatory Focus Questionnaire (RFQ).[30] The situational regulatory focus is experimentally manipulated using a priming technique, which involves framing worded statements as either promotion or prevention. The focus of this study is to understand whether or not patients' regulatory focus affects the behavior of statin medication adherence. Patients' situational regulatory focus was primed with promotion or prevention framed messages. Understanding patients' self-regulatory system when making a decision in regards to their medications will help us design better patient counseling strategies.

The process of engaging in a behavior to achieve a goal is complex. When considering goal-directed behaviors, such as taking statin medications to improve cardiovascular health or avoid a cardiovascular event, patients often form intentions. Behavioral intentions serve as an indicator of how hard an individual will try to achieve the goal-directed behavior.[34] They originate from the Theory of Reasoned Action and Theory Planned Behavior, and have been examined in the context of various behaviors.[35-41] Intentions have proven to explain only 20 to

30% of variance in a behavior.[42] Therefore, in our study in addition to intentions we are investigating other factors that may influence and explain the behavior of medication adherence. The factors chosen were patients' beliefs (self-efficacy and outcome expectancy), duration of medication therapy, presence of drug insurance, and the number of over-the-counter medication products taken. Next, we describe each of these factors.

Research studies have found that both self-efficacy and outcome expectancy beliefs are predictors of behavioral intentions.[43] Self-efficacy is defined as one's belief to successfully perform a specific behavior in particular situations and outcome expectancy is defined as one's belief about the likelihood of the specific behavior change leading to certain outcomes.[44] Self-efficacy is identified as a determinant of health behavior, health behavior change, and maintenance.[45.46] It is an indicator of the amount of effort and persistence one would engage in the face of obstacles and adverse experiences.[47] Self-efficacy has been examined in the following behaviors: exercise, weight control, contraceptive use, alcohol abuse, and cigarette smoking.[45] Findings indicate that self-efficacy has a strong relationship with health behavior change and maintenance. Self-efficacy and outcome expectancies were both studied in the context of regulatory focus and the behavior of adopting omega-3 foods and supplements.[48] Findings indicate that high self-efficacy beliefs enhanced intention to engage in the behavior only for the prevention framed message of outcome expectations, but not for the promotion outcome expectation framed messages.[48] In our study we framed promotion and prevention regulatory focus messages and investigated the how self-efficacy and outcome expectancy beliefs moderated patients intentions or motivation to engage in the behavior of adhering to statin medications. Another difference is that our study measured actual behavior, while the omega-3 study measured only intentions.

In addition to these patient-related factors affecting the behavior, we included several medication specific factors that are known to influence the behavior. Specifically, statin medication adherence research has demonstrated that over time adherence to statin medications could drop significantly from 50% at 6 months to 30-40% at 12 months and that cost of treatment may be a barrier to optimal statin medication adherence.[49-52] Therefore, in our study we investigated whether or not duration of therapy and cost may influence patients' intentions and motivation to engage in the behavior of adhering to statins. Knowing this information will help us better understand whether the two medication-related factors influence intentions and motivation. This will add to the knowledge of medication adherence research and help in future intervention design.

Next we also included non-prescription medications as a medication-related factor. Our patient population consists of older adults on a cholesterol lowering medication. National survey reports that 42% of older adults ages 57 to 85 years, take one or more non-prescription medications and 81% at least one prescription medication.[53] We investigated how the number of non-prescription medications taken in addition to the statin medication affected patients' intention and motivation in the context of regulatory focus. Specifically to statin therapy, non-prescription medications such as red yeast rice or plant sterols may be sought by patients experiencing myopathy.[54,55] Both red yeast rice and various plant have been demonstrated to reduce LDL and total cholesterol levels.[54,55] With approximately 10% of patients on statin therapy experiencing myopathy,[54] muscle side-effects, these alternatives may be used concurrently. As well, the availability of over-the-counter medication products may add value to patients' health in a cost-effective way, as each dollar spent on non-prescription medications saves $6 to $7 for the US health care system.[56] Including non-prescription medication use will

help us better understand how prescription and non-prescription medications taken concomitantly affect patient psychosocial factors.

The aims of this study are to better understand patients' intention and motivation to engage in the behavior of statin medication adherence. Specifically, the relationship between patients' regulatory focus and statin medication adherence was tested via a conditional indirect effect with behavioral intentions and motivational intensity serving as mediators, and self-efficacy, outcome expectancy, time on statin, insurance coverage, and the number of non-prescription medication products serving as moderators.

Aim 1 tested behavioral intentions as the mediator and aim 2 tested motivational intensity as the mediator between regulatory focus and statin medication adherence. Several moderators (self-efficacy, outcome expectations, time on statin, insurance coverage, number of non-prescription medication products) were tested for each aim. The supporting hypotheses for aim 1 were the following:

H1a: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the self-efficacy.

H1b: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the outcome expectations.

H1c: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the longer the statin therapy.

H1d: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence if insurance is present.

H1e: The regulatory focus of a person will influence behavioral intentions to engage in the behavior of statin medication adherence the higher the number of non-prescription medications present.

H2: The stronger the behavioral intentions the greater the statin medication adherence levels.

H3a: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the higher the self-efficacy.

H3b: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the higher the outcome expectations.

H3c: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the longer the statin therapy.

H3d: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence if insurance is present.

H3e: The regulatory focus of a person will influence motivational intensity to engage in the behavior of statin medication adherence the greater the number of non-prescription medications.

H4: The stronger the motivational intensity the greater the statin medication adherence levels.

Methods

Research Design

This was a randomized controlled field experiment. Patients prescribed a statin medication from a university health system were recruited to participate. Those who agreed to participate had the opportunity to complete two questionnaires (Appendices A and B) and were randomized to two experimental conditions of promotion or prevention. The assignment to the two groups

was done randomly via a computer generated system. One group of patients received the promotion regulatory focus manipulation while the other group received the prevention regulatory focus manipulation. The mediating, moderating, and dependent variables were measured variables in our questionnaires. The hypotheses for this study were tested via the conditional indirect effect analyses developed by Hayes (Appendix C).[57] The variables in our research design, presented in Figure 1, are the following:

1. A dichotomous manipulated independent variable (X) indicating exposure to one of the two experimental conditions of promotion or prevention regulatory focus. The promotion experimental condition was coded +1 and the prevention experimental condition was coded -1.
2. Two continuous mediating variables (M) that were behavioral intentions or motivational intensity were tested in two different models.
3. Five moderator variables (W), four of which are continuous: self-efficacy, time on statin therapy, number non-prescription medications, and one is dichotomous: insurance coverage for the statin therapy.
4. One continuous dependent variable (Y), reflecting patients' self-reported adherence to statin therapy.

Manipulation. The promotion focus manipulation consisted of priming patients with two promotion framed questions. Specifically, patients were asked to think and write down three past and three present *hopes, aspirations, and dreams*. For each of the three, patients were asked to indicate how strong each hope, aspiration, or dream was for them personally, with answer options ranging from *not at all strong* to *very very strong*. The prevention focus manipulation consisted of priming patients with two prevention framed questions. Specifically, patients were

asked to think and write down three past and three present *duties, obligations, and responsibilities*. For each of the three, patients were asked to indicate how strong each duty, obligation, or responsibility was for them personally, with answer options ranging from *not at all strong* to *very very strong*.

Participants and Procedures

Participants were recruited from a large university health system. A total of 1700 potential participants were invited to participate in the study using an initial mail contact. The inclusion criteria for the study were taking a statin medication at the time of the survey, 18 years of age or higher, and proficiency in the English language. The total number of participants with complete responses for all variables of interest was n=326.

Participants who agreed to participate in our study were asked to complete two online questionnaires, one at baseline and the second one two weeks later. The initial mail contact consisted of a cover letter inviting patients to participate in the study. The cover letter conveyed the purpose of the study, procedures for completing the two questionnaires, and incentives for completing the questionnaires. A $2 bill incentive was included with the cover letter. The incentive for completing the first questionnaire was $20 and the incentive for completing questionnaire two was $5. At the bottom of the cover letter a link to the first questionnaire was provided as well as a unique personal passcode for respondents to access the questionnaire. When participants completed the first questionnaire they were asked to enter their email address via which they received the second questionnaire two weeks later. This study was approved by the University's Institutional Review Board (IRB) (Appendix D).

Measures

Several measures were used in this study.

Independent variable. The independent variable, regulatory focus, was manipulated. The manipulation consisted of a priming technique of framed questions. The questions were framed as promotion or prevention. For promotion, the priming technique consisted of questions framed as *hopes, dreams, and aspirations* while for prevention, the priming technique consisted of questions frames as *duties, obligations, and responsibilities*.

Mediating variables. The mediated relationship between regulatory focus and statin medication adherence was tested via two mediators including behavioral intentions and motivational intensity. Each mediator was measured via two questions. The behavioral intention questions asked patients their *intention* and *plans* to take their statin medication as directed by their health care provider within the next two weeks. The answer options ranged from *strongly disagree* to *strongly agree*. The motivational intensity questions asked patients how *motivated* and *determined* they were to take their statin medication as prescribed. Answer options ranged from *not at all* to *extremely*. The two questions for each mediator were averaged to obtain one score for behavioral intentions and one score for motivational intensity.

Moderator variables. The variables tested as moderators were: self-efficacy, outcome expectancy, time on statin, statin insurance and the number of non-prescription medications. Self-efficacy was measured via two questions asking patients on a scale from *not at all* to *extremely* how *confident* and *certain* they were able to take their statin medication as directed. Outcome expectancy was measured via two questions asking patients on a scale from *not at all* to *extremely* how *promising* and *likely* they were able to take their statin medication as directed. The time on statin and number of non-prescription medications questions were open ended. The

insurance coverage question had answer options of *yes, no, and I don't' know*. The *no and I don't' know* answer options were grouped as '*no*'.

Dependent variable. The dependent variable, statin medication adherence (SMA), was measured via the single-item visual analogue rating scale (VAS). It was a single item asking patients to estimate along a continuum the percentage of medication dosages taken as prescribed during the past two weeks.[58-60] Patients' SMA was measured at baseline in the first questionnaire and two weeks after the intervention in the second questionnaire.

Analysis Approach

The conditional indirect effects were tested via the PROCESS macro tool,[57] and two models were tested (Figure 1). First, the mediator variable model was determined by the interaction effects of the independent variable (X) and the moderator (W) on the mediator (M). The following equation represents the mediator variable model:

$$\mathbf{M}=\beta_{10}+\beta_{11}\mathbf{X}+\beta_{12}\mathbf{W}+\beta_{13}\mathbf{X(W)}+\varepsilon_{1} \quad (1)$$

Second, the outcome variable model was determined by the effect of the mediator (M) on the outcome variable (Y) and by the direct effect of the independent variable (X) on the outcome variable (Y). The following equation represents the outcome variable model:

$$\mathbf{Y}=\beta_{20}+\beta_{21}\mathbf{X}+\beta_{22}\mathbf{M}+\varepsilon_{2} \quad (2)$$

There were some assumptions associated with these two equations. The assumptions were that the mediator and moderator variables were mean centered and that the residuals were normally distributed, independent, and had a common variance. The conditional indirect effect between the independent variable (X) and the outcome variable (Y) was considered successful when the

pathway from the independent variable (X) to the mediator (M) (β_{13}) and the pathway from the mediator (M) to the outcome variable (Y) (β_{22}) were statistically significant (Figure 1). Figure 1 presents pictorially the models of the study. [Figure 1a and 1b are similar, with one difference being the mediator variable tested. In Figure 1a the mediator variable is behavioral intentions while in Figure 1b the mediator variable is motivational intensity. In both figures the independent variable (X) is regulatory focus, the dependent variable (Y) is statin medication adherence, and the moderator variables (W) are self-efficacy, outcome expectancies, time on statin, insurance coverage, and the number of non-prescription medications.]

Results

From the 1700 potential participants, a total of 32.65% patients responded to the first questionnaire. A total of 58.74% of patients who responded to the first questionnaire completed the second one. The total number of complete responses for our variables of interest was n=326. There were no statistical significant differences between respondents to both questionnaires and respondents to the first questionnaire only, except for health insurance (Appendix E).

Patient demographic characteristics indicate that the majority of participants were white (87.1%) and 60 years of age or older (69.3%) (Table 2.1). Approximately half of participants were female (40.2%) and had an annual income of $60,000 or higher (56.8%). The majority of participants, 88.7%, reported their health to be good to excellent. Only 11.5% reported an overall health of fair to poor. A total of 91.7% of participants received a diagnosis from their health care professional of high cholesterol and 11.3% of patients experienced a heart surgery/procedure during their lifetime. A total of 87.4% of participants had been on a statin medication for 4 or more years for up to 30years. About half of participants (46.03%) were on 1 or 2 non-prescription medications; some participants were not taking any (14.1%), and others were taking

5 of more non-prescription medications (15.3%). A total of 22.1% of participants reported taking a medication for depression. Results of chi-square and t-tests indicated that there was no difference among all demographic and clinical characteristics between the promotion and prevention groups.

The reliability of variables in the study was measured via the Cronbach alpha (α). A general reliability value of ≥.70 is considered good. All study variables exhibited good reliability: α(behavioral intention) = .71, α(motivational intensity) = .93, α(self-efficacy) = .85, α(outcome expectancy) = .86, α(regulatory focus promotion) = .82, α(regulatory focus prevention)=.74. The distribution of the dependent variable, statin medication adherence, was skewed (mean = 96.3 ± 13.74). The statin medication adherence variable was transformed via a log-transformation and a two-step approach with results being slightly better towards normality; however, not statistically significant (indicated by the Kolmogorov-Smirnov and Shapiro-Wilk tests). Hence, we decided to use the original statin medication adherence results. The mean statin adherence at baseline was 95.67% ± 14.21. Intentions to engage in the behavior were explored as a possible dependent variable as well. The distribution of intentions was skewed (mean 4.85 ±.524). In the end, the behavior of adhering to statin medication was chosen as the dependent variable. Table 2.2 presents the results from the PROCESS analysis for conditional indirect effect between regulatory focus and statin medication adherence with behavioral intentions serving as the mediator. Table 2.3 presents the results from the results from the PROCESS analysis for conditional indirect effect between regulatory focus and statin medication adherence with motivational intensity serving as the mediator. Table 2.4 presents the conditional indirect effects for each mediator at different moderator values. Table 2.5 presents the study's hypotheses and results.

The results for the conditional indirect effect of regulatory focus on statin medication adherence with behavioral intentions serving as the mediator and the five moderators are shown in Figure 2.1a; Tables 2.2, and 2.4. Results indicate that behavioral intentions partially mediated the impact of patients' regulatory focus on statin medication adherence. Regulatory focus was a direct and indirect predictor of statin medication adherence. The direct effect showed that for one unit change in prevention regulatory focus there was a 1.73 units change in statin medication adherence (b=-1.73, p=.01). Prevention regulatory focus had a positive effect on statin medication adherence, when compared to promotion regulatory focus.

For the indirect effect, among all the moderators, time on statin therapy (b=.01, p=.03) and insurance coverage (b=.26, p=.00) moderated the relationship between regulatory focus and behavioral intentions at a statistical significant level. The longer the time on the statin therapy (95% CI .08, 2.66) and presence of insurance coverage (95% CI 1.07, 7.83), both, interacted with patients' regulatory focus resulting in higher behavioral intentions to engage in the behavior.

The results for the conditional indirect effect of regulatory focus on statin medication adherence with motivational intensity serving as the mediator and the five moderators are shown in Figure 2.1b; Tables 2.3 and 2.4. Results indicate that, similarly to behavioral intentions, motivational intensity partially mediated the impact of patients' regulatory focus on statin medication adherence. Regulatory focus served as a predictor of statin medication adherence directly and indirectly. The direct effect showed that for one unit change in prevention regulatory focus there was a 1.84 unit change in statin medication adherence (b=-1.84, p=.01). Prevention regulatory focus compared to promotion regulatory focus had a positive effect on statin medication adherence.

For the indirect effect, among all the moderators, self-efficacy (b=.08, p=.05) and number of non-prescription medications (b=-.05, p=.01) moderated the relationship between regulatory focus and motivational intensity. Higher self-efficacy (95% CI .01, 1.38) and lower number of non-prescription medications (95% CI .38, 2.19), both, interacted with prevention regulatory focus resulting in higher motivation to engage in the behavior. The number of prescription medications was tested as a moderator and was found to have no significant effect (the results are not shown).

In summary, regulatory focus is a significant predictor of statin medication adherence affecting the behavior directly and indirectly. The direct effect is positively influenced by prevention regulatory focus. The indirect effect is mediated by intentions or motivation and moderated by different medication and patient-related factors. Duration of therapy and insurance coverage influence patients' intentions while self-efficacy and number of non-prescription medications influence patients' motivation.

Discussion

Behavioral intentions and motivational intensity were mediating variables between patients' regulatory focus and statin medication adherence. Both are important factors in the decision-making process towards the goal-pursuit of cardiovascular health. Other factors influencing the behavior were patients' beliefs in their own ability to engage in the behavior, length of time on the statin medication, insurance coverage for statin, and the number of non-prescription medications. These factors interacted with patients' prevention regulatory focus, when compared directly to promotion regulatory focus, to influence either behavioral intentions or motivational intensity to engage in the behavior and ultimately influencing the behavior of SMA at a significant level.

Our study showed that that patients' prevention and promotion orientation impacts the behavior of statin medication adherence differently. Patients' prevention orientation in comparison to promotion positively impacted statin medication adherence. This finding is important as our behavior of interest of medication adherence is related and often framed in terms of 'preventing' a disease or condition or a future unwanted event from occurring. For example, statements related to heart disease on the Centers for Disease Control and Prevention website are worded as preventing heart disease with a focus on steps a patient must take to reduce risks for heart disease or tips to healthy living habits that patients need to consider to prevent heart disease.[61] Therefore, health care professionals are most likely to communicate with patients the recommended steps needed to reduce the risk for heart disease. Reducing the risk for heart disease or preventing heart disease are both statements that have a prevention regulatory focus associated with them, of avoiding unwanted events. In this case, the unwanted event would be a potential future heart attack or potential future diagnosis of cardiovascular disease. Specifically, pharmacists may encourage patients to take their statin medication to avoid any potential future heart disease. Therefore, this may be a likely explanation for why patients' prevention orientation, when compared to promotion, showed significant positive changes in statin medication adherence in our study.

Additionally, we identified that patients' behavioral intentions and motivational intensity were impacted by different patient and medication-related factors. Presence of insurance coverage for the drug and consistent behavior of taking the medication for long periods of time positively influenced behavioral intentions to take the statin medication as prescribed. In other words, behavioral intentions to adhere to statin medications were impacted by insurance related factors. Previous research findings indicate that adherence to statin medications drops over time

and cost of treatment can potentially be a barrier.[13,49-52] Cost is a known significant predictor for statin medication adherence.[62] Specifically, Piette et al. identified high out-of-pocket costs as a significant risk for non-adherence for both low and high trust levels between the patient and physician.[63] Furthermore, cost-related underuse of medications was related to patient trust in his/her physician.[63] For example, rates of underuse for patients with low trust in their physician were reported within the range of 4% to 30%.[63] The rest may be attributed to other factors, including patient psychosocial factors. Piette et al., states that patients who were non-adherent due to cost, reported other reasons for non-adherence, such as depressive symptoms. Considering the implications of cost for our sample population, a total of 91.72% of our patients had statin insurance and 25.5% reported an annual income of 100k or greater. Therefore, cost of therapy, most likely was not a barrier for majority of our patients. Identifying additional determinants, such as psychosocial patient factors, of statin adherence adds to our understanding on various ways to improve adherence once cost needs have been met for patients. Also, finding ways to eliminate the cost barriers for patients who cannot afford therapy treatment, by ensuring insurance coverage for statin therapy is essential as it may result in greater intentions for patients to adhere. Greater intentions to adhere may improve statin medication adherence over long periods of time.

Patients' motivational intensity was also impacted by different patient and medication factors. The greater patients' confidence in their ability to follow the prescribed therapy and the lower the number of non-prescription medications, the greater was the motivation to adhere to statin therapy. Self-efficacy has been studied in the context of intentions in other research and was found to predict intentions in general. Our study presents a novel finding where patients' self-efficacy impacted patients' motivational intensity to engage in the behavior of adhering to

statins, but not their behavioral intention. This may be due to the way we define self-efficacy, as one's confidence in his/her ability to engage in a behavioral goal. Hence, the self-efficacy construct influences one's motivation and determination to engage in a behavior instead of one's intention. The non-prescription medication finding may be due to the possibility that patients' motivation to take their statin medication as prescribed to manage their cardiovascular health eliminates the need to rely on other medication products that are sold without a prescription from a health care provider. This may be attributed to the effectiveness of statin therapy for our sample population. The high adherence levels and long duration of statin therapy indicates that majority of patients most likely have not experienced myopathy; hence reliance on statin therapy. Identifying the two drivers, higher self-efficacy and lower number of non-prescription medications, of patients' motivational intensity helps us better understand what factors contribute to patients' motivation to take medications as prescribed.

Our study makes important contributions to research in two meaningful ways. One, our research adds value to the medication adherence research. Regulatory focus is a new concept being investigated in the context of medication adherence research. Additionally, we have investigated the relationship between regulatory focus and statin medication adherence via a novel analytic technique, the conditional indirect effect analysis. This allowed us to test the effect of regulatory focus on medication adherence directly and indirectly with potential mediating and moderating variables. Our findings suggest that patients' prevention regulatory focus positively affects the behavior of statin medication adherence directly, when compared to promotion, and is partially mediated by patients' motivational intensity (the greater the self-efficacy and the lower the number of non-prescription the greater the motivational intensity) or

behavioral intentions (the greater the length of time on statin therapy and presence of insurance coverage the greater the behavioral intentions).

The second meaningful contribution of our study to the body of research is addition of a new behavior to the regulatory focus research. This is the first study to our knowledge applying the theory of regulatory focus to the behavior of medication adherence. So far, the regulatory focus theory has been studied in the context of decision-making and problem solving in various tasks, but not yet in the context of the behavior of medication adherence. One behavior it was applied was the behavior of supplementing with omega-3 products.[48] Findings indicate that prevention outcome expectations significantly interacted with self-efficacy to impact behavioral intentions to engage in the behavior of supplementing with omega-3 supplements and enriched foods. Promotion outcome expectations did not interact with self-efficacy beliefs, but did directly impact behavioral intentions.[48] In our study, prevention regulatory focus compared to promotion regulatory focus impacted the behavior of statin medication adherence and self-efficacy interacted with patients' motivational intensity to impact the behavior. This study did test the effect of outcome expectations as a moderator in both models; however no significant impact was found.

Applying the concept of regulatory focus to medication adherence and better understanding the mediating and moderating mechanisms involved in the process, helps us identify key variables that affect the behavior. This will help in intervention design to improve medication adherence. For example, if we know that prevention regulatory focus positively impacts statin medication adherence compared to control, pharmacists could frame medication messages with a prevention focus when communicating with patients about their statin

medication in order to activate patients' prevention orientation. In doing so, based on this study's findings, we expect statin medication adherence levels to improve.

Our study's findings also contribute to pharmacy practice. First, our results of prevention regulatory focus, when compared to promotion regulatory focus, leads to positive changes in statin medication adherence levels. Additional studies are needed to compare prevention regulatory focus to control and promotion regulatory focus to control. These studies will help us identify framing strategies for messages. For example, framing messages in terms of prevention - avoiding a risk- may be more effective than framing messages in terms of promotion – approaching a hope or desire related specifically to the behavioral goal, or vice versa. Framing strategies of avoiding risk may take a similar approach to loss framing while those of approaching a hope may take a similar approach to gain framing. Investigating which approach may work best for the behavior of medication adherence in the context of cardiovascular health for different patients will be helpful for pharmacy practice.

Additionally, our findings indicate that insurance coverage for statins is important and that the longer patients take their statin therapy the better. These two factors led to greater behavioral intentions to adhere to medications. Pharmacists as health care professionals that have direct contact with patients have an opportunity to help patients with insurance coverage questions or challenges they may have in regards to continuing on statin therapy for a long period of time to ensure optimal health outcomes. And lastly, focusing on patients' belief in their ability to take their statin medication as indicated, pharmacists' have the opportunity to increase patients' motivational intensity to improve behavior.

Future research needs to test whether prevention regulatory focus positively affects medication adherence for other medications and conditions. For example, the behavior of taking

a statin medication targets reduction of a cardiovascular risk factor to prevent heart disease. Will similar results be found for depression medications or medications treating a cold/virus? These questions will be interesting to be investigated.

In this study, we utilized a technique consisting of priming individuals with framed messages as promotion or prevention. Knowing which orientation affects a specific behavior in a positive way, we can tailor communication with framed messages that match a particular orientation. For example, health care professionals, such as pharmacists, during patient consultation interactions can frame the communication messages as prevention in order to positively affect adherence levels. Additionally, pharmacists may ask patients about their confidence in their ability to take their statin medication as directed. By doing so, if, for example the pharmacist identifies that the problem is a lack of information about the medication, he/she would provide the information to increase patients' self-efficacy beliefs. Increasing patients' self-efficacy beliefs will in turn increase patients' motivational intensity to engage in the behavior; therefore the patient would be more likely to adhere to the medication.

Additionally, next research steps are to develop and test the idea of regulatory focus and strategic means by investigating the effect of fit versus non-fit on the behavior of statin medication adherence. This will provide a better understanding on whether a fit between patients' regulatory focus and a strategic means positively affect the behavior of statin medication adherence or not. Fit studies in other behaviors have proven to improve outcomes, therefore testing whether or not a fit intervention will positively affect the behavior of statin medication adherence will provide us with a simple, yet powerful, intervention technique to improve behavior.

Limitations

Our study has several limitations. One limitation of the study is the generalizability of our results. The findings of the study apply to our sample population consisting of older adults, mostly white, in the higher income bracket, who are part of a university health system. In our study, participants were randomly assigned to the two groups, promotion and prevention. Therefore, it is unlikely that any differences were attributed to preexisting characteristics.

Secondly, in our study comparison of prevention or promotion groups can be done relative to each other. However, in order to be able to conclude how prevention or promotion orientations each operate, inclusion of a control group where neither manipulation is given to patients is needed. This will allow us to identify whether promotion or prevention framed messages are most effective to affect the behavior of statin adherence.

Another limitation of this study is the recall and social desirability biases potentially present. This is due to the nature of data collection method used, as data were collected via questionnaires. Therefore, the potential of failure to remember specific information and the desire to respond differently than the actual reality is possible is possible. It is most likely that the most adherent patients respond to studies; therefore it is more challenging to detect differences among variables between adherent and non-adherent patients.

The strength of our study was measuring the actual behavior of adhering to statin medications. The behavior was measured two weeks after the intervention to test its effects. The levels of adherence in this study were very high. The discrepancy between the published literature results and our findings, may be due to the social desirability and recall bias, or it may be possible that our sample population is adherent to the statin therapy indeed. Statin medication adherence was measured via a single-item, the visual analogue scale (VAS). VAS is proven to be as effective as unannounced pill-counts[58,59] and was chosen to capture adherence levels while

reducing response burden. Including additional items would have increased response burden in this study, but could be pursued in future studies. With different statin medication adherence results we may detect different mediation and moderation relationships between variables of interest. It is also possible that our results may look different for a more diverse population sample in age, gender, race, and income. Our present sample represented mainly white older individuals with moderate to high income.

Conclusion

Patient psychosocial factors, such as patients' regulatory focus, behavioral intentions, and motivational intensity have a significant impact on the behavior of statin medication adherence. Additional patient and medication factors - patients' self-efficacy beliefs, duration of therapy, insurance coverage, and non-prescription medications taken concomitantly with prescription medications – play an essential role influencing patients' behavioral intentions or motivational intensity to engage in the behavior. Our study provides insights for future research on improving the behavior of medication adherence. Specifically, our research provides insights on potential aspects of patient psychosocial factors pharmacists may focus on when interacting with patients or thinking of strategies for interventions to improve patients' medication adherence.

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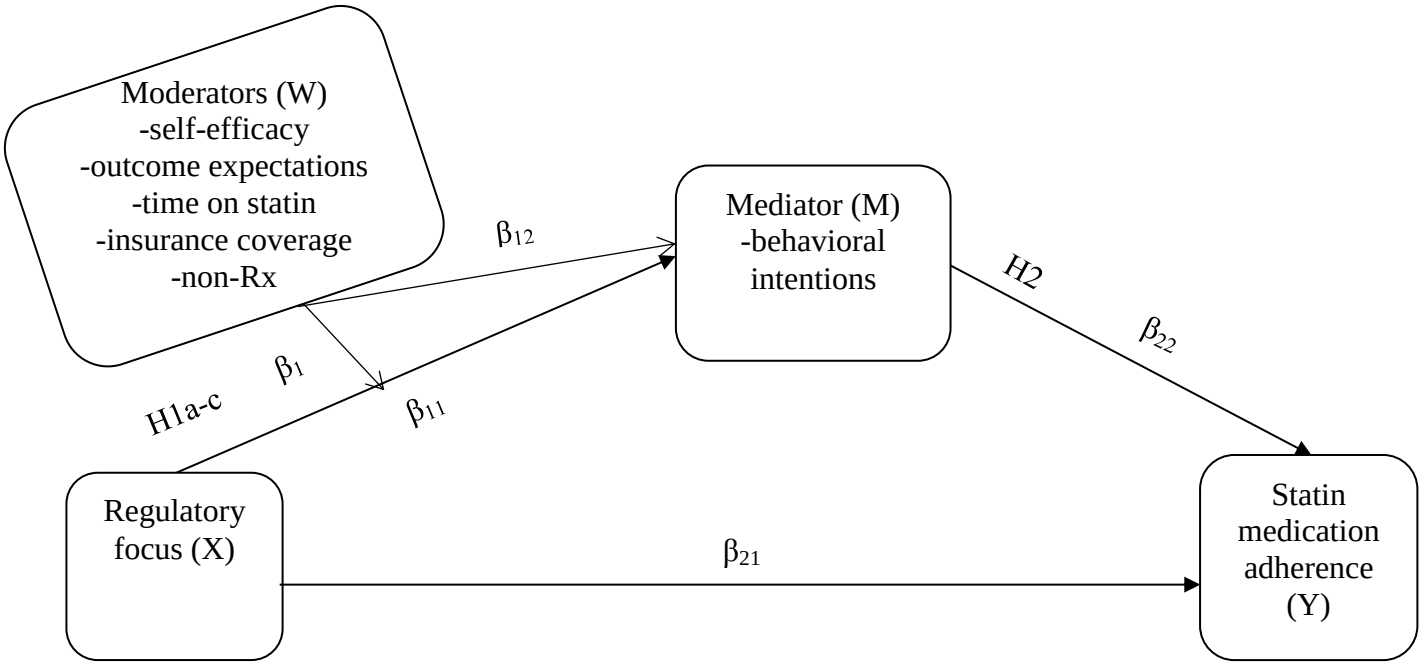
Table 2-1. Respondent Demographic and Clinical Characteristics (N=326)

Characteristic	Percentage
Age	
≥60years	69.3
Gender (Female)	40.2
Race	
White-American	87.1
Income	
≤19,999/year	8.3
$20,000 - $39,000	12.6
$40,000 - $59,999	17.8
$60,000 - $79,999	15.3
$80,000 - $99,000	16.0
≥$100,000/year	25.5
Had heart disease	25.2
Had a heart surgery	11.3
Diagnosed with high cholesterol	93.6
Insurance coverage for cholesterol medication	91.7
Taking a medication for depression	22.1
Time on statin	
1	2.15
2-3	10.4
4-6	27.9
7-10	27.9
≥11	31.6
Number of daily Rx	
1	10.1
2-3	31.0
4-7	43.0
≥8	15.9
Number of non-Rx	
0	14.1
1	24.2
2	21.8
3	13.2
≥4	26.7
Overall Health	
Excellent	17.8
Very good	37.1
Good	33.8
Fair	9.50
Poor	1.80

Rx - prescription medications; non-Rx – non-prescription medications. Note: Chi-square and t-test results indicate that there was no difference found among all these variables between the promotion and prevention groups

Figure 2-1. Theoretical and Analytical Framework for Regulatory Focus Predicting Statin Medication Adherence

a The Conditional Indirect Effect of Regulatory Focus on Statin Medication Adherence with Behavioral Intentions serving as the Mediator



b The Conditional Indirect Effect of Regulatory Focus on Statin Medication Adherence with Motivational Intensity serving as the Mediator

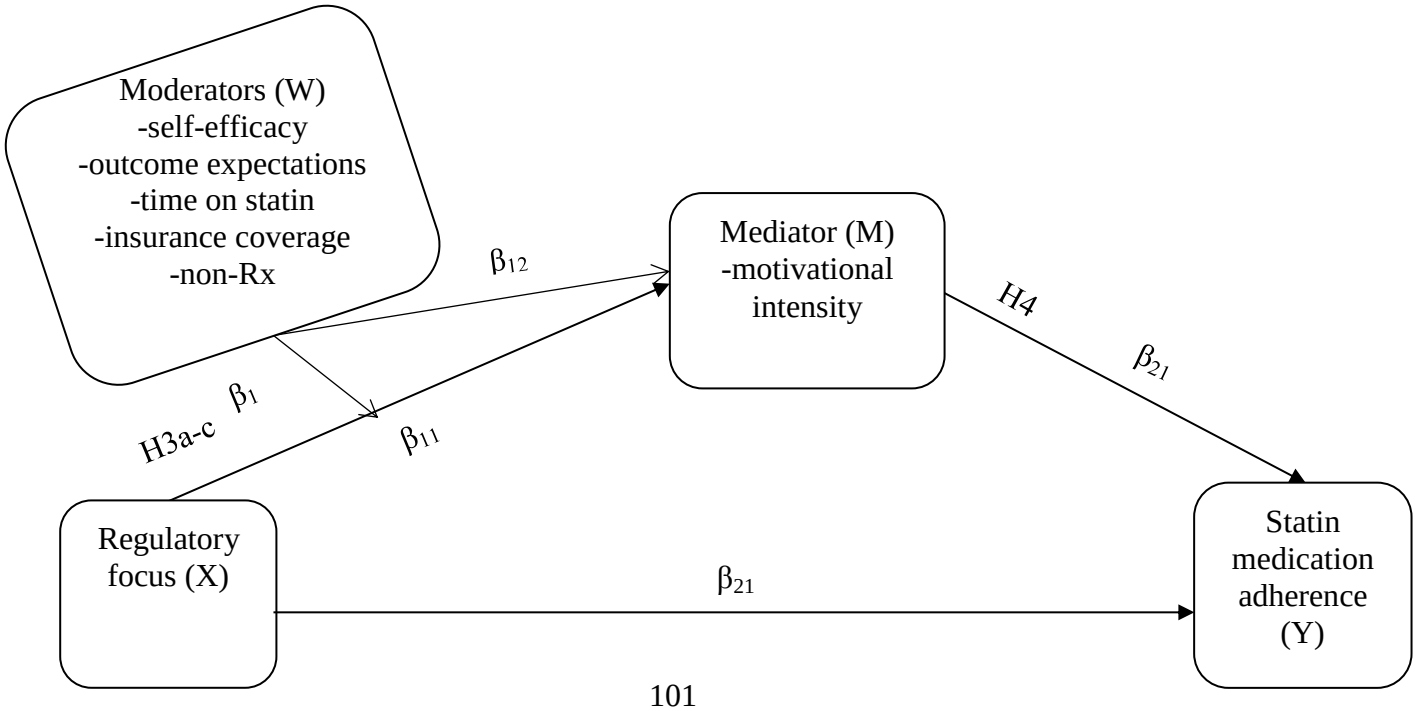


Table 2-2. Conditional Indirect Effect of Regulatory Focus on Statin Medication Adherence with Behavioral Intentions as the Mediator

Moderator (W)	**Self-efficacy**		**Outcome expectancies**		**Time on statin therapy**		**Statin insurance**		**Nr non-Rx med products**	
Mediator Variable Models	R^2=.03, p=.01		R^2=.03, p=.03		R^2=.01, p=.18		R^2=.03, p=.02		R^2=.02, p=.16	
M=β_{10}+β_{11}X+β_{12}W+β_{13}X(W)+ε_1	**b**	**p**	**b**	**p**	**b**	**p**	**b**	**p**	**b**	**p**
X: manipulation β_{11}	.00	.92	.00	.99	.01	.59	.01	.61	.01	.68
W: moderator β_{12}	.08	.00*	.08	.00*	.00	.77	-.12	.19	.03	.03*
X*W: interaction β_{13}	.01	.64	-.01	.64	.01	.03*	.26	.00*	-.00	.89

Outcome variable (Y)	**Statin Medication Adherence (SMA)**	
Outcome Variable Model	R^2=.23, p=.00	
Y=β_{20}+β_{21}X+β_{22}M+ε_2	**b**	**p**
X: manipulation β_{21}	-1.73	.01*
M: behavioral intentions β_{22}	13.84	.00*

*p≥.05; X manipulation, W moderator, M mediator, X*W interaction term

N=326

Table 2-3. Conditional Indirect Effect of Regulatory Focus on Statin Medication Adherence with Motivational Intensity as the Mediator

Moderator (W)	**Self-efficacy**		**Outcome expectancies**		**Time on statin therapy**		**Statin insurance**		**Nr non-Rx med products**	
Mediator Variable Models	R^2=.21, p=.00		R^2=.25, p=.00		R^2=.03, p=.01		R^2=.01, p=.17		R^2=.02, p=.049	
M=β_{10}+β_{11}X+β_{12}W+β_{13}X(W)+ε_1	**b**	**p**	**b**	**p**	**b**	**p**	**b**	**p**	**b**	**p**
X: manipulation β_{11}	-.00	.93	-.02	.52	.05	.22	.04	.34	.04	.35
W: moderator β_{12}	.36	.00*	.41	.00*	.02	.00*	-.26	.10	.02	.42
X*W: interaction β_{13}	.08	.05*	.07	.09	.01	.33	.18	.26	-.05	.01*

Outcome variable (Y)	**Statin Medication Adherence (SMA)**	
Outcome Variable Model	(R^2=.17, p=.00)	
Y=β_{20}+β_{21}X+β_{22}M+ε_2	**b**	**p**
X: manipulation β_{21}	-1.84	.01*
M: behavioral intentions β_{22}	6.93	.00*

*p≥.05; X manipulation, W moderator, M mediator, X*W interaction term

N=326

Table 2-4. Conditional Indirect Effects for Behavioral Intentions and Motivational Intensity as Mediators

Moderators	**SMA (M: Behavioral Intentions)**		**SMA (M: Motivational Intensity)**	
Self-efficacy	Effect	95% CI	Effect	95% CI
W=-1SD (-.97)	-.13	(-2.04, .86)	-.56	(-2.06, .33)
W=0	-.03	(-.83, .63)	-.02	(-.67, .49)
W=+1SD (.97)	.20	(-.28, .99)	.51	(.01, 1.38)*
Outcome expectancy	Effect	95% CI	Effect	95% CI
W=-1SD (-.95)	.17	(-1.76, 1.13)	-.64	(-2.19, .24)
W=0	-.00	(-.90, .59)	-.18	(-.91, .30)
W=+1SD (.95)	-.17	(-.93, .74)	.29	(-.21, 1.08)
Time on statin	Effect	95% CI	Effect	95% CI
W=-1SD (-6.04)	-.58	(-2.13, .30)	.08	(-.94, .93)
W=0	.19	(-.51, .84)	.37	(-.13, 1.08)
W=+1SD (6.04)	.95	(.08, 2.66)*	.67	(-.03, 1.80)
Statin insurance	Effect	95% CI	Effect	95% CI
W=-1SD (-.08)	-.12	(-1.05, .50)	.19	(-45, .85)
W=+1SD (.92)	3.46	(1.07, 7.83)*	1.43	(-.46, 4.30)
Nr non-Rx med	Effect	95% CI	Effect	95% CI
W=-1SD (-2.20)	.19	(-1.07, 1.16)	1.10	(.38, 2.19)*
W=0	.15	(-.67, .77)	.28	(-.28, .92)
W=+1SD (2.20)	.09	(-.57, .71)	-.53	(-1.61, .22)

SMA - statin medication adherence, M – mediator, W – moderator (+1 low, 0 moderate, -1 high, levels), SD - standard error,
Effect – conditional indirect effect, 95% CI – bootstrap 95% confidence intervals for conditional indirect effect, Rx – prescription

N=326

Table 2-5. Regulatory Focus Study Hypotheses and Results

	Hypothesis	**Finding**
H1a	The regulatory focus of a person will influence intentions to engage in the behavior the higher the self-efficacy.	H1a is not supported. (β_{13} =.01, p=.64)
H1b	The regulatory focus of a person will influence intentions to engage in the behavior the higher the outcome expectancies.	H1b is not supported. (β_{13} =-.01, p=.64)
H1c	The regulatory focus of a person will influence intentions to engage in the behavior the longer a person has been on a statin.	H1c is supported. (β_{13} =.01, p=.03*)
H1d	The regulatory focus of a person will influence intentions to engage in the behavior if insurance is present.	H1d is supported. (β_{13} =.26, p=.00*)
H1e	The regulatory focus of a person will influence intentions to engage in the higher the number of non-Rx medication products.	H1e is not supported. (β_{13} =-.00, p=.89)
H2	The stronger the behavioral intentions the greater the statin medication adherence levels.	H2 is supported. (β_{22} =13.84, p=.00*)
H3a	The regulatory focus of a person will influence motivation to engage in the behavior the higher the self-efficacy.	H3a is supported. (β_{13} =.08, p=.05*)
H3b	The regulatory focus of a person will influence motivation to engage in the behavior the higher the outcome expectancies.	H3b is not supported. (β_{13} =.07, p=.09)
H3c	The regulatory focus of a person will influence motivation to engage in the behavior the longer a person has been on a statin.	H3c is not supported. (β_{13} =.01, p=.33)
H3d	The regulatory focus of a person will influence motivation to engage in the behavior if insurance is present.	H3d is not supported. (β_{13} =.18, p=.26)
H3e	The regulatory focus of a person will influence motivation to engage in the behavior the higher the number of non-Rx medication products.	H3e is supported. (β_{13} =-.05, p=.01*)
H4	The stronger the motivational intensity the greater the statin medication adherence levels.	H4 is supported. (β_{22} =6.93, p=.00*)

*p≥.05, H – hypothesis, Rx - prescription

Chapter 3 - **PAPER 2: THE EFFECT OF A REGULATORY FIT INTERVENTION ON STATIN MEDICATION ADHERENCE**

Abstract

Background: Regulatory Fit between a person's orientation and strategic means used to accomplish a goal leads to higher motivation in goal pursuit, to greater enjoyment during the goal pursuit, and to better feelings in the process of decision making. For example, regulatory fit would be achieved when a promotion regulatory orientation matches a promotion strategic approach to achieve a goal; same for prevention. Regulatory fit, applied to various health behaviors from academic writing to cancer detection results in positive outcomes. This principle of regulatory fit has not been yet studied in the behavior of medication adherence. Applications of regulatory fit interventions could improve the behavior of adhering to medications.

Aim: Investigate the effect of a regulatory fit intervention on the behavior of statin medication adherence.

Methods: Patients taking a statin medication participated in a randomized, prospective field experiment. The three study groups were fit, non-fit and control. Patients completed two online questionnaires designed to capture patient variables and deliver the intervention, and two weeks later to assess subsequent behavior. The intervention consisted of manipulations priming patients with framed messages that created a fit or non-fit between patients' motivational orientation and implementation intentions. ANOVA pairwise comparisons were run to determine the significance of between and within group differences.

Results: Patients in the regulatory fit group experienced greater statin medication adherence levels compared to the patients in the non-fit and control groups. When patients' motivational intensity, behavioral intentions, self-efficacy, and outcome expectancies were strong, there was no difference in statin medication adherence levels between the fit, non-fit, and control groups. A statistical significant difference was detected among the fit and non-fit and fit and control groups for the weak condition for both intention and motivation. A difference between only the fit and non-fit groups was seen when patients' outcome expectancies were weak. Regardless of the strength of self-efficacy, there was no difference between any of the groups in statin medication adherence levels. Within group differences between the weak and strong points of intentions and motivation were detected only for the non-fit and control groups.

Conclusions: Patients receiving the Fit intervention had higher statin medication adherence, when patients' intention, motivation, self-efficacy, or outcome expectation were weak. Therefore, there is an opportunity to improve the behavior of statin medication adherence, when patient-related factors are weak, as there were significant differences found between the Fit and Non-fit/Control intervention groups.

Introduction

Goals and the pursuit of goals are part of everyday life for most people. Whether it's pursuing an academic, career, personal, health, or an organizational goal – in its pursuit we make decisions and engage in actions. While exploring how and why individuals are able to manage themselves in goal pursuit, Higgins developed the concept of regulatory focus, proposing two independent human motivational systems that drive goal-directed behaviors.[1-4]

The two human motivational systems defined by Higgins are: promotion and prevention.[1-4] The promotion and prevention orientations operate to meet different human needs. The promotion motivational system operates to meet the survival need of nurturance (nourishment) while the prevention motivational system operates to meet the survival need of obtaining security. Therefore, the promotion focus is characterized by "ideals" which include hopes, wishes, and aspirations as maximal goals to be reached. Prevention focus, on the other hand, is characterized by "oughts" which include duties, obligations, and responsibilities as minimal goals to be met.

The needs of nourishment and security are present in all people in different degrees leading to chronic individual differences, with some individuals being more promotion oriented and others more prevention oriented.[5] Some studies suggest that the two chronic orientations are not bipolar constructs.[4] Therefore, the orientations can be activated momentarily in different situations.[1,5] The activation technique involves manipulating the regulatory orientation via the framing of messages with either promotion or prevention words, also called priming. All people can be primed with both promotion and prevention focus, at different points in time.[5] We utilized this priming technique to activate patients' promotion/prevention orientation.

What is also notable is that when a person's orientation towards a goal – either promotion or prevention – matches the strategy used to pursue a goal, then a state of regulatory fit is produced.[2,5,6] This state of regulatory fit creates a feeling of rightness that leads to higher motivation to engage in the tasks necessary to accomplish a goal. In addition, a state of regulatory fit leads to feeling better, to being more alert about a decision, and to enjoying goal pursuit more.[3]

The regulatory fit theory has been studied in the context of a variety of behaviors, such as physical activity, fruit and vegetable consumption, writing, unhealthy snacking habits, supplementing with omega-3 products, and cancer detection.[7-11] The definition of regulatory fit among studies differs with regulatory focus (promotion and prevention) being constant while the strategy/means used to accomplish the goal varies from tailored outcome messages,[6,7] implementation intentions,[9] or emotions.[11]

While motivation is important, translating goals into actions can be challenging. One strategic self-regulatory tool used to overcome obstacles in goal-pursuit is implementation intentions.[12] Proven to be effective in completing personal goals and in taking immediate action, the mechanism suggested by which implementation intentions do so is via a heightened mental representation of a potential situation which leads to easier recognition, recall, and engagement when the specific situation arises.[12-14] In other words, implementation intentions make action initiation easier by linking a goal-directed response to a situation or situational cues.[12] For example, linking a situation X to behavior Y by thinking *when X occurs, I will perform response Y,* a person will make specific decisions of *when, where, and how* to engage in the behavior, so that action is automatized.[12-14] Specifically to statin medications, a patient would think *when I wake up in the morning, I will take my statin medication as soon as I wake up, in the kitchen, as I prepare my morning coffee/tea.*

Studied in the context of a variety of behaviors, implementation intentions serve as an effective tool in reducing dietary fat intake, in achieving greater weight loss among obese women, in reducing drinking and smoking, in increasing attendance for cervical screening, in increasing physical activity in children, and in increasing the inclusion of healthy foods, such as more fruits in one's diet. [15-24] Moreover, when combining implementation intentions with a

motivational theory-based intervention, such as a decision balance sheet, a dramatic effect in increased exercise behavior was seen.[17,18] Motivational intervention by itself produced significant effects on intentions only, yet not on exercise behavior.[17] Studied in the context of self-monitoring blood glucose, implementation intentions together with implementation desire were found to be mediators between goal intentions and the blood glucose monitoring.[25]

Together with regulatory focus, implementation intentions were studied in the context of the behavior of healthy snacking.[9] A match between implementation intentions and regulatory focus was defined as regulatory fit and a mis-match as non-fit. Findings indicate that formation of implementation intentions that match regulatory orientation results in a state of regulatory fit, which in turn heightens motivational intensity to attain a specific goal. Similarly, our study investigated the effect of implementation intentions together with patients' regulatory focus on the behavior of medication adherence, when a match versus a mis-match exists.

The specific medication adherence behavior in this study was statin medication adherence. Medication adherence is defined as the extent to which a patient takes a prescribed medication according to the prescribed schedule by their health care provider.[26-29] Being adherent to statin medications has proven to be effective in the treatment and prevention of cardiovascular diseases and reducing cardiovascular mortality.[29-31] Despite their effectiveness, patients have challenges in continuing to take statin medications, with adherence rates ranging from 25 to 48%.[31-33] SMA levels, measured as the percentage of patients achieving MPR ≥80%, were reported in the most recent review to be between 18.3% to 91.9%.[34] Statin medication adherence is thus considered a goal behavior.

Predictors to better understand the behavior of statin medication adherence have been studied and identified and include medication,[30,33,35] patient,[29-31,33,36-39] provider,[31,36,37] and system factors.[30,31,33,40] Yet, no one single variable or factor on its own can explain the reason behind statin non-adherence in all patients. Therefore, identifying the factors influencing statin medication adherence for a patient or a group of patients may be a good strategy to start with when thinking of solutions or design of interventions. For this study, we chose to focus on patient psycho-social factors to better understand the behavioral goal of statin medication adherence.

The patient psycho-social factors chosen were motivational intensity, behavioral intentions, self-efficacy, and outcome expectancies. We chose motivational intensity because regulatory fit produces a feeling of rightness and leads to higher motivation.[2] Motivational intensity, to our knowledge, has not yet been investigated in the behavior of medication adherence. This will be the first study to do so. Behavioral intentions are included in our study as they capture a person's motivational factors that influence behavior and are an indication of the effort one will invest in to achieve a goal. Behavioral intentions are part of the Theory of Planned Behavior and it has been used to study medication use.[41-43] Their focus is to predict and explain behavior; however they do so at modest levels of 20 to 30% of variance.[12] Pairing behavioral intentions with implementation intentions, therefore, is essential in helping patients translate their intentions into actions to achieve a goal. We have included both, behavioral intentions and implementation intentions, in this study.

Next, in addition to intentions, we included patient beliefs, such as self-efficacy, and patients' outcome expectancies, to better understand the behavioral goal of taking statin medications as prescribed. Behavior change according to Bandura's Social Learning Theory[44,45]

is a function of the person's beliefs about one's ability to engage in the behavior, termed as self-efficacy (SE), and of the person's expectations about the outcome, termed as outcome expectations (OE).

Self-efficacy, described as the belief in one's abilities to perform in behavioral domains, encompasses personal competencies and self-regulation.[46] Self-efficacy influences directly or acts as a mediator for a variety of behaviors including cigarette smoking cessation, condom use, alcohol use, exercise, recovery from bulimia, weight reduction, coping with severe and chronic illness, recovery from myocardial infarction, and disease management.[45-49] Individuals with higher self-efficacy levels may be more likely to sustain healthy behaviors.[49]

Self-efficacy is also known to predict medication adherence to some medications as several measures have been designed to assess the concept of self-efficacy in certain conditions and in specific populations. Examples of such measures are MASES – Medication Adherence Self-Efficacy Scale in hypertensive African Americans,[50] LTMBSES – Long-Term Medication Behavior Self-Efficacy Scale tested in adhering to an immunosuppressive regimen,[51] SEAMS – Self-efficacy for Appropriate Medication Use developed to assess medication self-efficacy in chronic disease management,[52] MUSE- the Medication Understanding and USE Self-Efficacy Scale to determined medication use,[53] SEOMA – Self-Efficacy for osteoporosis medication adherence.[54] OEOMA – Outcome Expectations for osteoporosis medication adherence was developed and tested as a reliable and valid measure of medication adherence.[54] Self-efficacy beliefs and outcome expectancies are both predictors of behavioral intentions[55] and of behavior change.[45,56] Investigating the role of self-efficacy and outcome expectancies on the behavior of statin medication adherence as moderators will help us better understand how psycho-social

factors affect the behavior of adhering to medications. This in turn will help us design better interventions targeted to improve medication adherence.

In summary, this study designed an intervention based on the Regulatory Fit Theory and tested it on the behavior of adhering to statin medications. The objective of the study was investigate how Regulatory Fit affects the behavior of statin medication adherence compared to Non-Fit and Control considering several patient psycho-social factors serving as mediators or moderators. Regulatory Fit was defined as a match between one's manipulated regulatory orientation and framed implementation intentions. The study's hypotheses are the following:

H1: There is no difference between regulatory Fit, Non-Fit, and Control groups when it comes to statin medication adherence at weak versus strong variables of motivational intensity, behavioral intentions, self-efficacy, and outcome expectations.

H2: There is no difference between the weak and strong motivational intensity/behavioral intentions/self-efficacy/outcome expectations variable groups when it comes to statin medication adherence within each of the regulatory Fit, Non-Fit, and Control group.

Methods

Design

The effect of regulatory fit and non-fit was evaluated in older adults taking a statin medication as part of a field experiment using a randomized design (Figure 3.1). The experiment consisted of two Qualtrics® questionnaires with priming manipulations. The manipulations in this study were priming patients' regulatory focus and formed implementation intentions. Specifically, the priming technique consisted of framing messages as either promotion or prevention.

Patients were randomly assigned by the Qualtrics® survey system into two groups, promotion or prevention. The promotion group was primed with promotion framed messages, while the prevention group was primed with prevention framed messages. The formation of implementation intention plans was manipulated as well. Patients in the two orientation groups, promotion and prevention, were randomly assigned by the Qualtrics® survey system into three groups: promotion implementation intentions, prevention implementation intentions, and no implementation intentions.

The research study was approved by the University's Institutional Review Board (Appendix D).

Participants

Participants in the study were recruited from the University of Michigan Health System. The inclusion criteria for the study were being 18 years of age or higher, ability to speak English, and taking a statin medication at the time of participation in the study.

Data Collection

Data were collected via two online Qualtrics® questionnaires. A cover letter was mailed to 1,700 potential participants meeting the inclusion criteria inviting them to participate in the study. The letter, addressed to each patient, described the purpose of the study and an invitation to participate. A link to survey one was provided in each cover letter and a $2 bill was included as an incentive. Patients who chose to participate and completed survey one received a $20 visa gift card in the mail as an appreciation for their time and participation. Patients who completed survey one were invited to complete survey two by asking them to provide an email address.

Survey two was emailed two week later, and patients who completed survey two received an additional $5 reward.

Questionnaires (Appendices A and B)

The two questionnaires were designed based on theories and concepts used in the social-psychology and pharmacy fields to better understand goal-pursuit and behavior change. Specifically, the regulatory focus and fit concepts were based on the regulatory focus[1-4] and regulatory fit theories,[2,5,6] respectively. The concept of behavioral intentions was derived from the theory of planned behavior.[43] The concepts of self-efficacy and outcome expectancies were derived from Bandura's social learning theory.[44,45]

Questionnaire one was distributed via Qualtrics® and consisted of 47 questions for the promotion and prevention groups and of 45 for the control group. It included questions that determined eligibility to participate in the study, questions about medications and overall health, and demographic questions. Patients were asked two questions to determine their statin medication adherence via the visual analogue rating scale.[57,58] Patients' regulatory focus was primed via two questions and then measured with the promotion or prevention regulatory focus questions. The regulatory focus questions were derived from the Regulatory Focus Questionnaire designed by Higgins and modified by Bagozzi.[3,9] Patients' intentions, motivation, self-efficacy, and outcome expectations were measured with two questions each. Patients were primed with implementation intentions framed as either promotion or prevention. One group of patients served as the control group, therefore receiving no implementation intentions.

Questionnaire two consisted of four questions. Similarly to the first questionnaire, two questions measured the behavior of statin medication adherence via the visual analogue rating

scale (VAS).[57,58] Question three was designed to capture potential reasons for statin medication non-adherence. And the last question asked patients of their intention to adhere to their statin medication in the next two weeks.

Measures

Regulatory Focus (RF). Regulatory focus was manipulated. Manipulation consisted of priming patients with two promotion or two prevention framed questions. The promotion framed questions asked patients to *think about **past** and **present** hopes, aspirations, and dreams* and list three of them. The prevention framed questions asked patients to *think about **past** and **present** duties, obligations, and responsibilities* and list three of them. Question one for each manipulation focused on the past and question two focused on the present. The success of the manipulation was checked with nine promotion or prevention questions derived from the Regulatory Focus Questionnaire (RFQ) and designed by Bagozzi.[3,9] Seven-point scales with response options from (1) *Does not describe me at all* to (7) *Describes me extremely well* were used. The 18 item Regulatory Focus Questionnaire was inspired from the original 11 items RFQ developed by Higgins (α=0.91 for the promotion scale; α=0.93 for the prevention scale).[3,9] Higgins' RFQ was modified by eliminating the parental oriented questions such as "how often did you obey rules and regulations that were established by your parents?" so that the questionnaire is applicable to adult sample populations. A sample item of promotion-focus scale is "I am typically able to get what I want out of life" and a sample item of prevention-focus scale is "I frequently think about how I can prevent failures in my life".

Implementation Intentions (ii). The formation of implementation intention plans has been studied and applied in other studies.[12-14] In this study, implementation intentions were manipulated by framing implementation intention messages as promotion, prevention, or none.

The promotion and prevention implementation groups each received two questions framed as either promotion or prevention. The control group did not receive any implementation intention questions.

In the first question the promotion implementation intentions group was asked to think of the *benefits* of taking their cholesterol medication and to list at least three things that they could do that could help them to *take* their cholesterol medication. In the second question, then they were asked to imagine *when, where, with whom,* and *in what situations* they will *take* their statin medication. The prevention implementation intention group was asked to think of the *drawbacks* of not taking their cholesterol medication and list three things they could do that would help to *avoid not taking* their cholesterol medication.

Regulatory Fit (RFit). Regulatory Fit in this study was manipulated and defined as the match between a patient's orientation (RF) and implementation intentions. A fit was experienced when a patient with a promotion orientation formed promotion implementation intentions or when a patient with a prevention orientation formed prevention implementation intentions. A misfit was experienced when a patient with a promotion orientation formed prevention implementation intentions or when a patient with a prevention orientation formed promotion implementation intentions. Fit was coded 1, Non-Fit -1, and control 0. Control represented groups that formed no implementation intentions.

Behavioral Intention (BI). Behavioral intention was assessed via two questions in this study. Participants were asked on a scale from *strongly disagree* to *strongly agree* to answer two questions on intending and planning to take their cholesterol medication as prescribed during the next 2 weeks. The behavioral intentions variable was further dichotomized by averaging *strongly*

disagree, disagree, neither disagree/agree as together as 'weak' and averaging *agree* and *strongly agree* as 'strong'. The effect of regulatory fit on statin medication adherence was tested when behavioral intentions were strong versus weak.

Motivational Intensity (MI). Motivational intensity was assessed via two questions in this study. MI was measured via two constructed questions asking participants how *motivated* and *determined* they are to take their cholesterol medication as prescribed. The response options ranged from *not at all* to *extremely*. Motivational intensity was dichotomized by averaging *not at all, somewhat, and moderately* together as 'weak' and *very and extremely* as 'strong'. The effect of regulatory fit on statin medication adherence was tested when motivational intensity was strong versus weak.

Self-efficacy (SE). Self-efficacy was assessed via two constructed questions asking patients how *confident* and *certain* they are in their ability to take their cholesterol medication as directed. Response options ranged from *not at all* to *extremely confident* for each question. Self-efficacy was dichotomized by averaging *not at all, somewhat, and moderately* together as 'weak' and *very and extremely* as 'strong". The effect of regulatory fit on statin medication adherence was tested when self-efficacy was strong versus weak.

Outcome Expectancies (OE). Outcome expectancies was assessed via two questions by asking patients how *promising* or *likely* is that their heart will improve or their risk for heart disease will be reduced if cholesterol medication will be taken as directed. Response options range from *not at all* to *extremely certain*. Outcome expectancies was dichotomized by averaging *not at all, somewhat, and moderately* together as 'weak' and *very and extremely* as 'strong". The effect of

regulatory fit on statin medication adherence was tested when a patient's outcome expectations were strong versus weak.

Statin Medication Adherence (SMA). Statin medication adherence was measured via the two surveys at baseline and two weeks later. The item used to collect data on statin medication adherence was the single-item visual analogue rating scale (VAS).[57,58] The VAS has been successfully tested and used to measure adherence to antiretroviral therapy.[59] VAS is a single item visual analogue scale that asks individuals to estimate along a continuum the percentage of medication dosages taken as prescribed during a specified period of time. The continuum ranges from 0% to 100% of medication doses taken as prescribed. VAS, administrated via a computer, demonstrated adherence estimates that paralleled unannounced pill counts, electronic medication monitoring, unannounced monthly pill counts, and self-reported recall.[57,58]

Other Variables. Demographic variables such as gender, age, race, and income were collected in this study. Data on clinical variables such as having a diagnosis of heart disease, high cholesterol, had heart surgery, currently taking a statin medication, the length of time being on the statin medication, insurance coverage, number of Rx medications taken daily, number of over the counter products, and perceived overall health were collected as well.

Summary Design (Figure 3.1) The simple effect analysis variables can be summarized as follows:

1) manipulated variable RFit (X): defined as the match/fit between a patient's regulatory focus orientation and implementation intention plans. Fit was coded 1, Non-Fit -1, and Control 0. Control represented groups that formed no implementation intentions,

2) categorical independent variables: motivational intensity (MI), behavioral intentions (BI), self-efficacy (SE), and outcome expectancies (OE),

3) one continuous outcome variable (Y): statin medication adherence (SMA).

Analysis

For analysis, descriptive and frequency distributions were computed to describe demographics and health characteristics. Behavioral intentions, motivational intensity, self-efficacy, and outcome expectancies were recoded as 'strong' and 'weak'. A 2 (independent variable: weak vs strong) x 3 (Regulatory: Fit vs Non-Fit vs Control) ANOVA with statin medication adherence (SMA) as the dependent variable was conducted. Pairwise comparisons were run to determine the significance of differences between groups. For each of the 'weak' and 'strong' groups, it was tested whether there was a statistical significant difference in statin medication adherence between the Fit, Non-Fit, and Control groups.

Results

A total of 1700 patients from a university affiliated health system were invited to participate in the study; responses were received from 555 patients to questionnaire one and to both questionnaire from 326 patients. Differences in variables of interest were tested between respondents to both questionnaires and those who responded to only questionnaire one. Results indicated a significant difference between respondents and non-respondents in health insurance (Appendix E). Table 3.1 presents patient demographic and clinical characteristics. The majority of patients (69.32%) were 60 years of age or higher and identified themselves as white (87.17%). Patients' economic status represented in terms of income ranged from ≤$19k/year (9.2%) to $100k/year or ≥ (24.2%); about half of participants had an income of $60k/year or greater. The

majority of patients (88.65%) reported to be very good to excellent overall health. A total of 93.56% reported a high cholesterol diagnosis, with 25.15% having a heart disease/condition and 11.35% reported to have experienced heart surgery. The respondents were on a statin medication for a long period of time, for up to 30 years and they were taking other prescription medications in addition to the statin. There was no significant difference between the Fit, Non-Fit, and Control groups in demographics or clinical characteristics.

Overall, the mean for Statin medication adherence (SMA) at two weeks was 96.3% ± 13.74; while at baseline was 95.67% ± 14.21. The dependent variable was skewed, and it was transformed via a two-step approach and a log-transformation. Both transformations resulted in slightly better results towards normality; however, the results were not statistically significant (indicated by the Kolmogorov-Smirnov and Shapiro-Wilk tests). Therefore, we used the original statin medication adherence results for analyses. For each group, SMA was the following: SMA (Fit) = 98.25%, SMA (Non-Fit) = 95.64%, SMA (Control) = 94.89% ($F=1.81$, $p=.165$). The behavior of statin medication adherence (SMA) was predicted as a function of regulatory fit (RFit) and independent variables, including motivational intensity (MI), behavioral intentions (BI), self-efficacy (SE), and outcome expectations (OE). In addition to statin medication adherence, intentions were explored as a possible dependent variable. Intentions' distribution was skewed (mean 4.85 ± .524); therefore the behavior of adhering to statin medication was chosen as the dependent variable. The average promotion and prevention scores were calculated to test whether manipulation worked. The manipulation was successful: RF (promotion) average score was 5.02 (.90) and RF (prevention) average score was 5.65 (.79).

Figure 3.2 and Table 3.2 represent the results of the ANOVA analysis of the difference between groups (H1). When patients' motivational intensity, behavioral intentions, self-efficacy,

and outcome expectations were strong, there was no difference in statin medication adherence levels between the Fit, Non-Fit, and Control groups. When patients' motivational intensity and behavioral intentions were weak, statin medication adherence in the Fit group was higher than in the Non-Fit and in the Control group. There was no statistically significant difference between the Non-Fit and Control groups. When patients' self-efficacy was weak, there was no difference between any of the groups in statin medication adherence levels. When patients' outcome expectations were weak, statin medication adherence was higher in Fit versus Non-Fit group ($p=.023$).

Table 3.3 represents the results of the ANOVA analysis of the differences within groups (H2). There is a statistical significant difference for the Non-Fit and Control groups for patients who have weak versus strong motivational intensity and behavioral intentions, but not for weak versus strong self-efficacy. Weak versus strong outcome expectations were significant only in the Non-Fit condition. For the Fit group, there is no difference for patients with weak and strong aspects of all variables.

Discussion

This study examined the effect of a fit intervention on the behavior of statin medication adherence. Specifically, the intervention was designed to examine potential strategies patients may use in their decision-making process to engage in the behavioral goal of adhering to their statin medication. The strategic compatibility between patients' regulatory focus and formed implementation intentions was tested in this intervention.

Findings indicate that patients who experienced a Fit versus Non-Fit or versus Control had greater statin medication adherence levels at weak psychosocial factors such as motivational

intensity, behavioral intentions, and outcome expectations. When these patient psychosocial factors were strong, there was no statistical significant difference in statin medication adherence levels among the groups. Additionally, findings suggest that when patients' self-efficacy is weak or strong there is no difference in statin medication adherence levels between the Fit, Non-Fit, and Control groups. These findings indicate that when patients' motivational intensity, behavioral intentions, and outcome expectations are weak, there is an opportunity to improve statin medication adherence via a Fit intervention.

The results of this Fit intervention are similar with findings from with previous regulatory fit studies.[1,6-9,11] The Fit intervention consisted of matching patients' primed regulatory focus with framed implementation intentions. Implementation intentions served as strategic means to patients' regulatory focus. Other studies have utilized strategic means such as framing health outcomes,[6] tailoring messages,[7,8] taking on eagerness versus strategic approach,[6] thrill versus worry emotional approaches,[11] and framed implementation intentions.[9] Regardless of the strategic means chosen in each study, the suitability of strategic means to patients' regulatory orientation is what created a 'value from fit'.[4] This 'value from fit' effect led to a feeling of rightness in the decision-making process, increased motivation to engage in the specific behavior, and feeling better and more alert about the decision.[4] In the context of the behavior of choice of this study, statin medication adherence, when experiencing a fit, patients would be more likely to be motivated to take their medication and feel better as a result of making the decision to take their medication as directed by their health care provider.

Patients' regulatory focus in this study was manipulated. Other studies manipulated participants' regulatory focus as well,[7,9,11] while others measured participants' chronic regulatory focus.[6,8] One study measured participants chronic regulatory focus and also manipulated it;

similar findings were reported for the two.[9] Since the effect of both measured and manipulated regulatory focus was found to be similar, we chose to test the effect of patients' manipulated regulatory focus with promotion and prevention framing messages on the behavior of statin medication adherence. Testing the effects of this priming manipulation on the behavior of statin medication adherence provides us with an intervention tool that can be applied to improve adherence behavior.

This study adds value to the body of research as it is the first study to investigate the effect of the regulatory fit theory on the behavior of statin medication adherence. This study took on an intervention approach of manipulating both regulatory focus and implementation intentions. One study investigated the behavior of healthy snacking behavior with a similar approach and had some similar findings to this study.[9] Findings indicate that, similarly to statin medication adherence, the snacking behavior was affected differently at weak versus strong unhealthy snacking habits. The difference being that the healthy snacking behavior was changed only at strong unhealthy habits when there was a fit, while at weak habits the behavior was changed either when there was a fit or non-fit. For the behavior of statin medication adherence, at weak patient psychosocial factors the behavior was greater for the fit versus non-fit and versus control, while at strong psychosocial factors the behavior of adhering to medications was similar among the groups. These findings indicate that a fit intervention is most effective when unhealthy habits are strong and psychosocial factors are weak; hence, more potential for behavior change. Applying the theory of regulatory fit via similar fit interventions to other medications and/or conditions will help us better understand whether patients' self-regulatory processes are similar or different in their decision-making process to take and adhere to their medications.

More recent research in medication adherence trajectories is promising. Trajectories of non-adherence identified for coronary heart disease, for example are: 1) nearly always adherent patients, 2) an early gap in adherence with a later recovery, 3) brief gaps in medication use or occasional users, 4) a slow decline in adherence, and 5) a fast decline.[60] Predictions of statin adherence trajectories were identified based on patterns of statin filling over a year following therapy initiation.[61] The best prediction trajectory was using 3 months statin initial adherence and worst using just baseline variables. Future studies investigating how our results may be similar or different by trajectories of statin adherence are needed in order to identify how patient psychosocial factors impact adherence levels at different stages during therapy.

Implications for pharmacy practice can be drawn from the results of the fit intervention. Specifically, the fit design presents an opportunity for future tailored communication between the health care provider and the patient. The communication would be tailored to be patient specific according to each patient's regulatory focus (chronic or manipulated). In this context, considering the behavior of statin medication adherence, pharmacists would tailor their communication by framing strategic means to match patients' orientation. This approach can be applied during a patient consultation or during a motivational interview session. Both encounters are opportunities for pharmacists to tap into the motivational sources for patients' decision to engage in the behavior of taking their statin medication. In either encounter, pharmacists would inquire about patients' goals as a result of taking the medication and based on answers received would tailor communication. For example, if the patient states his/her goal being to avoid a stroke event as a result of taking the statin medication, then the pharmacist would tailor their response as 'avoid stroke, as a result of taking the statin medication'; this representing a prevention fit communication between pharmacist and the patient. However, if the patient thinks

in terms of promotion outcomes, as a result of chronic or manipulated promotion regulatory focus orientation, the pharmacist would tailor communication accordingly. A promotion cardiovascular goal may be to 'improve heart health and live a long life to see my great grandkids'. Another approach pharmacists may use is to assess patients' motivational intensity, behavioral intentions, and outcome expectations in regards to their behavior of taking their medication. If those are high, then there is no need to tailor communication. However if they are low, pharmacists have an opportunity to tap into patients' intrinsic motivational factors and help them move towards positive medication adherence behavior change via tailored 'fit' communication.

Future studies investigating the effect of fit interventions in various medications and disease conditions will provide us with insights to design messages for patients that will improve behavior change for each medication and condition. These fit interventions can be designed to deliver tailored communication face-to-face or via mobile technologies. The goal of positive behavior change is to improve patients' overall health and well-being.

Limitations of this study include the potential patient response bias in the questionnaires. The statin medication adherence levels in this study are high compared to the previously reported statin adherence levels. This may be due to the self-report nature of the study leading to over-reporting due to potential social desirability to indicate high adherence values or potentially due to recall bias leading to patients inaccurately remembering their adherence behavior. It may also be likely that patients participating in the study were more inclined to seek engagement in various health behaviors, including taking statin medications, in pursuit of improving their cardiovascular and overall health. Furthermore, statin medication adherence was measured via the visual analogue scale (VAS), consisting of a single item. This measure was chosen to capture

the adherence levels while reducing response burden. Including additional items could be pursued in future studies, but would increase response burden. With different statin medication adherence levels, we may detect different results.

Study generalizability is another limitation. The results of this study are applicable for one segment of a specific population, specifically patients on a statin medication in a specific geographical area. It is likely, that given a more diverse population sample, our results may have been different. For example, a different distribution in race and income may result in different statin medication adherence levels as well as different levels in behavioral intentions, motivational intensity, self-efficacy, and outcome expectations. Our study design did include randomizing patients to different groups and assessed behavior two weeks after delivering the regulatory fit intervention. Therefore, the generalizability of the results from our controlled study to a similar sample of patients is scientifically sound. Potential future research applications are to test the effect of Regulatory Fit interventions in other medications and patient populations and design tailored messages delivered by pharmacists face-to-face or via mobile technologies.

Conclusions

The regulatory fit intervention resulted in higher statin medication adherence levels for the fit versus the non-fit and versus the control groups. Furthermore, when patients' behavioral intentions, motivational intensity, and outcome expectations were weak, differences in statin medication adherence levels between the fit and non-fit and between the fit and control groups were significant, presenting an opportunity for adherence improvement via interventions. Future research expanding the effect of regulatory fit for various medications and patient populations is needed. Pharmacists have a unique opportunity to apply regulatory fit interventions in their practice to improve the behavior of medication adherence.

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Table 3-1. Patient Demographic and Clinical Characteristics by Intervention Group

Variable	Fit	Non-Fit	Control	Total	
Sample size	112	110	104	326	p-value
Demographics					
Age (≥60y)	69.64%	70.00%	68.27%	69.32%	.715
Female	40.18%	38.18%	42.31%	40.18%	.828
White	88.39%	89.09%	83.65%	87.17%	.937
Income (>60k)	57.94% (n=107)	67.62% (n=105)	52.52% (n=99)	59.49%	.384
Clinical					
Heart disease (yes)	28.57%	21.82%	25.00%	25.15%	.645
Heart surgery (yes)	11.61%	12.73%	9.61%	11.35%	.644
High cholesterol (yes)	90.18%	94.54%	96.15%	93.56%	.196
Depression meds (yes)	22.32%	19.09%	25.00%	22.09%	.580
Rx ≤ 5	73.21%	72.73%	61.54%	69.32%	.147
Time on statin ≤10y	74.11%	64.54%	66.35%	68.40%	.135
Overall health (good to excellent)	86.61%	91.82%	87.50%	88.65%	.760

*p<.05

Table 3-2. Mean Differences in Statin Medication Adherence between Weak and Strong variables at Different Points of Fit

Variable	**Weak**		**Strong**	
	mean diff (se)	p-value	mean diff (se)	p-value
Motivational Intensity				
Fit : Non-Fit	14.3 (3.73)	.000*	.293 (1.87)	.875
Fit : Control	17.4 (4.36)	.000*	2.19 (1.86)	.240
Non-Fit : Control	3.12 (4.53)	.492	1.89 (1.84)	.304
Behavioral Intentions				
Fit : Non-Fit	29.5 (8.82)	.001*	1.60 (1.70)	.349
Fit : Control	54.5 (9.52)	.000*	1.83 (1.73)	.289
Non-Fit : Control	25.0 (9.52)	.009	.236 (1.73)	.892
Self-efficacy				
Fit : Non-Fit	4.00 (2.30)	.083	.77 (3.04)	.801
Fit : Control	3.90 (2.38)	.102	3.14 (3.00)	.296
Non-Fit : Control	-.10 (2.43)	.968	2.38 (2.91)	.414
Outcome Expectancies				
Fit : Non-Fit	5.62 (2.45)	.023*	-.598 (2.73)	.827
Fit : Control	3.77 (2.45)	.125	2.89 (2.82)	.305
Non-Fit : Control	-1.84 (2.52)	.465	3.49 (2.75)	.205

mean diff – mean difference, se – standard error, *p<.05

Table 3-3. Mean Differences in Statin Medication Adherence between the Fit, Non-Fit, and Control groups at Weak and Strong Variables

Variable (weak vs strong)	Fit		Non-Fit		Control	
	mean diff (se)	p	mean diff (se)	p	mean diff (se)	p
Motivational Intensity	-5.47 (2.82)	.053	-19.48 (3.07)	.000*	-20.70 (3.81)	.000*
Behavioral Intentions	.259 (6.35)	.967	-27.64 (6.35)	.000*	-52.41 (7.30)	.000*
Self-Efficacy	-2.33 (2.72)	.393	-5.56 (2.66)	.038	-3.08 (2.70)	.254
Outcome Expectancies	-1.25 (2.60)	.629	-7.47 (2.59)	.004*	-2.14 (2.68)	.426

*p<.05

Figure 3-1. Study Design

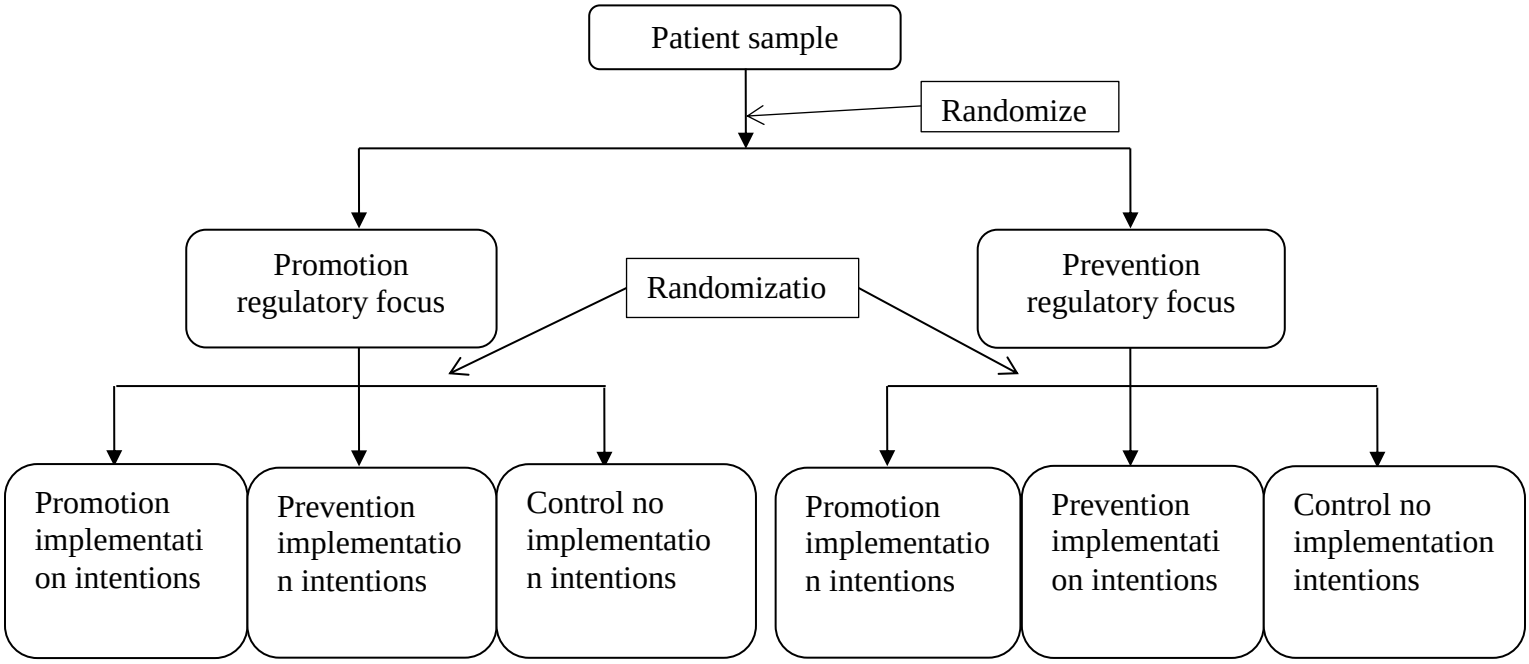
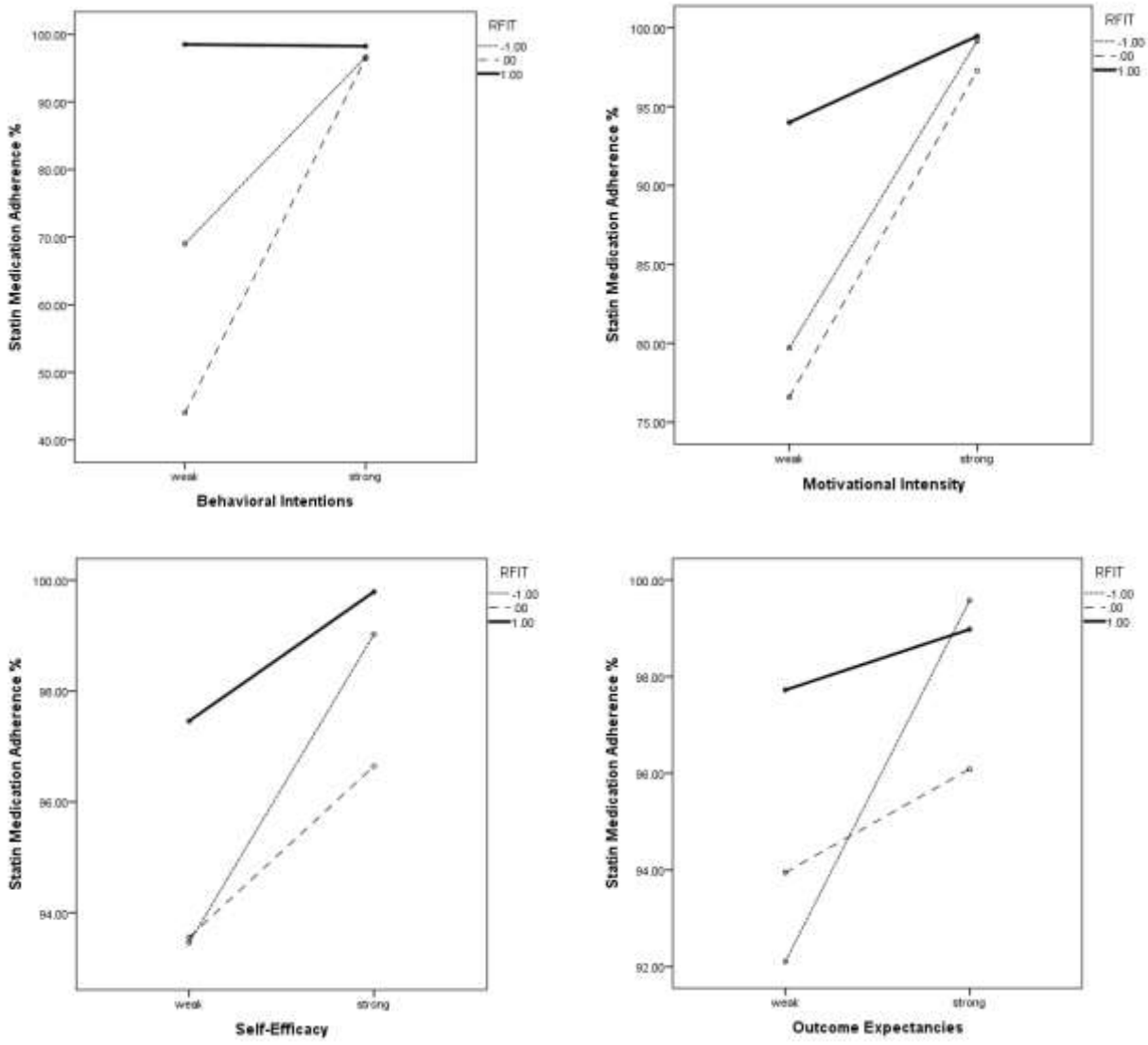


Figure 3-2. Statin Medication Adherence as a Function of Regulatory Fit and Patient Psychosocial Variables



Chapter 4 - **PAPER 3: OPTIMISM'S EFFECT ON STATIN MEDICATION ADHERENCE**

Abstract

Background: Optimism is linked to positive outcomes in a variety of behaviors, including cardiovascular health and medication adherence. The mechanisms via which it does so are not yet understood. This is important because it may provide a better understanding for future intervention design to improve health behaviors.

Aim: To test the conditional indirect effect of optimism on statin medication adherence with various psychosocial factors mediating and moderating the relationship as potential mechanisms.

Methods: Adults on a statin medication proficient in English were recruited from a Midwestern academic health system to participate in the study. Patients who agreed to participate completed two questionnaires assessing various psycho-social factors in questionnaire one and the behavior of statin medication adherence in questionnaire two. Optimism was measured via the Life Orientation Test Revised tool. The effect of optimism on statin medication adherence was determined via a conditional indirect effect using the PROCESS macro tool.

Results: The conditional indirect effect of optimism on statin medication adherence with behavioral intentions serving as the mediator and low-to-moderate levels of self-efficacy or outcome expectation levels serving as the moderator was statistically significant. Similarly, the conditional indirect effect of optimism on statin medication adherence with motivational

intensity intentions serving as the mediator and low-to-moderate levels of self-efficacy or outcome expectation levels serving as the moderator was statistically significant.

Conclusion: Optimism affected the behavior of statin medication adherence via a conditional indirect effect with various patient psychosocial factors serving as mediators and moderators. This is a novel predictor for statin medication adherence that should be considered when designing interventions to improve medication adherence. Furthermore, our research provides a framework for potential mechanisms via which optimism affects behavior.

Introduction

Optimism, an inherent part of human nature, is a beneficial psychological characteristic defined as the global expectancy that good things will be plentiful in the future and bad things scarce.[1,2] This personality variable categorizes people as optimists or pessimists, with a range from very optimistic to very pessimistic. Optimists expect good things to happen to them while pessimists expect the opposite.[2] Optimism is known to influence a variety of behaviors.

Research indicates that optimism is associated with greater persistence in educational, athletic, military, occupational, and political success; benefits in the socioeconomic world; better relationships; popularity; better health; and with long life. [1,2] Specifically to health behavioral outcomes, optimism is linked to higher levels of engagement coping, better subjective well-being in times of difficulty, and to greater likelihood of taking proactive steps to protect one's health.[2] In the context of cardiovascular health, optimism is associated with reduced pain, distress, and cardiovascular reactivity in healthy adults primed with neutral words.[3] For older adults, optimism has a protective effect on all-cause cardiovascular mortality and the risk of stroke is lower for optimists compared to pessimists.[4,5]

Being optimistic is associated with positive outcomes for patients who have experienced one or more cardiovascular events. Specifically, optimism is associated with a faster rate of physical recovery after coronary artery bypass graft (CABG) surgery during the period of rehospitalization, with a faster rate of return to normal life activities once discharged from the hospital, and with lower rates of rehospitalization after CABG surgery.[6] Moreover, being optimistic is linked to higher response rates to depression treatment in depressed post-CABG surgery patients,[7] and to greater success in achieving lower levels of saturated fat, body fat, global coronary risk, and higher aerobic capacity in cardiac patients.[8]

Optimism is a patient characteristic that has been studied little in in the context of medication adherence. There is one study that investigated the effect of optimism on medication adherence in a sample population of people living with HIV/AIDS.[9] The finding of this dissertation research study indicates that optimism is positively associated with medication adherence. Additional factors suggested to influence this relationship are presence of depression, quality of life and self-efficacy. The mechanisms of optimism's effect on the behavior medication adherence, however, are not yet examined. Therefore, this study will serve as a foundational research in better understanding the mechanisms via which optimism affects the behavior of statin medication adherence.

Approximately 50% of patients with cardiovascular disease are reported to have poor medication adherence.[10] Aligned with the American Heart Association's goal of improving the cardiovascular health of Americans by 10% by the year 2020, [11,12] we are interested in improving the cardiovascular health of patients. Specifically, we are focusing on improving one of the cardiovascular health behaviors patients must engage in to achieve cardiovascular health, that is

attaining cholesterol levels of <200mg/Dl.[12] One pathway to achieve this goal is taking a statin medication. Therefore, our focus is on investigating the behavior of statin medication adherence.

The behavior of medication adherence is an important behavior of focus for several reasons. One, with 50% of patients in the US not taking their medications as prescribed,[13] medication nonadherence is costing the US between $100 to $300 billion USD annually of avoidable health care costs.[10] In addition to increased health care costs, other negative consequences of medication nonadherence are worsening of condition, increased comorbid diseases, higher hospitalization rates, and death.[14] Better medication adherence leads to positive outcomes. Examples include lower hospitalization rates and cost offsets of medical costs for some chronic conditions,[15] lower rates of major adverse cardiovascular events and cost savings,[16] and improved health outcomes and reduced annual costs for secondary prevention of coronary artery disease.[17] Therefore, improving the behavior of medication adherence is a worthwhile goal.

Adhering to statin therapy is an important clinical issue as statin medications have shown to play an essential role in the treatment and prevention of heart disease.[18,19] Despite being safe and effective in reducing cardiovascular mortality and morbidity, half of patients discontinue therapy within the first year and statin adherence levels are reported to be as low as 25% and as high as 48%.[18,19,20] The most recent review documents statin medication adherence levels between 18.3% to 91.9%; SMA was measured as the percentage of patients achieving MPR ≥80%.[21] Consequences for medication non-adherence are poor outcomes, increased healthcare utilization, and increased overall costs; specifically, non-adherence for cardiovascular medications consequences are increased risks of morbidity and mortality.[22] Reasons for statin nonadherence are multifactorial and complex, ranging from patient to health care system

factors.[19,22] Specific examples for statin discontinuation include adverse effects, lack of efficacy, motivation, cost, polypharmacy, drug interactions, age, ethnicity, gender, type of exercise, presence of other diseases, adverse publicity in the media, and others.[23]

This study focused on investigating patient psycho-social factors to better understand the behavior of statin medication adherence. Specifically, we focused on investigating how patients' optimism affects the behavior of statin medication adherence with behavioral intentions, motivational intensity, self-efficacy, and outcome expectations potentially mediating or moderating this relationship. Behavioral intentions, derived from The Theory of Reasoned Action and The Theory of Planned Behavior, capture a person's motivational factors that influence behavior and are an indication of how hard a person will try in order to achieve a behavior.[24] The concepts of self-efficacy and outcome expectations originate from Bandura's Social Learning Theory proposing that behavior change is a function of one's expectations about the outcome and one's ability to engage in behavior.[25,26] Self-efficacy is defined as one's belief about his/her ability to successfully perform specific behaviors in particular situations to produce the outcomes and outcome expectations is defined as the belief about the likelihood of the behavior leading to certain outcomes.[25,27] Motivational intensity measures the degree of motivation one would engage in a behavior and it is linked to the self-regulatory fit theory.[28] These four patient psycho-social factors are identified as important in goal behaviors. Hence, they are included in this study as potential variables investigating the mechanism of optimism on statin medication adherence.

The aims of this study were to understand how optimism affects the behavior of statin medication adherence. Specifically, the relationship between patients' optimism and statin medication adherence was tested via a conditional indirect approach with behavioral intentions

and motivational intensity serving as mediators, and with patients' self-efficacy and outcome expectancies serving as moderators.

First, the conditional indirect effect of patients' optimism on statin medication adherence was tested with behavioral intentions as the mediator and the two moderators of self-efficacy and outcome expectancies. The hypotheses tested were:

H1: The greater the optimism the greater the intentions to engage in the behavior.

H2a: Behavioral intentions will influence the behavior of statin medication adherence the greater the self-efficacy.

H2b: Behavioral intentions will influence the behavior of statin medication adherence the greater the outcome expectations.

H3: Optimism affects statin medication adherence directly.

Second, the conditional indirect effect of patients' optimism on statin medication adherence was tested with motivational intensity as the mediator and the two moderators, self-efficacy and outcome expectancies. The hypotheses for this model include:

H4: The greater the optimism the greater the motivation to engage in the behavior.

H5a: Motivational intensity will influence the behavior of statin medication adherence the greater the self-efficacy.

H5b: Motivational intensity will influence the behavior of statin medication adherence the greater the outcome expectations.

H6: Optimism affects statin medication adherence directly.

Methods

Research Design

This was a prospective study and data collection was done via two designed questionnaires (Appendices A and B). Questionnaire one focused on patient psychosocial factors, and questionnaire two focused on the behavior of adherence to the statin medication.

Patients who were taking a statin medication during the time of study were identified at a large university health care system. A total of 1700 potential patient participants were invited to take part of our study. The invitation consisted of a cover letter consisting of the purpose of the study and invitation to participate, a link to complete the survey online, and a $2 incentive. The link was the same for all potential participants and a unique code was provided for each participant to access the survey. Participants who completed the first survey received an incentive of $20 and were invited to complete the second survey. The second survey was sent to participants' emails two weeks from completing the first survey. Participants who successfully completed the second survey received an additional $5 incentive. University of Michigan Institutional Review Board (IRB) approval was granted to initiate and complete the study.

Participants

Patients on a statin medication, proficient in English, 18 years of age or higher were included in the study. Patients who did not meet our inclusion criteria were excluded from the study.

Measures

Independent variable: Optimism

The independent variable, optimism, was measured via the Life Orientation Test Revised (LOT-R).[29,30] The LOT-R is a 10-item scale that was adapted from the LOT instrument developed to asses individual differences in generalized optimism versus pessimism. The LOT-R scale was constructed by eliminating two items dealing with coping style rather than with positive expectations for future outcomes. The items in the LOT-R consist of 3 positive worded items, 3 negative worded items, and 4 filler items. The LOT-R items are scored 1-5, with 1 indicating *strongly disagree*, 2 *disagree*, 3 *neutral*, 4 *agree*, and 5 *strongly agree*. Total score is the sum of 6 items; the other four items are filler items. The filler items are *its easy for me to relax, I enjoy my friends a lot, it's important for me to keep busy, I don't get upset too easily*.. The three negatively worded items are reverse coded before scoring; *if something can go wrong for me it will, I hardly ever expect things to go my way, I rarely count on good things to happen* (0=4, 1=3, 2=2, 3=1, 4=0). Specific items 1,3,4,7,9, and 10 are summed to obtain an overall score, and the possible range for the total score is 6 to 30. The higher the value implies higher optimism. The LOT-R has good internal consistency with a Cronbach's α=0.78 and its test-retest reliability is 0.68 at 4 months and 0.79 at 28 months.

Dependent variable: Statin medication adherence (SMA)

Statin medication adherence was assessed using the single-item visual analogue rating scale (VAS).[31,32] It consists of a single item that asked participants to estimate, along a continuum of 0 to 100, the percentage of medication dosages taken as prescribed during a specified time period.[31,32,33] VAS was used to successfully measure adherence to antiretroviral therapy[33] and has demonstrated adherence estimates that paralleled unannounced pill counts, electronic medication monitoring, unannounced monthly pill counts, and self-reported recall.[31,32]

Statin medication adherence was assessed at baseline and two weeks after completing questionnaire one.

Mediator variables: Behavioral intentions and Motivational intensity

Behavioral intentions (BI)

The variable of behavioral intentions served as a mediator in this study and was assessed via two questions. The two questions consisted of asking participants to rate on a scale from *strongly disagree* to *strongly agree* their *intention* to take the cholesterol medication as prescribed in the next two weeks and on a scale from *very unlikely* to *very likely* how likely is the intention to take their cholesterol medication as prescribed. The scores for the two questions were averaged. The answer options for both questions were on a scale of 1 to 5.

Motivational intensity (MI)

The variable of motivational intensity served as a mediator in this study as well and was assessed via two questions. The two questions asked participants on a scale of *not at all* to *extremely* how *motivated* and *determined* they were to take their cholesterol medication as prescribed. To obtain one score for the motivational intensity variable, the scores for the two questions were averaged. The answer options for both questions were on a scale from 1 to 5.

Moderator variables: Self-efficacy and Outcome expectancies

Self-efficacy (SE)

The variable of self-efficacy served as one of the moderator variables. It was tested via two questions asking participants on a scale of *not at all* to *extremely* how *confident* they were that their cardiovascular health will improve as a result of taking their cholesterol medication as

directed and how *certain* they were that they will be able to avoid cardiovascular disease as a result of taking their cholesterol medication as directed. The average of the two questions was calculated into one self-efficacy score. The answer options were on a scale from 1 to 5.

Outcome expectancies (OE)

The variable of outcome expectancies served as a moderator in this study as well and was measured via two questions. One question asked participants how *promising* it was that their health would improve if they took their cholesterol medication as directed. The second question asked participants how *likely* it was that they will reduce their risk of heart disease if they took their cholesterol medication as directed. Both questions had answer options ranging from *not at all* to *extremely*, and the scores for the two questions were averaged to obtain one score. The answer options were on a scale from 1 to 5.

Participants in the study also answered questions about their overall and cardiovascular health, other medications, and demographic characteristics.

Analysis

The PROCESS marco[34] (Appendix C) was applied to test the hypotheses in this study. Figure 1 represents the model with the variables included in the model. The conditional indirect effect of X on Y via mediators M and moderators V is tested via two subset models: the mediator variable model and the outcome variable model.

The mediator variable model is determined by the effect of the independent variable (X) on the mediator (M). The equation for the mediator variable model is:

$$\mathbf{M}=\beta_{10}+\beta_{11}\mathbf{X}+\varepsilon_{1} \quad (1)$$

The outcome variable model is determined by the direct effects of the independent variable (X) on the independent variable (Y) and by the interaction effects of the mediator (M) with the moderator (V) on the independent variable. The equation for the outcome variable model is:

$$\mathbf{Y}=\beta_{20}+\beta_{21}\mathbf{X}+\beta_{22}\mathbf{M}+\beta_{23}\mathbf{V}+\beta_{24}\mathbf{M(V)}+\varepsilon_2 \quad (2)$$

The conditional indirect effect of optimism on statin medication adherence is found to be successful when β_{11} and the β_{24} coefficients are statistically significant.

Results

Demographic and clinical patient characteristics represented in Table 1 indicate that our sample was comprised of predominantly white (87.1%) and ≥60y of age (69.3%) adults. The female and male populations were similar in number and approximately half of the sample had an annual income of $60k or higher. The majority of patients perceived themselves as being in good to excellent health (88.7%). Approximately 1/3 indicated taking a depression medication at the time of study completion. Analyses between respondents to both questionnaires versus respondents to questionnaire one only indicate no significant differences between majority of variables, except health insurance (Appendix E).

Cronbach alpha (α) tests determined the reliability of the measures in our study. Considering the general rule in social sciences of a reliability measure of ≥.70 being good, all variables tested exhibited good reliability: α(behavioral intentions) = .71, α(motivational intensity) = .93, α(self-efficacy) = .85, α(outcome expectancies) = .86, α(optimism) = .81. The distribution of the dependent variable Statin medication adherence (SMA) was 96.3% ± 13.74. Baseline statin medication adherence was 95.67% ± 14.21. Intentions were considered as a potential dependent variable tool. Similarly to statin medication adherence, the distribution of

intentions was skewed (mean 4.85 ± .524). For analyses, we chose the behavior of adhering to statin medication as the dependent variable. The two-step and log-transformation approaches were used to transform the statin medication adherence variable. Slightly better results towards normality resulted. However, the transformation results were was not statistically significant as indicated by the Kolmogorov-Smirnov and Shapiro-Wilk tests. The original statin medication adherence results were used for analyses.

Figure 1 represents pictorially the model with the independent variable being optimism (X), the mediating variables being behavioral intentions and motivational intensity (M), and the moderating variables being self-efficacy and outcome expectancies (V). The three main findings from testing the model were:

1. Optimism did not influence the behavior of statin medication adherence directly.
2. Optimism did influence the behavior of statin medication adherence via a conditional indirect effect with behavioral intentions mediating the relationship and with self-efficacy or outcome expectancies serving as moderators.
3. Optimism did influence the behavior of statin medication adherence via a conditional indirect effect with motivational intensity mediating the relationship and with self-efficacy or outcome expectancies serving as moderators.

The conditional indirect effect of optimism on statin medication adherence was established when behavioral intentions or motivational intensity served as the mediator and when self-efficacy or outcome expectancies served as the moderator (Figure 4.1; Table 4.2). Specifically, behavioral intentions mediated the relationship between patients' optimism and behavior of adhering to statin medications (b=.01, p=.04). Furthermore, self-efficacy or outcome expectancy

values moderated the degree to which patients' intentions influenced the behavior (b=-10.88, p =.00). Specifically, low and moderate levels of self-efficacy and outcome expectations interacted behavioral intentions to affect statin medication adherence (Table 4.4). Since, there was not a direct effect of optimism on the behavior of statin medication adherence, we can say with statistical confidence that intentions fully mediated the impact of optimism on statin medication adherence in this model.

Similarly to intentions, motivation was found to fully mediate the impact of optimism on statin medication adherence. The conditional indirect effect of optimism on statin medication adherence was established when motivational intensity served as the mediator (b=.04, p=.00) and when self-efficacy (b=-2.77, p=.00) or outcome expectancies (b=-1.79, p=.048) served as the moderator (Table 4.3). Specifically, low and moderate levels of both moderators significantly interacted with motivational intensity to affect statin medication adherence (Table 4.4).

Discussion

Psychosocial factors are essential determinants of human behaviors. Optimism is a novel patient psychosocial factor investigated in the context of the health behavior of statin medication adherence. This study sought to test the effect of optimism on the behavior of statin medication adherence. Specifically, this study aimed to better understand the mechanisms via which optimism may impact the behavior by focusing on patients' behavioral intentions, motivational intensity, self-efficacy, and outcome expectations as potential influencing factors. Our main finding was that optimism is a predictor of statin medication adherence and it affects it via a conditional indirect effect.

Our findings provide insights into potential mechanisms of how optimism affects the behavior of medication adherence for patients who are at risk for cardiovascular disease.

Specifically, our study identified that optimism does not affect the behavior of statin medication adherence directly. Utilizing a conditional indirect analysis approach, optimism was identified to influence patients' behavioral intentions and motivational intensity to engage in the behavior of taking statin medications as prescribed. This relationship was further influenced by patients' self-efficacy and outcome expectations. Low and moderate self-efficacy or outcome expectations interacted with patients' behavioral intentions or motivational intensity to positively affect behavior.

Optimism is associated with a variety of health benefits, including lower risk of stroke;[5] reduced all-cause mortality in old age;[2] greater success in achieving lower levels of saturated fat, body fat, and global coronary risk, and with greater success in increasing aerobic capacity;[8] with lower rate and risk of rehospitalization after coronary artery bypass graft (CABG) surgery;[6,7] with better physical health;[2] with benefits in the socioeconomic world;[2] with more persistence in educational efforts and with higher level of income;[2] with faring better in relationships;[2] with reduced risk of incidence of coronary heart disease;[35] with positive mood, good morale, perseverance, problem solving, success, popularity, good health, long life;[1] and with medication adherence.[9] The mechanisms for these positive associations of optimism to outcomes are not yet fully understood.

Kim et al., suggests as a potential mechanism that optimism may protect against stroke through different pathways, including health behaviors.[5] This study demonstrated that optimism positively affects the behavior of statin medication adherence. The mechanism via which it does so is via one's formed behavioral intentions or via one's motivational intensity to engage in the behavioral goal. Carver et al. further suggests that optimism is associated with taking proactive steps to protect one's health, hence behavioral patterns of optimists may provide models of living

for others to learn.[2] Desirable characteristics linked to optimism are happiness, perseverance, achievement, and health.[1] In addition to focusing on behavioral intentions and motivational intensity as approaches to improve behavioral goals, striving to emulate these characteristics may be one approach to cultivate optimism.

Self-efficacy and outcome expectations are known predictors of behavioral intentions.[36] Tested as potential moderators, low to moderate self-efficacy and outcome expectations interacted with behavioral intentions and motivational intensity to impact the relationship between patients' optimism and the behavior of statin medication adherence. Another study indicated positive associations between optimism and confidence to take medications.[9] Hence, it may be possible that strong self-efficacy and outcome expectations may serve as mediators of optimism and behavior rather than moderators. Future research is needed to investigate further the relationship between optimism and these factors.

It is possible for optimism to be learned, although generally it is described as a trait-like characteristic.[2] The questions that need to be answered are how much of it can be learned for what period of time? Cognitive behavioral therapies are one approach to reduce negative cognitive distortions and allow room for positive ones.[2] Cancer cognitive-based intervention focused on cognitive and emotional-focused coping strategies and resulted in reduced stress.[37] As health care professionals, pharmacists can focus on fostering positive thoughts and affects to their patients in regards to their statin medication and cardiovascular health. This can be accomplished via questions of patients' positive expectations as a result of taking their medication for their cardiovascular health, well-being, and quality of life in general. Additional research is needed to identify exact questions and framing strategies to use during an interaction or intervention in order to achieve positive results. By instilling optimism in patients, they may

be more likely to adhere to their medication and to take proactive actions to optimize health.[2] The challenge for pharmacists is familiarizing professionals with the ways to instill optimism and identify appropriate strategies to nurture optimism in patients at appropriate times.

This was the first study to our knowledge investigating the effect of optimism on the behavior of statin medication adherence with other psychosocial factors influencing this relationship. Patients' behavioral intentions and motivational intensity mediate the effect of optimism on the behavior of adhering to statins and both intentions and motivation in turn interact with low and moderate self-efficacy and outcome expectations to affect behavior. These findings are important for both optimism and health behavior research in the following way. For optimism research, we are presenting potential mechanisms via which optimism affects behavior. For health behavior research, we are expanding the research on medication adherence by presenting novel ways in which psychosocial factors can be studied in the context of this behavior. For clinical research and practice, an important patient factor, optimism, is presented to potentially be used to design interventions and applied in practice to improve medication adherence.

Our study was faced with some limitations. One limitation is the generalizability of the results. The findings of the study apply only to our sample population consisting of older mostly white adults that are in the higher income bracket and part of a university health system. These findings may be similar or different in other sample populations. Also there may be cultural differences in optimism results between North Americans, Asians, and Europeans.[2] More research is needed to investigate the effects of optimism on the behavior of medication adherence among different cultural, ethnic, and race groups. Second, there are potential recall and social

desirability biases present, both being associated with answering questionnaires. These biases most likely contributed to increased reported statin medication adherence levels.

Furthermore, the measure used for statin medication adherence was a single item. Including additional items would increase response burden. Therefore, although not included in this study, they could be pursued in future studies. Different statin medication adherence levels may impact the results. It is also likely that investigating these psychosocial factors in different sample populations, with different race and income distributions, may produce different results. Additionally, it may be likely that adherent patients are more likely to volunteer to participate in studies compared to nonadherent patients.

Conclusion

Optimism is a predictor of statin medication adherence. It influences statin medication adherence via a conditional indirect effect with various patient psychosocial factors influencing this relationship. Patients' optimism together with behavioral intentions, motivational intensity, self-efficacy, and outcome expectations are important factors to consider when examining the behavior of statin medication adherence.

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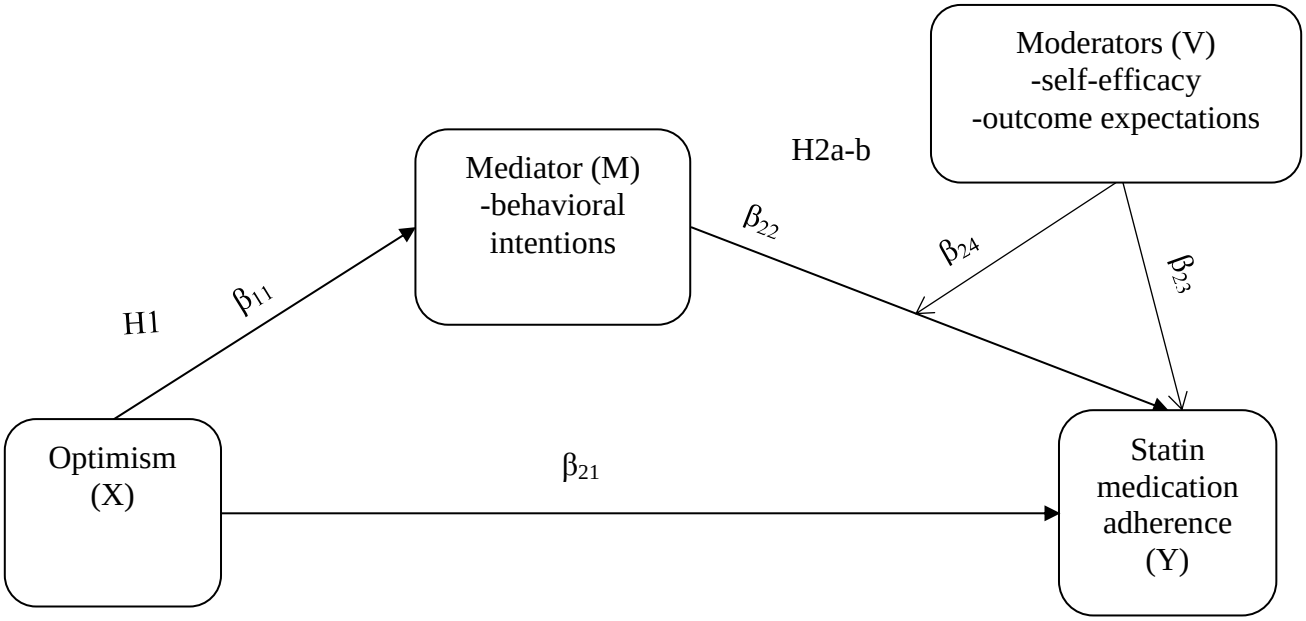
Figure 4-1. Theoretical and Analytical Framework for Optimism Predicting Statin Medication Adherence

a The Conditional Indirect Effect of Optimism Regulatory Focus on Statin Medication Adherence with Behavioral Intentions serving as the Mediator



b The Conditional Indirect Effect of Optimism Regulatory Focus on Statin Medication Adherence with Motivational Intensity serving as the Mediator

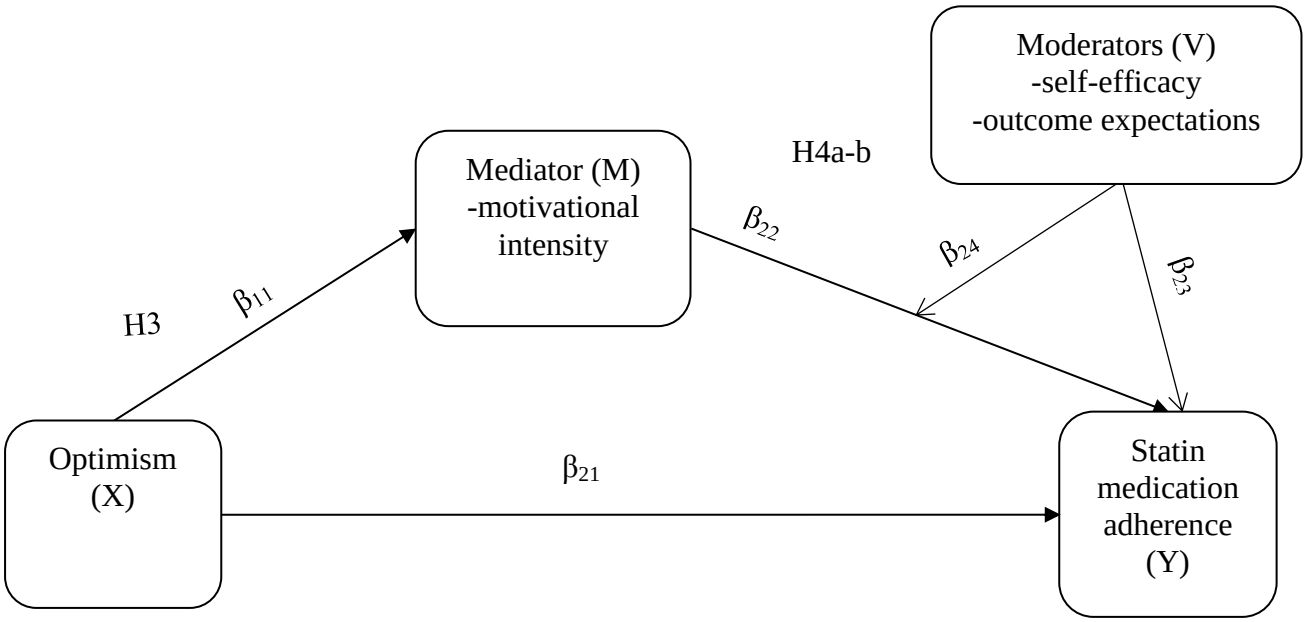


Table 4-1. Respondent Demographic and Clinical Characteristics

Characteristic	Percentage
Age	
≥60years	69.3
Gender (Female)	40.2
Race	
White-American	87.1
Other/no answer	12.9
Income	
≤19,999/year	8.3
$20,000 - $39,000	12.6
$40,000 - $59,999	17.8
$60,000 - $79,999	15.3
$80,000 - $99,000	16.0
≥$100,000/year	25.5
Had heart disease	25.2
Had a heart surgery	11.3
Diagnosed with high cholesterol	93.6
Insurance coverage for cholesterol medication	91.7
Taking a depression medication	22.1
Overall Health	
Excellent	17.8
Very good	37.1
Good	33.8
Fair	9.5
Poor	1.8

N = 326

Table 4-2. Model 1a Conditional Indirect Effect of Optimism on Statin Medication Adherence with Behavioral Intentions as the Mediator

Mediator (M)	**Behavioral intentions**			
Mediator Variable Model	R^2=.01, p=.04			
M=$\beta_{10}+\beta_{11}X+\varepsilon_1$	**b**		**b**	
X: Optimism β_{11}	.01		.04*	
Outcome variable (Y)	**Statin Medication Adherence (SMA)**			
Moderator (V)	**Self-efficacy**		**Outcome expectancies**	
Outcome Variable Model	R^2=.29, p=.00*		R^2=.24, p=.00*	
Y=$\beta_{20}+\beta_{21}X+\beta_{22}M+\beta_{23}V+\beta_{24}M(V)+\varepsilon_2$	**b**	**p**	**b**	**p**
X: independent variable β_{21}	.13	.43	.21	.22
M: mediator β_{22}	6.19	.00*	10.98	.00*
V: moderator β_{23}	1.86	.01*	1.11	.13
M*V: interaction β_{24}	-10.88	.00*	-3.57	.01*

*p≤.05; X manipulation, M mediator, V moderator, M*V interaction term

N=326

Table 4-3. Model 1b Conditional Indirect Effect of Optimism on Statin Medication Adherence with Motivational Intensity as the Mediator

Mediator (M)	**Motivational intensity**			
Mediator Variable Model	R^2=.05, p=.00*			
M=$\beta_{10}+\beta_{11}X+\varepsilon_1$	**b**		**p**	
X: Optimism β_{11}	.04		.00*	
Outcome variable (Y)	**Statin Medication Adherence (SMA)**			
Moderator (V)	**Self-efficacy**		**Outcome expectancies**	
Outcome Variable Model	R^2=.18, p=.00*		R^2=.17, p=.00*	
Y=$\beta_{20}+\beta_{21}X+\beta_{22}M+\beta_{23}V+\beta_{24}M(V)+\varepsilon_2$	**b**	**p**	**b**	**p**
X: independent variable β_{21}	.15	.41	.19	.29
M: mediator β_{22}	5.25	.00*	5.92	.00*
V: moderator β_{23}	.38	.65	-.36	.68
M*V: interaction β_{24}	-2.77	.00*	-1.79	.048*

*p≤.05; X manipulation, M mediator, V moderator, M*V interaction term

N=326

Table 4-4. Conditional Indirect Effects: Optimism and Statin Medication Adherence

Moderators	**SMA (M: Behavioral Intentions)**		**SMA (M: Motivational Intensity)**	
Self-efficacy	Effect	95% CI	Effect	95% CI
V=-1SD (-.97)	.22	(.04, .56)*	.35	(.14, .69)*
V=0	.08	(.01, .25)*	.23	(.10, .44)*
V=+1SD (.97)	-.06	(-.35, .10)	.11	(-.07, .36)
Outcome expectancy	Effect	95% CI	Effect	95% CI
V=-1SD (-.95)	.19	(.01, .49)*	.34	(.15, .66)*
V=0	.14	(.01, .38)*	.26	(.10, .52)*
V=+1SD (.95)	.10	(-.01, .51)	.18	(-.04, .52)

SMA - statin medication adherence, M – mediator, V – moderator, SD - standard error, Effect – conditional indirect effect, 95% CI – bootstrap 95% confidence intervals for conditional indirect effect

N=326

Table 4-5. Optimism Study Hypotheses and Results

	Hypothesis	**Finding**
H1	The greater the optimism the greater the intentions to engage in the behavior.	H1 is supported. (β_{11} =.01, p=.04*)
H2a	Behavioral intentions will influence the behavior of statin medication adherence the greater the self-efficacy.	H2a is not supported. (β_{24} =-10.88, p=.00*)
H2b	Behavioral intentions will influence the behavior of statin medication adherence the greater the outcome expectancies.	H2b is not supported. (β_{24} =-3.57, p=.01*)
H3a	Optimism affects statin medication adherence directly.	H3 is not supported. (β_{21} =.13, p=.43) SE (β_{21} =.21, p=.22) OE
H4	The greater the optimism the greater the motivation to engage in the behavior.	H4 is supported. (β_{11} =.04, p=.00*)
H5a	Motivational intensity will influence the behavior of statin medication adherence the greater the self-efficacy.	H5a is not supported. (β_{24} =-2.77, p=.00*)
H5b	Motivational intensity will influence the behavior of statin medication adherence the greater the outcome expectancies.	H5b is not supported. (β_{24} =-1.79, p=.048*)
H6	Optimism affects statin medication adherence directly.	H6 is not supported. (β_{24} =.15, p=.41) SE (β_{21} =.19, p=.29) OE

Chapter 5 - **DISCUSSION**

This is the first randomized field study focused on investigating unique patient psychosocial factors and the effects of a fit intervention on the behavior of statin medication adherence. We created and delivered a fit intervention to better understand its effects on statin medication adherence; the results of which will help with future communication intervention design. Additionally, our study investigated how unique patient and medication-related factors affect the behavior; specifically patients' regulatory focus and optimism are first in research history to be investigated in the context of statin medication adherence. Next, a summary of findings for each aim is provided followed by the study's limitations, potential future directions, and conclusions.

Summary of Study Aims

Aim1

Using the theory of regulatory focus, social learning theory, and the theory of planned behavior, two questionnaires were created to investigate the effect of patients' regulatory focus on the behavior of statin medication adherence with behavioral intentions, motivational intensity, and other medication-related factors serving as mediators and moderators. To test the effect of regulatory focus, patients' orientation was manipulated via messages framed as either promotion or prevention. This technique enabled us to prime patients' orientation into promotion or prevention regulatory focus orientation and test the effect of one orientation versus another on the behavior of statin medication adherence. The approach of manipulating regulatory focus has been successfully applied to a variety of studies and behaviors.[1-9] Tam et al., is an example of a

study where both manipulated and chronic regulatory orientation were examined in behavior change.[8] Findings indicate both approaches to be effective. However, manipulating regulatory focus via priming is the preferred method, as measuring chronic regulatory focus may not be feasible in a practice setting.

Our findings indicate that regulatory focus predicted the behavior of statin medication adherence. Specifically, prevention orientation positively impacted the behavior when compared to promotion. Future studies need to identify the effect of prevention and promotion regulatory focus compared to control. We believe that the reasons for this finding may be related to the nature of the behavior of taking medications. For example, our behavior of taking statin medications as indicated by a health care provider is one which patients engage in to either prevent a cardiovascular event from occurring based on a lab value, usually a high LDL-cholesterol value, or to prevent another heart event from occurring. Both goals encompass the idea of preventing an unwanted event to happen in the future. This prevention orientation is part of prevention regulatory focus described by Higgins via the regulatory focus theory. The regulatory focus theory distinguishes self-regulation with a promotion from prevention focus.[1] A person's prevention focus is governed by security needs, strong oughts, and specific situations of nonloss-loss and is sensitive to absence of presence of negative outcomes.[1] When a person is prescribed a statin medication, it may automatically imply prevention of an unwanted future event. Taking the statin medication may represent to many patients the hope of meeting that security need, may represent meeting a responsibility given by their health care provider, and may represent the fear of loss of their cardiovascular health as a result of failing to take the statin medication. The promotion focus, conversely, is governed by nurturance needs, strong ideals, and specific situations of gain-nongain and is sensitive to the presence or absence of positive

outcomes.[1] When a patient is told that he/she is at high risk of cardiovascular disease, or is diagnosed with a heart condition, or has experienced a heart procedure - all may trigger a prevention orientation versus promotion. More studies are needed to determine how each promotion or prevention orientation operates when compared to control. Additionally, further studies are needed to determine whether these results are similar or different for different population samples.

Furthermore, we found that several patient psychosocial and medication-related factors impact the relationship between prevention regulatory focus and statin medication adherence. Specifically, patients' motivational intensity and behavioral intentions partially and separately mediate this relationship; each patient factor, in turn, is affected by different medication-related factors. As a theory attempting to answer how people are motivated to achieve a goal, motivational intensity is a key variable assessed in regulatory focus studies.[4] Patients' motivational intensity was found to mediate the relationship between regulatory focus and statin medication adherence. Furthermore, motivational intensity was influenced by patients self-efficacy and number of non-prescription medications. Specifically, the greater patients' self-efficacy and the lower the number of non-prescription medications, the greater the motivational intensity. The higher patients' confidence in their ability to take their statin medication as prescribed, the greater their motivation to engage in the behavior. Similarly, the lower the number of non-prescription medications a patient was taking, the greater their motivation to engage in the behavior. This may be due to patients' confidence in the effectiveness of their prescribed medication for their specific diagnoses or condition compared to the non-prescribed over the counter medications. This confidence may be linked to our patient's high adherence

levels of adherence and long duration of statin therapy, indicating low likelihood of adverse side-effects, such as myopathy.

Patients' intentions too partially mediated the relationship between regulatory focus and statin medication adherence. Intentions were influenced by different medication-related factors than motivational intensity. Specifically, presence of insurance coverage for statins and duration of statin therapy positively influenced intentions to engage in the behavior of statin medication adherence. Presence of statin drug insurance and longer time on statin resulted in greater intentions. Lower costs for statins and familiarity with drug therapy positively affected patients' intentions to engage in the behavior. Therefore, ensuring affordable costs for statins for all patients and encouraging patients to remain on therapy are essential to improving patients' intention to engage in the behavior and ultimately to improve statin medication adherence.

Intentions, derived from the Theory of Reasoned Actions and the Theory of Planned Behavior, control people's actions via attempts to engage in a behavior and motivational intensity measures the degree of motivation one has to make a goal happen.[4,10] Both factors partially interacted with prevention regulatory focus in predicting the behavior of statin medication adherence. The mechanisms via which they do so are different. We identified that intentions and motivation are driven by different patient and medication-related factors. Peoples' attempts to engage in the behavior of statin medication adherence are determined by drug therapy cost and familiarity. Peoples' motivation to engage in the behavior is determined by their confidence and belief in the effectiveness of their medication.

Similarly to this study, prevention orientation had a positive effect on the behavior of taking omega-3 health supplements. The omega-3 study indicated that prevention compared to

promotion positively influenced the behavior of supplementing with omega-3 supplements or omega-3 enriched products.[11] The difference between the omega-3 study and this medication adherence study is that outcome expectations were framed as promotion or prevention in the omega-3 study, while in our study the regulatory focus messages were framed as promotion or prevention and outcome expectations were measured via two questions. Findings of the omega-3 study indicated that the prevention outcome expectations only (not promotion) and intentions were strengthened at high levels of self-efficacy to affect the behavior of supplementing with omega-3 products.[11]

These are important findings because this is the first study to our knowledge in which the regulatory focus theory was applied to the behavior of medication adherence. The theory of regulatory focus goes beyond the hedonic principle of people approaching pleasure and avoiding pain and explains the two distinct self-regulatory modes of promotion and prevention to achieve a goal.[1] Identifying that one mode of self-regulation, prevention, predicts the behavior of statin medication adherence, when compared to promotion, is an important finding in the medication adherence research. A better understanding how patients' self-regulate during the decision-making process to engage in the behavior of taking medications as prescribed will help health care providers, such as physicians and pharmacists to better address patients' needs. Furthermore, patient and statin-medication specific factors found to partially impact patients' self-regulation to adherence. The conditional indirect approach used in this study is a novel approach in the medication adherence research thus far. This approach may be applied to studying adherence to other medications. As a result, we will better understand whether these mediation and moderator factors affect statin medication adherence specifically or adherence to other medications as well.

Knowing that prevention regulatory focus, when compared to promotion, positively predicts statin adherence has implications in practice as well. One implication is that health care providers could focus on communicating with patients at risk or diagnosed with cardiovascular disease with a prevention frame when encouraging adherence to statin therapy. An example of a prevention framed message a pharmacists may be one emphasizing the importance of taking statin medications to avoid an unwanted cardiovascular event. A promotion framed message emphasizing the importance of taking the statin medication to approach the goal of being healthy and live a long life enjoying more time with grandchildren may be less beneficial in this case. Ensuring that patients have insurance coverage for their statin medications, finding ways to encourage patients to take their statin medication over a long period of time, and assess patients' confidence levels in their ability to take their statin medication as indicated, and inquiring about any other non-prescription medication patients' may be taking at the time of therapy – are action steps health care professionals may take to increase patients' intentions and motivation to adhere.

Overall, this study was successful at investigating the effect of regulatory focus theory via a conditional indirect effect testing various patient and medication-related factors as potential mediators and moderators on the behavior of statin medication adherence. This study answered the question of how patients who are on statin therapy self-regulate when deciding to take their statin medication as prescribed. The next step was to examine patients' self-regulation and strategies used to achieve the goal of statin medication adherence.

Aim2

This study sought to examine how various strategies used in the decision making process to engage in the behavioral goal of adhering to statin medications interacted with patients' regulatory focus. These strategies are referred to as strategic means. When there is a strategic

compatibility between the means and orientation, a fit is experienced. The effect of a fit intervention was tested on the behavior of statin medication adherence.

The fit intervention consisted of experimentally priming patients' regulatory focus with framed promotion or prevention messages and by priming patients with framed (promotion or prevention) and non-framed implementation intentions. A fit was defined as a match between patients' orientation (promotion/prevention) and implementation intentions (promotion/prevention), such as promotion-promotion or prevention-prevention. The suitability of strategic means to patients' regulatory orientation generates 'value from fit' which explains how a goal pursuit is carried out.[4] Consistent with previous studies, [1,5-9] regulatory fit resulted in greater statin medication adherence levels compared to non-fit and to control. These results are promising as we now have a better understanding of best strategies to use for patients with different orientations to achieve better statin medication adherence.

Of equal importance, findings of this study indicated that various patient psycho-social factors affected statin medication adherence differently between the fit, non-fit, and control groups. Specifically, at weak patient psychosocial factors (intentions, motivation, outcome expectations) statin medication adherence levels were significantly different between the fit and non-fit and between the fit and control groups. However, at strong levels of the same patient psychosocial factors (intentions, motivation, outcome expectations) statin medication adherence levels were not significantly different between the fit, non-fit, and control groups. These findings suggest that when patients' motivation, intentions, and outcome expectations are weak, there is an opportunity to improve statin medication levels with a Fit intervention. However, when patients' motivation, intentions, self-efficacy, and outcome expectations are strong, statin medication adherence levels are similar among all groups.

Our findings were similar to a fit intervention study examining the behavior of healthy snacking; the behavior was affected differently at weak versus strong unhealthy snacking habits. For the weak unhealthy snacking habits, regardless of the kind of implementation intentions formed, the healthy snacking behavior was higher compared to when no implementation intentions were formed while for strong unhealthy snacking habits, the behavior was broken and people snacked more healthfully only when there was a fit between implementation intentions and regulatory focus.[8] Similarly, this study found that statin medication adherence was affected differently at weak versus strong factors. At weak behavioral intentions, motivational intensity, and outcome expectancies, statin medication adherence was greater when there was a fit between regulatory focus and implementation intentions formed compared to when there was a non-fit or when no implementation intentions were formed.

Being the first regulatory fit intervention applied to the behavior of medication adherence, research on better understanding the processes through which people decide to adhere or not adhere to their medications will inform health care professionals how to best help people adhere to their medications and improve their health. Extending similar interventions in other medications and conditions will help to better understand whether our findings are statin specific or whether they can be applied to other conditions. Additionally, future studies testing the effect of patients' prospective feelings about a choice they make of taking or not taking their medication when regulatory fit is higher and examining whether patients' retrospective evaluations of past decisions or goal pursuits are more positive when regulatory fit is higher will add to the understanding of the 'value from fit' concept in the context of medication adherence.

This study presented an effective regulatory fit intervention demonstrating improved statin adherence levels at weak psychosocial factors as behavioral intentions, motivational

intensity, and outcome expectations. Similar future interventions could be applied in population samples of patients who may display weak behavioral intentions, motivational intensity, expectations of outcomes, and are in need to improve medication adherence levels. The fit intervention presents an opportunity for future tailored communication that is patient specific to their regulatory focus. In this case, considering the behavior of statin medication adherence, health care professionals may tailor communication via framing strategic means that match patients' primed orientation. Tailored communication strategies between the health care professional and the patient could be implemented face-to-face during a patient consultation or during motivational interviewing. The patient counseling may be extended beyond to just purposes of taking the medication to patients' goals as a result of taking the medication. One of the four general principles of motivational interviewing is *developing discrepancy* between present behavior and goals or values that are important to the person.[12] Identifying patients' goals that are important to them is an essential step.

Here, pharmacists have an opportunity to identify the goal and tailor communication that is aligned with patients' goals. For example, in the contexts of cardiovascular health and medication adherence, the pharmacist would ask the patient what his/her goals are in regards to their cardiovascular health and why the mentioned goals are important to them. Then, based on the patients' answers, if, for example the answer is 'my goal is to avoid a stroke or heart attack', the pharmacist would tailor their communication with that of the patient's, with the choice of words 'avoid stroke or heart attack as a result of taking your medication'. On the other hand, if the patient would mention that his/her goal is 'to stay healthy and be able to live long and enjoy more time with grandchildren', then the pharmacist would tailor communication with that of the patient's with the choice of words 'live long and enjoy more time with grandchildren as a result

of taking your medication'. As a result of this tailored communication a fit will be created. Therefore, a feeling of rightness will be created in patients, their motivation to take the medication will be increased, and it is likely that patients will even feel better and more alert about their decision to take their medication as their health care provider has indicated to do. In other words this tailored communication strategy will create a 'value from fit' effect'[2] in patients' decision process.

Motivation is what provides the drive for patients' focus, effort, energy needed to move through processes of change described in the transtheoretical model of intentional human behavior change (TTM).[12] The Fit strategy is likely to increase patients focus, effort, energy at all points of behavior change. This is likely to happen by carefully tailoring each stage back to patients' goal mentioned in the *developing discrepancy* step.

Assessing patients' intentions, motivation, self-efficacy, and outcome expectations in regards to behavior is important, as we have identified different adherence levels at weak versus strong patient psychosocial factors. The last step of motivational interviewing is assessing and supporting patients' self-efficacy. In addition to self-efficacy, pharmacist could assess patients' motivation, and their outcome expectations they have in regards to taking their medication. Miller states that when motivational interviewing is done well, then it is the client that gives a voice to his/her concerns, reasons for change, self-efficacy, and intentions to change.[12] In this case, the client is the patient and the pharmacist's role is to tap into patient's intrinsic motivational factors and help the patient move towards positive behavior change. This study provides an innovative strategy to tailor communication between the pharmacist and patient that can be implemented in the motivational interviewing setting and potentially in other counseling environments.

In addition to the face-to-face interaction, this study provides the opportunity to tailor medication messages via mobile technologies. Future studies will investigate the possibility of delivering tailored messages via a fit intervention design. This fit intervention, delivered face-to-face or via mobile technologies, will help patients improve their medication taking behavior, and ultimately improve their health.

Aim3

To better understand what other factors may influence the behavior of statin medication adherence, this study focused on examining the effect of optimism on the behavior. This effect was tested via the conditional indirect approach with motivational intensity or behavioral intentions as the mediator and with self-efficacy or outcome expectations as the moderator. This is the first study to our knowledge investigating optimism in the context of the behavior of statin medication adherence.

Optimism can be a trait (captures optimism levels generally experienced for each individual) or described as a state (captures optimism based on situation or contextual factors).[13] Optimism is known to be positively linked to a variety of health benefits;[14-21] however, the mechanisms via which it does so are not yet fully understood. The findings of this study provide insights into potential mechanisms via which optimism affects the behavior of statin medication adherence.

Optimism acted as a significant predictor of the behavior of statin medication adherence. It affected the behavior via a conditional indirect effect, but not directly. Specifically, patients' behavioral intention or motivational intensity levels to engage in the behavior were positively affected by optimism levels, but only when levels of self-efficacy and outcome expectations

were low or moderate. From previous research it is known that self-efficacy and outcome expectations are predictors of behavioral intentions.[22] Additionally, one specific study found positive associations between optimism and confidence to take medications.[23] Tested as potential moderators, self-efficacy and outcome expectations impacted the relationship between patients' optimism and the behavior of statin medication adherence differently. It may be possible that strong self-efficacy and/or strong outcome expectations may act as mediators of patients' positive expectations of the future and behavior. Future research efforts are needed to investigate additional mechanisms between these psychosocial factors.

This study has important implications for both, research and practice. In the realm of research opportunities, this is a cornerstone step in investigating the effect and mechanisms of a trait/state characteristic in the behavior of statin medication adherence. Future research is needed to test how optimism may affect adherence in a variety of medications and conditions. This will allow us to further understand the mechanisms via which optimism does affect adherence. By doing so, we will be better equipped to design interventions delivered in practice to positively influence behavior.

In the context of cardiovascular health and pharmacy practice, pharmacists have the opportunity to foster positive thoughts in patients related to statin medication and cardiovascular health. The cognitive behavioral therapy approach focuses on reducing negative cognitive distortions, hence making room for positive ones.[15] Identifying such distortions during pharmacist-patient communication and replacing with positive one, may be a good starting point in instilling optimism in patients. Research to answer the questions of the feasibility and power of training optimism in patients is much wanted.

Limitations

Our study may present some generalizability challenges as it consisted of a certain demographic sample population. Due to the randomized nature of our design, we can generalize our findings to similar populations engaging in a similar behavior. Our sample population consisted of volunteers; hence it is likely that our participants were already interested in improving their medication adherence behavior. Our findings indicate statin medication adherence levels were higher than the average levels indicated in previous studies; this could be due to the self-report nature of the study, thus presenting the possibility of social desirability and recall biases. Or it may be that we truly captured the actual adherence levels representative for this population sample.

Future Directions

This is the first cutting-edge research investigation to analyze the psychosocial driving forces behind the behavior of statin medication adherence. Findings provide insights into potential mechanisms, but there is much more to be understood in the realm of the behavior of adhering to medications. Considering the importance of patient-centered care and that much of human behavior is driven by internal factors, heightened understanding of the role of psychosocial factors in adherence will play a vital role in intervention design to improve behavioral health outcomes.

Future research investigating the effect of psychosocial factors in patients from diverse backgrounds is warranted. Specifically, research is needed to determine how psychosocial factors affect behavior similarly or differently in patients from different cultural, ethnic, racial, economic, generational backgrounds. Moreover, understanding the effect of these factors across

medications and conditions is important, as the mechanisms may differ depending on type and disease severity.

Driving motivational forces and mechanisms for statin medication adherence identified that prevention orientation positively affected the behavior when compared to promotion. Future studies are needed to better understand whether prevention regulatory focus orientation positively affects adherence levels similarly or differently in other medications and/or conditions. It is also important to understand whether prevention or promotion orientation would positively affect the behavior of medication adherence when compared to control. Future regulatory focus studies are needed in the domain of medication adherence research. A better understanding of patients' motivational orientation will better equip us to tailor communication more effectively between the patient and health care provider.

Additionally, designing and delivering 'Fit' tailored messages for patients during face-to-face patient-provider interactions or via mobile technologies will aid in improving patients' medication adherence and health outcomes. Moving forward testing Fit interventions across populations and conditions is imperative. And finally, a better understanding of how optimism affects medication adherence and finding ways to improve patients' optimism levels will serve as an innovative way to improve medication adherence.

Conclusions

In sum, this study found that patients' prevention regulatory focus predicted statin medication adherence directly and indirectly via several patient psychosocial and medication-related factors. Directly, it predicted statin medication adherence with prevention focus positively affecting the behavior compared to promotion focus. Indirectly, it predicted statin

medication adherence with intentions or motivation serving as mediators and different factors serving as moderators (insurance and time on statin for intentions; self-efficacy and number of non-prescription medications for motivational intensity). Furthermore, the intervention of matching patients' regulatory orientation with implementation intentions as strategic means was found to be an effective intervention that resulted in greatest statin medication adherence levels for the fit condition. At weak behavioral intentions, motivational intensity, and outcome expectations the greatest the differences between the fit versus non-fit and between fit versus control groups; hence, the greatest potential for a fit intervention. Lastly, the behavior of statin medication adherence was influenced by patients' optimism levels via a full conditional indirect effect with behavioral intentions or motivational intensity serving as the mediator and low/moderate self-efficacy or outcome expectations serving as the moderator. Optimism is an important patient psychosocial factor found to positively impact the behavior of statin medication adherence when self-efficacy and outcome expectations were low/moderate.

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APPENDICES

APPENDIX A

A. Questionnaire One

The next few questions will determine if you are eligible for our study:

1. Has your doctor ever told you that you have heart disease?

   □ yes □ no □ do not know

2. Have you had heart surgery?

   □ yes □ no □ do not know

3. Has your doctor ever told you that you have high cholesterol?

   □ yes □ no □ do not know

4. Are you currently taking a statin medication to lower your cholesterol?

   □ yes □ no

5. Are you currently taking a medication for depression?

   □ yes □ no

- *For patients who answer Yes to question # 4 and No to question # 5, the following message will appear: "Thank you very much! You are eligible for the study. Please proceed to the next page.*"
- *For patients who answer No to question # 4 and Yes to question #5, the following message will appear: "Thank you for your interest to in our study. Unfortunately, you are not eligible to participate. Thank you for your time!*"

Hello:

We are doing a research study about cardiovascular health. The purpose of this study is to test how people make decisions about their cholesterol medications. Please follow the instructions in each section of this survey till your complete it. It will take you approximately 15 to 20 minutes to take the entire survey.

Participating in this study is completely voluntary. There are no foreseeable risks associated with your participation. However, if you feel uncomfortable or stressed answering any question you may skip it or you can discontinue participation from this study at any point. Your responses and all data from this research are completely confidential. The benefit of your participation in this study is helping research advance in the area of cholesterol medication adherence and cardiovascular health. There are no foreseeable risks associated with this study.

If you have any questions or comments, please feel free to contact any member of our research team.

Thank you for your time!

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In the next set of questions we would like to ask you about your medications and health.

1. How many different prescription medications do you take daily? _____
2. How long have you been on your cholesterol lowering medication? _____
3. Is your cholesterol medication covered by your insurance?

   □ yes □ no □ do not know

4. How many different over the counter products (those purchased without a prescription)? do you take daily_____
5. Overall in the past month, how would you rate your health?

   □ Excellent

   □ Very good

   □ Good

   □ Poor

   □ Very poor

The next set of questions asks about your cholesterol medication.

Most people have many medications to take at different times during the day and many find it hard to remember to take them. We need to understand what people are really doing with their medications. It is okay to tell us exactly how you take your cholesterol medication. Please tell us what you are actually doing in your personal situation.

1. Please put an "X" on the line below, between 0% and 100%, at the point showing your best guess about how much of your cholesterol medication you have taken in the last two weeks.

0% means you have taken none of the drug

50% means you have taken the drug half of the time

100% means you have taken every single dose of the drug on each day it is to be taken

2. Over the last 14 days, how many days were you able to take your cholesterol medication exactly as prescribed?

0 days	1day	2days	3days	4days	5days	6days	7days	8days	9days	10days	11days	12days	13days	14days

3. Now, specifically, in the last 7 days, how many days were you able to take your cholesterol medication exactly as prescribed?

0 days	1day	2days	3days	4days	5days	6days	7days

- *For the Regulatory Focus Manipulation participants are randomly assigned to 2 groups: promotion and prevention. The promotion group receives a promotion message, while the prevention group receives a prevention message.*

Promotion:

For the next few questions please think about your past hopes, aspirations, and dreams and list 3 of them. Next to each hope, aspiration, or dream, tell us how strong this hope/aspiration/dream is for you personally:

	Not at all strong	Somewhat strong	Moderately strong	Very strong	Very Very strong
1.Past hope/aspiration	1	2	3	4	5
2.Past hope/aspiration	1	2	3	4	5
3.Past hope/aspiration	1	2	3	4	5

Now, please think about your current hopes, aspirations, and dreams and list 3 of them. Next to each hope, aspiration, or dream, tell us how strong this hope/aspiration/dream is for you personally:

	Not at all strong	Somewhat strong	Moderately strong	Very strong	Very Very strong
1.Current hope/aspiration	1	2	3	4	5
2.Current hope/aspiration	1	2	3	4	5
3.Current hope/aspiration	1	2	3	4	5

Prevention:

For the next few questions please think about your past duties, obligations, and responsibilities and list 3 of them. Next to each duty, obligation, or responsibility, tell us how strong this duty/obligation/responsibility is for you personally:

	Not at all strong	Somewhat strong	Moderately strong	Very strong	Very Very strong
1.Past duty/obligation	1	2	3	4	5
2.Past duty/obligation	1	2	3	4	5
3.Past duty/obligation	1	2	3	4	5

For the next few questions please think about your current duties, obligations, and responsibilities and list 3 of them. Next to each duty, obligation, or responsibility, tell us how strong this duty/obligation/responsibility is for you personally:

	Not at all strong	Somewhat strong	Moderately strong	Very strong	Very Very strong
1.Current duty/obligation	1	2	3	4	5
2.Current duty/obligation	1	2	3	4	5
3.Current duty/obligation	1	2	3	4	5

For the next 9 questions, please indicate the extent to which each statement describes you extremely well or not at all by selecting one answer for each statement:

Promotion Focus	Does not describe me at all					Describes me moderately well		Describes me extremely well
1. I am typically able to get what I want out of life.	1	2	3	4	5	6	7	
2. I often accomplish things that get me excited or motivated to work even harder.	1	2	3	4	5	6	7	
3. I often do well at different things that I try.	1	2	3	4	5	6	7	
4. When it comes to achieving things that are important to me, I find that I don't perform as well as I would like to do.	1	2	3	4	5	6	7	
5. I feel like I have made progress towards being successful in my life.	1	2	3	4	5	6	7	
6. My job or studies capture my interests and motivate me to put considerably effort into them.	1	2	3	4	5	6	7	
7. I feel that I am succeeding well in terms of goals that I have set.	1	2	3	4	5	6	7	
8. I see myself as someone who is primarily striving to reach my "ideal self" —to fulfill my hopes, wishes, and aspirations.	1	2	3	4	5	6	7	
9. I frequently imagine how I will achieve my hopes and aspirations.	1	2	3	4	5	6	7	

Prevention Focus	Does not describe me at all			Describes me moderately well		Describes me extremely well
1. I seldom break my obligations.	1	2	3	4	5	6	7
2. Obeying rules is important to me.	1	2	3	4	5	6	7
3. I generally fulfill my duties.	1	2	3	4	5	6	7
4. I find myself doing things that are forbidden or frowned upon.	1	2	3	4	5	6	7
5. I usually honor rules and regulations.	1	2	3	4	5	6	7
6. Being a responsible person is a value I hold.	1	2	3	4	5	6	7
7. I seldom do things that others disapprove of me doing.	1	2	3	4	5	6	7
8. I see myself as someone who is primarily striving to become the self I "ought" to be — to fulfill my duties, responsibilities and obligations.	1	2	3	4	5	6	7
9. I frequently think about how I can prevent failures in my life.	1	2	3	4	5	6	7

The next set of questions asks you about your plans to take your cholesterol medication. Please indicate how much you agree or disagree with the following questions:

1. I <u>intend</u> to take my cholesterol medication as prescribed during the next 2 weeks:

1	2	3	4	5
strongly disagree	disagree	neither disagree/agree	agree	strongly agree

2. How likely or unlikely is it that you intend to take your cholesterol medication as prescribed during the next 2 weeks:

1	2	3	4	5
Very unlikely	Likely	neither unlikely/likely	Likely	Very likely

- *For the implementation intention manipulation, among our three groups (promotion, prevention, control), only the promotion and prevention groups will receive the Implementation Intention Questions. In the promotion group, ½ of the participants will receive promotion worded implementation intentions and the other ½ will receive prevention worded implementation intentions. Similarly, in the prevention group, ½ of the participants will receive promotion worded implementation intentions and the other ½ will receive prevention worded implementation intentions.*

Question 1

According to medication experts, the most effective way to improve taking your cholesterol medication is to focus on the benefits of taking your cholesterol medication (*drawbacks of not taking your cholesterol medication*) for you personally and to commit yourself to taking your cholesterol medication as directed. Please list at least 3 things you could do that will help you to take (*avoid not taking*) your cholesterol medication within the next few days.

1_____
2_____
3_____

Question 2

Now, imagine as vividly as possible, when you will take (*avoid not taking*) your cholesterol medication, where you will take (*avoid not taking*) it, and other details of the situation you anticipate to take (*avoid not taking*) your cholesterol medication. Next we ask you to let us know approximately when, where, with whom, and in what situations you will take (*avoid not taking*) your cholesterol medication.

When? _____
Where? _____
With whom? _____
In what situations? _____

The next 10 questions tell us about you.

Please be as honest and accurate as you can throughout. Try not to let your response to one statement influence your responses to other statements.

There are no ‘correct’ or ‘incorrect’ answers. Answer according to your own feelings, rather than how you think ‘most people’ would answer.

Using the scale below, write the appropriate number beside each statement.

1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree

1) In uncertain times, I usually expect the best _____

2) It’s easy for me to relax _____

3) If something can go wrong for me it will _____

4) I’m always optimistic about my future _____

5) I enjoy my friends a lot _____

6) It’s important for me to keep busy _____

7) I hardly ever expect things to go my way _____

8) I don’t get upset too easily _____

9) I rarely count on good things happening to me _____

10) Overall, I expect more good things to happen to me than bad _____

The next set of questions asks you about your cholesterol medication. Please select one answer for each question.

1. How confident are you that your cardiovascular health will improve as a result of taking your cholesterol medication as directed?
    a. Not at all confident
    b. Somewhat confident
    c. Moderately confident
    d. Very confident
    e. Extremely confident
2. How certain are you that you will be able to avoid cardiovascular disease as a result of taking your cholesterol medication as directed?
    a. Not at all certain
    b. Somewhat certain
    c. Moderately certain
    d. Very certain
    e. Extremely certain
3. How promising is it that your heart health will improve if you take your cholesterol medication as directed?
    a. Not at all promising
    b. Somewhat promising
    c. Moderately promising
    d. Very promising
    e. Extremely promising
4. How likely is it that you will reduce your risk of heart disease if you take your cholesterol medication as directed?
    a. Not at all likely
    b. Somewhat likely
    c. Moderately likely
    d. Very likely
    e. Extremely likely
5. How motivated are you to take your cholesterol medication as prescribed?
    a. Not at all motivated
    b. Somewhat motivated

c. Moderately motivated
d. Very motivated
e. Extremely motivated

6. How determined are you to take your cholesterol medication as prescribed?
    a. Not at all determined
    b. Somewhat determined
    c. Moderately determined
    d. Very determined
    e. Extremely determined

Please let us know your intention of taking your cholesterol medication as directed during the next 2 weeks.

1. I intend to take my cholesterol medication as prescribed by my health care provider during the next 2 weeks:

    1 = strongly disagree
    2 = disagree
    3 = neither disagree/agree
    4 = agree
    5 = strongly agree

In the next set of questions we would like to ask you a bit about yourself.

1. What is your gender:

□ male □ female

2. What is your age: _____

3. What is your race:

□ Caucasian-American □ African-American □ Asian-American □ Hispanic-American □ prefer not to answer

4. What is your income:

□ below $19,000/year

□ $20,000-$39,000

□ $40,000-$59,000

□ $60,000-$79,000

□ $80,000- $99,000

□ ≥$100,000/year

Thank you for your participation in this survey!

Please fill out your name and address so we will know where to send your gift card for participating in our survey.

Please tell us your email address so that we can send you the second survey about two weeks from now. It will only have 5 questions and you will receive an additional gift for completing it.

Thank you!

APPENDIX B

B. Questionnaire Two

This survey has 5 questions about your cholesterol medication.

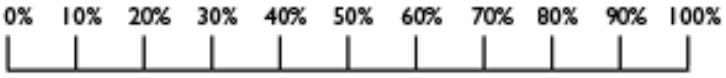
Most people have many medications to take at different times during the day and many find it hard to remember to take them. We need to understand what people are really doing with their medications. It is okay to tell us exactly how you take your cholesterol medication. Please tell us what you are actually doing in your personal situation.

1. Put an "X" on the line below, between 0% and 100%, at the point showing your best guess about how much of your cholesterol medication you have taken in the last two weeks.

0% means you have taken none of the drug

50% means you have taken the drug half of the time

100% means you have taken every single dose of the drug on each day it is to be taken



2. Over the last 14 days, how many days were you able to take your cholesterol medication exactly as prescribed?

0 days	1day	2days	3days	4days	5days	6days	7days	8days	9days	10days	11days	12days	13days	14days

3. Now, specifically, in the last 7 days, how many days were you able to take your cholesterol medication exactly as prescribed?

0 days	1day	2days	3days	4days	5days	6days	7days

4. When you were not able to take your cholesterol medication as prescribed, how many days did it happen in the past 7 days for each of the following reasons?

0 days	1day	2days	3days	4days	5days	6days	7days

I had side effects from my cholesterol medicine

I did not have money to pay for my cholesterol medicine

I was not comfortable taking it for personal reasons (for example: I was traveling…)

I was not comfortable taking it for social reasons (for example: I was with friends….)

I don't think I need my cholesterol medicine anymore

I don't think that my cholesterol medicine is working for me

I sometimes skip my cholesterol medicine to see if it is still needed

I am concerned about possible side-effects from my cholesterol medicine

I am concerned about long term effects from my cholesterol medicine

I had difficulty opening the container

I had difficulty swallowing my cholesterol medicine

I didn't have my cholesterol medicine because the pharmacy was out of this medicine

I didn't have my cholesterol medicine because I didn't have a ride to the pharmacy

I am not sure how to take my cholesterol medicine

I have trouble managing all the medicines I have to take

I would have taken it but simply missed it

I would have taken it but missed it because of busy schedule

I would have taken it but have problems forgetting things in my daily life

I do not consider taking my cholesterol medicine as a high priority in my daily life

Please let us know your intention of taking your cholesterol medication as prescribed during the next 2 weeks.

5. I intend to take my cholesterol medication as prescribed during the next 2 weeks:
   1 = strongly disagree

   2 = disagree

   3 = neither disagree/agree

   4 = agree

   5 = strongly agree

Thank you for your participation in this survey!

Please fill out your name and address so we will know to upload your additional money on your gift card.

Thank you!

APPENDIX C

C. PROCESS Analysis Model

The conditional process analysis model is used when the analytical goal is to describe and understand the conditional nature of the mechanisms by which a variable transmits its effect on another. Mediation analysis establishes to what extent a causal variable X influences an outcome Y through a mediation variable. Moderation analysis on the other hand, determines whether the sign or size of the effect of the causal variable X on outcome Y depends on a third moderation variable. The mediation and moderation analyses are combined into a moderated mediation analysis, termed as conditional process analysis.

The mechanisms linking X to Y can be said to be conditional if the indirect effect of X on Y through M is contingent on a moderator. There are many ways this could happen. We considered two in this research.

1. The indirect effect of X is conditional on W through moderation of M on Y. W moderates the indirect effect through its moderation effect of X on M. The equations are:

$$M = i_1 + a_1X + a_1W + a_1XW + e_M \quad (1)$$

$$Y = i_2 + b_1M + e_Y \quad (2)$$

X exerts its effect on Y through both direct and indirect pathways. The direct effect links X to Y independent of M and the effect of X on Y through M, is the products of paths linking X to Y through M. The first of these components of the indirect effect is the path from X to M, where the effect of X on Y is a function of W, estimated by equation 1. The second component is the path from M to Y, estimated by equation 2.

2. The indirect effect of X is conditional on V through moderation of M on Y effect by V. The equations are:

$$M= i_1+ a_1X + e_M \quad (3)$$

$$Y = = i_2+ c'_1X + b_1M+ b_2V + b_3Mv + e_Y \quad (4)$$

X exerts its effect on Y through both direct and indirect pathways. The direct effect links X to Y independent of M and the effect of X on Y through M, is the products of paths linking X to Y through M. The first of these components of the indirect effect is the path from X to M, estimated by equation 3, and the second component is the path from M to Y, where the effect of M on Y is a function of V, estimated by equation 4.

Reference

Hayes, A.F. (2013). Introduction to mediation, moderation, and conditional process analysis: a regression-based approach. The Guilford Press: New York, London.

APPENDIX D

D. IRB Documentation

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Road, Building 520, Room 3214, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

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To: Karen Farris

From:

Michael	Geisser
Alan	Sugar

Cc:

Ala	Iaconi
Steven	Erickson
Karen	Farris
John	Piette
Richard	Bagozzi
Michael	Dorsch

Subject:Initial Study Approval for [HUM00078405]

SUBMISSION INFORMATION:
Study Title: The moderated mediation of regulatory focus and fit on statin adherence
Full Study Title (if applicable):
Study eResearch ID: HUM00078405
Date of this Notification from IRB:11/22/2013
Review:Expedited
Initial IRB Approval Date: 11/22/2013
Current IRB Approval Period:11/22/2013 - 11/21/2014
Expiration Date: Approval for this expires at 11:59 p.m. on 11/21/2014
UM Federalwide Assurance (FWA): FWA00004969 (For the current FWA expiration date, please visit the UM HRPP Webpage)
OHRP IRB Registration Number(s): IRB00001999

Approved Risk Level(s):

Name	Risk Level
HUM00078405	No more than minimal risk

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRBMED has reviewed and approved the study referenced above. The IRB determined that the proposed research conforms with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents.

APPROVAL PERIOD AND EXPIRATION:
The approval period for this study is listed above. Please note the expiration date. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

IMPORTANT REMINDERS AND ADDITIONAL INFORMATION FOR INVESTIGATORS

APPROVED STUDY DOCUMENTS:
You must use any date-stamped versions of recruitment materials and informed consent documents available in the eResearch workspace (referenced above). Date-stamped materials are available in the "Currently Approved Documents" section on the "Documents" tab.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

AMENDMENTS:
All proposed changes to the study (e.g., personnel, procedures, or documents), must be approved in advance by the IRB through the amendment process, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

AEs/ORIOs:
You must inform the IRB of all unanticipated events, adverse events (AEs), and other reportable information and occurrences (ORIOs). These include but are not limited to events and/or information that may have physical, psychological, social, legal, or economic impact on the research subjects or other.

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance (http://www.med.umich.edu/irbmed/ae_orio/index.htm), and not implementing any changes to the research without IRB approval of the change via an amendment submission.

When changes are necessary to eliminate apparent immediate hazards to the subject, implement the change and report via an ORIO and/or amendment submission within 7 days after the action is taken. This includes all information with the potential to impact the risk or benefit assessments of the research.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AEs/ORIOs in the eResearch workspace for this approved study (referenced above).

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: www.research.umich.edu/hrpp.

Michael Geisser
Co-chair, IRBMED

Alan Sugar
Co-chair, IRBMED

UNIVERSITY OF MICHIGAN
eResearch.umich.edu

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Road, Building 520, Suite 3214, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

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To: Dr. Karen Farris

From:

Michael Geisser
Alan Sugar

Cc:

Richard Bagozzi
Karen Farris

John	Piette
Ala	Iaconi
Michael	Dorsch
Steven	Erickson

Subject: Scheduled Continuing Review [CR00059639] Approved for [HUM00078405]

SUBMISSION INFORMATION:
Study Title: The moderated mediation of regulatory focus and fit on statin adherence
Full Study Title (if applicable):
Study eResearch ID: HUM00078405
SCR eResearch ID: CR00059639
SCR Title: HUM00078405_Continuing Review - Wed Jan 25 11:16:15 EST 2017
Date of this Notification from IRB:2/1/2017
Review: Expedited
Date Approval for this SCR: 2/1/2017
Current IRB Approval Period: 2/1/2017 - 1/31/2018
Expiration Date: Approval for this expires at 11:59 p.m. on 1/31/2018
UM Federalwide Assurance:FWA00004969 (For the current FWA expiration date, please visit the UM HRPP Webpage)
OHRP IRB Registration Number(s): IRB00000244

Approved Risk Level(s) as of this Continuing Report:

Name	Risk Level
HUM00078405	No more than minimal risk

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRBMED has reviewed and approved the scheduled continuing review (SCR) submitted for the study referenced above. The IRB determined that the proposed research continues to conform with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents.

APPROVAL PERIOD AND EXPIRATION DATE:
The updated approval period for this study is listed above. Please note the expiration date. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established, except as necessary to eliminate apparent immediate hazards to research subjects or others. Should the latter occur, you must notify the IRB Office as soon as possible.

IMPORTANT REMINDERS AND ADDITIONAL INFORMATION FOR INVESTIGATORS

APPROVED STUDY DOCUMENTS:
You must use any date-stamped versions of recruitment materials and informed consent documents available in the eResearch workspace (referenced above). Date-stamped materials are available in the "Currently Approved Documents" section on the "Documents" tab.

In accordance with 45 CFR 46.111 and IRB practice, consent document(s) and process are considered as part of Continuing Review to ensure accuracy and completeness. The dates on the consent documents, if applicable, have been updated to reflect the date of Continuing Review approval.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

AMENDMENTS:
All proposed changes to the study (e.g., personnel, procedures, or documents), must be approved in advance by the IRB through the amendment process, except as necessary to eliminate apparent immediate hazards to research subjects or others. Should the latter occur, you must notify the IRB Office as soon as possible.

AEs/ORIOs:
You must continue to inform the IRB of all unanticipated events, adverse events (AEs), and other reportable information and occurrences (ORIOs). These include but are not limited to events and/or information that may have physical, psychological, social, legal, or economic impact on the research subjects or others.

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance (http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/adverse-events-aes-other-reportable-information-and-occurrences-orios-and-other-required-reporting), and not implementing any changes to the research without IRB approval of the change via an amendment submission. When changes are necessary to eliminate apparent immediate hazards to the subject, implement the change and report via an ORIO and/or amendment submission within 7 days after the action is taken. This includes all information with the potential to impact the risk or benefit assessments of the research.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AE/ORIO reporting in the eResearch workspace for this approved study, referenced above.

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: http://research-compliance.umich.edu/human-subjects.

Michael Geisser
Co-chair, IRBMED

Alan Sugar
Co-chair, IRBMED

APPENDIX E

Table A-E. Differences between Respondents and Non-respondents

Variables	**Respondents to both Questionnaires (N=326)**	**Non-respondents to the second Questionnaire (N=229)**	**Differences between groups**
SMA baseline	95.67 (14.21)	95.49 (14.06)	p=.894
Behavioral intentions	4.86 (.46)	4.82 (.52)	p=.359
Motivational intensity	4.30 (.80)	4.28 (.81)	p=.770
Self-efficacy	3.35 (.98)	3.34 (1.00)	p=.992
Outcome expectations	3.44 (.96)	3.50 (.95)	p=.500
Optimism	22.41 (4.04)	22.60 (3.87)	p=.627
RFocus			
Promotion	5.01 (.92)	4.86 (1.19)	p=.326
Prevention	5.65 (.79)	5.78 (.91)	p=.228
Number of Rx	4.73 (3.19)	5.44 (4.25)	p=.060
Number of Non-Rx	2.53 (2.20)	2.60 (2.33)	p=.739
Time on statin	9.45 (6.09)	9.60 (6.88)	p=.809
Statin Insurance			p=.025*
Yes	91.72%	96.99%	
No	8.28%	3.01%	
Age	64.19 (10.14)	64.34 (10.44)	p=.881
Gender			p=.991
Female	40.18%	40.13%	
Male	59.82%	59.87%	
Race			p=.218
White	87.12%	82.89%	
Other	12.88%	17.11%	
Income			p=.763
<19k/y	8.68%	12.67%	
20-39k/y	13.18%	12.67%	
40-59k/y	18.65%	16.00%	
60-79k/y	16.08%	16.67%	
80-99k/y	16.72%	14.00%	
>100k/y	26.69%	28.00%	
Overall health			p=.755
Excellent	17.79%	16.26%	
Very good	37.17%	32.53%	
Good	33.74%	37.35%	
Fair	9.51%	12.95%	
Poor	1.84%	1.81%	

APPENDIX F

Table A-F. Baseline Data for all Respondents

Variable	Average	Standard Deviation
Behavioral Intentions	4.86	.46
Motivational Intensity	4.30	.80
Self-efficacy	3.34	.98
Outcome Expectation	3.43	.96
Optimism	22.41	4.04
Statin Medication Adherence	95.67	14.21

N=326