THE ROLE OF SELF-EFFICACY IN PATIENTS WITH COMORBID TYPE 2 DIABETES AND CORONARY ARTERY DISEASE IN THE BYPASS ANGIOPLASTY REVASCULARIZATION INVESTIGATION 2 DIABETES (BARI 2D) TRIAL

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OBJECTIVES: Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are highly comorbid conditions that are affected by psychological factors, such as self-efficacy. Psychological factors can either hinder or promote medical interventions. Self-efficacy, the belief that one is able to make changes necessary for self-management, is associated with glycemic control and cardiac symptom burden, as well as behaviors that affect CAD prevention and outcomes.

METHODS: Using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, we assessed the relationship between self-efficacy and the treatment, risk factor control, and cardiac outcomes of patients with T2DM and CAD.

RESULTS: The first paper (N=889) showed no significant relationships between self-efficacy and randomized treatment for CAD (revascularization vs. medical therapy β=0.06, p=0.66) and T2DM (insulin sensitizers vs. insulin providers β=0.06, p=0.65) in patients with baseline self-efficacy scores $\leq$8. The second paper (N=1,562) verified a negative association between baseline self-efficacy and follow-up HbA1c (β=-0.03, p<.001) and a positive association with self-efficacy and physical functioning in which time negatively modified the association

(interaction p=0.02). A lagged association (feedback loop) was shown between self-efficacy and HbA1c, physical functioning, and BMI over time. The feedback loops were stronger in White non-Hispanic patients compared to minority patients. In the third paper (N=1,817), poor baseline self-efficacy was associated with an increased risk of a composite endpoint of death/myocardial infarction/stroke (hazard ratio [HR] =1.34, p=0.01), subsequent revascularizations (HR=1.30, p=0.004), subsequent PCIs (HR=1.43, p<.001), and angina (odds ratio [OR] =1.11, p<.001) compared to Fair-Excellent self-efficacy, but not after adjusting for baseline covariates. A decrease in self-efficacy from baseline to Year 1 was positively associated with all-cause mortality (adjusted HR=2.32, p<.001) and death/MI/stroke (adjusted HR=1.79, p<.001).

CONCLUSIONS: In summary, self-efficacy was associated with clinical risk factors and cardiac outcomes in patients with CAD and T2DM. This is of public health significance because it stresses the importance of improving a patient's confidence in managing their conditions outside of the medical setting.

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PREFACE

I would like to acknowledge all those who have helped me along the way in my career and my education. I would like to dedicate my dissertation to a most outstanding and wonderful investigator and mentor, Dr. Katherine Detre. It is my deepest regret that she was unable to see me attain my degree, for she has helped me tremendously. I would like to thank my committee members for all of their help, especially Dr. Maria Brooks whose brilliance and patience was instrumental in honing my statistical skills. I would also like to thank Dr. Stephen Thomas for his input on racial disparities; Dr. Gale Richardson for her insights on psychiatric epidemiology; Dr. Karen Matthews for her overall judicious insight; and Dr. Marike Vuga for her constant positive outlook.

I would also like to thank the faculty and staff of BARI 2D, EDC, and CMH for providing with a career experience that has provided me with new skills and have positively shaped my character.

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1.0 SPECIFIC AIMS

Despite the comorbid nature of T2DM and CAD, self-efficacy has not been studied in persons with both of these conditions, nor has it been studied longitudinally. Most studies have focused on self-efficacy in persons with CAD and in persons with T2DM, and are cross-sectional in design. Given the variety of therapies used to treat these conditions, it is not known whether self-efficacy varies by the type of glycemic control (insulin-sensitizing drugs versus insulin-providing drugs) or by the extent of glycemic control as measured by hemoglobin A1c (HbA1c). In addition, little is known about cardiac treatment and the psychological factors of self-efficacy in persons with T2DM and CAD.

The objective of the study is to examine how self-efficacy is related to the management, treatment, and clinical outcomes of persons with both T2DM and CAD using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial. BARI 2D is a National Institutes of Health (NIH)-sponsored, multi-center, randomized clinical trial of patients with T2DM and angiographically-documented stable CAD. The proposed research topics to be addressed are:

1. How does self-reported self-efficacy differ between patients on insulin-sensitizing drug therapy compared to insulin-providing drug therapy over time? How does self-

efficacy differ between patients whose CAD was treated with initial cardiac revascularization compared to initial medical therapy over time?

2. What is the relationship between self-efficacy and the clinical risk factors of HbA1c, blood pressure, low density lipids (LDL), and physical functioning over time? Does race/ethnicity serve as an effect modifier for these associations?
3. What is the relationship between self-efficacy and clinical endpoints (death, a composite of death/myocardial infarction [MI]/stroke, subsequent revascularizations, and angina) in patients overall and by type of randomized cardiovascular therapy (medical therapy or immediate revascularization)?

2.0 INTRODUCTION

The management of T2DM and CAD is not uniform and is a multifaceted process. Universally, all patients must make lifestyle changes that involve diet, exercise, foot care, and medication adherence. The various types of medication and hospital interventions include a diverse range of therapies, each differing in patient-physician involvement, pain, relief of pain, and complexity. The level of difficulty involved in managing one's health can be the pivotal transitioning factor that advances a person from knowing (s)he should do a behavior, to the assessment of his or her ability to carry out the behavior, and finally to the execution and maintenance of that behavior according to social learning theory (Albert Bandura, 1991). Maintenance/adherence is influenced by both behavior difficulty and outcome satisfaction.

To provide a better of understanding of the topics of interest, the background chapter will present the definition and epidemiology of T2DM, CAD, and self-efficacy. It will also include the risk factors, management, and complications of T2DM and CAD. Next, the literature review will address studies that provide the basis for the proposed objectives. These articles focus on what is known in the literature regarding psychosocial factors related to CAD and T2DM, and how the proposed objectives can address what is not known. This will be followed by a description of the BARI 2D study and its data, which were used for the analyses.

This research is important to both patients and healthcare professionals. From the patient's perspective, it explains why some people are likely to adhere to a physician's request. However, from the health professional's perspective, it explains why certain treatment not only aids patients, but also how it helps their self-confidence to manage other comorbid conditions. BARI 2D provides a strong setting to investigate the role of self-efficacy, treatment, and treatment outcomes in patients with comorbid diseases.

2.1 BACKGROUND

2.1.1 Type 2 Diabetes Mellitus

2.1.1.1 Definition

Diabetes mellitus is a metabolic disorder defined by chronic hyperglycemia (high blood sugar) and the inability to properly secrete or metabolize glucose. Characteristic symptoms of diabetes mellitus include polydipsia (increased thirst), polyuria (increased frequency in urination), polyphagia (increased appetite), blurred vision, and weight loss (Alberti, Zimmet, & Consultation, 1998; Engelgau, et al., 2004). There are two major types of diabetes: 1) Type 1 diabetes in which the onset is primarily in childhood; and 2) Type 2 diabetes (T2DM) in which the onset is primarily after the age of 45 years, but can occur at any age (Alberti, et al., 1998). T2DM begins with the body's resistance to insulin production (ADA, 2009). In order to compensate, the pancreas over-secretes insulin to the point at which it can no longer effectively produce enough. This proposal will focus only on T2DM, because it is the most prevalent form of diabetes mellitus.

2.1.1.2 Epidemiology

Approximately 23.6 million people in America have T2DM (17.9 million diagnosed and 5.7 million undiagnosed), and the lifetime prevalence is 17% (NIDDK, 2007). This is not only a growing problem in America, but across the world. It is estimated that 125 million people

worldwide have diabetes, with over 90% of the cases being T2DM. Due to environmental, behavioral, lifestyle, and dietary changes, the prevalence of T2DM worldwide continues to increase at an epidemic rate. Projections state that by the year 2025, 324 million people will have T2DM (Zimmet, 2003; Zimmet, Alberti, & Shaw, 2001).

2.1.1.3 Risk Factors

Non-modifiable risk factors for T2DM include having a family history of diabetes, being of racial/ethnic minority status, and older age (ADA, 2004, 2009; Engelgau, et al., 2004). Modifiable risk factors include being overweight, having a sedentary lifestyle, and poor diet. Additional risk factors for T2DM include: 1) pre-diabetes, a condition in which hemoglobin HbA1c levels are higher than normal (7.0%), but not high enough for a clinical diagnosis of T2DM; 2) gestational diabetes, which occurs during pregnancy; 3) delivering a baby over nine pounds; and 4) polycystic ovary syndrome. If left untreated through lack of diet modification and exercise, pre-diabetes can eventually progress into T2DM.

2.1.1.4 Management

Management of T2DM includes glycemic control and control of CAD risk factors such as high levels of low density lipids (>100) and hypertension (130/80 mmHg). This management protocol is known as the "ABCs" of diabetes care – normal levels of Hb**A**1c (<7%), aggressive management of **B**lood pressure and additional cardiovascular risk factors (i.e., dyslipidemia and microalbuminuria), and normal **C**holesterol levels through medications and lifestyle interventions (Gavin, Peterson, & Warren-Boulton, 2003; Ripsin, Kang, & Urban, 2009; Wattana, Srisuphan, Pothiban, & Upchurch, 2007).

T2DM is defined by the body's resistance to insulin, decreased insulin secretion, and increased hepatic glucose output (Ripsin, et al., 2009). Diabetes is commonly treated with insulin-sensitizing therapy, insulin-providing therapy, or a combination therapy. Both insulin-sensitizing drugs and insulin-providing drugs are equally efficient in managing T2DM in persons with CAD (BARI_2D_Study_Group, 2009). Insulin-sensitizing drugs such as thiazolidinediones and Biguanide (metformin) make fat, muscle, and liver cells more sensitive to the body's natural insulin and decrease hepatic glucose output (Magee & Isley, 2006). They are taken orally in the form of a pill. Insulin sensitizers are often used as first line agents in patients whose T2DM is fairly under control. Insulin drug use is indicative of treatment for more severe diabetes. Insulin drugs either provide the body with insulin or stimulate the pancreas to produce more insulin (insulin secretagouges) (Magee & Isley, 2006). Insulin comes in liquid form and as a suspension that is injected subcutaneously, several times a day (American_Society_of_Health-System_Pharmacists, 2009). It can be prescribed in conjunction with insulin-sensitizing drugs to assist in glycemic control (Ripsin, et al., 2009).

2.1.1.5 T2DM Complications

If untreated or poorly managed, T2DM can result in blindness, amputations, end stage renal disease (ESRD), and cardiovascular complications such as myocardial infarction (heart attack) and stroke (NIDDK, 2007). In 2004, CAD disease accounted for 68% of the deaths in people with T2DM aged 65 years or older (NIDDK, 2007). Based on 20 years of surveillance data, the Framingham Heart Study found that patients with diabetes had a two- to three-fold increased risk of CAD compared to patients without diabetes (Kannel & McGee, 1979).

2.1.2 Coronary Artery Disease

2.1.2.1 Definitions

Coronary artery disease (CAD) is characterized by atherosclerotic plaque build-up in the arteries, resulting in inadequate circulation of blood to the heart, brain, and surrounding tissues. Atherosclerosis is a condition that begins in childhood as a fatty streak within the endothelial cells, and due to years of accumulation of low density lipoproteins (LDL) and triglycerides, macrophage white blood cells, and other fatty deposits. It progresses throughout adulthood into calcification and/or a lesion(s). CAD is a specific type of cardiovascular disease. Cardiovascular disease is a class of diseases that affects the cardiovascular system – the heart, arteries, and veins. Types of cardiovascular disease include coronary heart disease, congestive heart failure (CHF), angina, aneurysm, peripheral vascular disease, myocardial infarction (MI), and stroke. MI and stroke are also considered to be adverse outcomes of cardiovascular disease.

MI is a rapid necrosis of the myocardium due to interrupted blood flow from the arteries. The plaque in an atherosclerotic artery can rupture with thrombus (blood clot) formation, occluding blood flow. This results in the severe inability of the artery to meet the oxygen the demands of the heart (ischemia). Without proper medical response within 20 to 40 minutes, irreversible death of the myocardium results. The myocardium will continue to die for six to eight hours, and scar tissue forms in its place (Burke & Virmani, 2007).

A stroke (cerebrovascular accident) is developing brain damage caused by interrupted blood flow to the brain due to a hemorrhage (bleeding in the brain) or ischemia (restricted blood flow). The brain suffers from a lack of oxygen and necrosis results. Warning signs of a stroke include sudden: 1) numbness or weakness of the face, arm, or leg, especially on one side of the

body; 2) confusion, trouble speaking or understanding; 3) vision problems in one or both eyes; 4) trouble with gait, balance, and coordination; and 5) severe headache. Depending on the affected area of the brain and the severity of the damage, a stroke can result in mild to severe paralysis, aphasia (loss of speech or comprehension of speech), or blindness in one side of the visual field (AHA, 2009a).

Angina is a treatable cardiovascular complication characterized by marked intermittent chest pain due to reduced oxygen to the heart (Campeau, 1975). Classic angina as defined by the Canadian Cardiovascular Society (CCS) Functional Classification of Angina is based on the activity that evokes pain and physical limitations (Campeau, 1975):

- Class I: Prolonged exertion, no physical limitations
- Class II: Walking more than two blocks or more than one flight of stairs, slight physical limitations
- Class III: Walking more than two blocks or more than one flight of stairs, marked physical limitations
- Class IV: Minimal or at rest, severe physical limitations

Angina equivalents are a group of symptoms other than angina such as light headedness, dyspnea, or pain in the arm or jaw (MediLexicon_International_Ltd, 2009).

2.1.2.2 Epidemiology

Approximately 80 million adults in America (approximately 1 in 3) have some form of CAD, and CAD was the leading cause of death in 2005 (CDC, 2008). In fact, CAD and cancer are the leading causes of morbidity and mortality in industrialized countries, and are steadily eclipsing infectious disease and malnutrition worldwide (CDC, 2008).

2.1.2.3 Risk Factors

Non-modifiable risk factors for CAD include being of racial/ethnic minority status, male sex, older age, and having a family history of CAD (especially before the age of 60). Modifiable risk factors are smoking/smoke exposure, high cholesterol, T2DM, sedentary lifestyle, high body mass index, unhealthy diet, and hypertension (AHA, 2009a). These risk factors are similar to those of T2DM, which partially explains why these two chronic conditions are often comorbid. Despite these shared risk factors, data from the National Health and Nutrition Examination Study (NHANES) showed that the reduction in CAD risk factors and improved heart disease treatment was less effective in reducing mortality in people with T2DM compared to those without T2DM, especially in women (CDC, 1996; Gu, Cowie, & Harris, 1999).

2.1.2.4 Treatment

Treatment options for CAD include 1) medical management with diet, exercise, and medicine; and/or 2) revascularization either by CABG or PCI. CABG is an invasive procedure in which a healthy blood vessel is grafted onto the heart to bypass the blocked part of the coronary artery. This attached artery improves blood flow to the heart muscle. Depending on the number of blocked arteries, patients can have multiple grafts (AHA, 2009). PCI is a less invasive procedure in which a balloon–tipped catheter is placed into the diseased artery of the heart (AHA, 2009). The balloon is inflated, which compresses the plaque in the arterial wall in order to widen the lumen and improves blood flow. Often, a bare metal stent or drug eluting stent (mesh wire tube) is inserted to prop open the inflated arteries (AHA, 2009a).

2.1.2.5 CAD Complications

Adverse outcomes that are commonly associated with CAD are MI, stroke, and angina. These can result in death, disability, and/or reduced quality of life. The risk of CAD-related complications in those with T2DM is 2 to 4 times greater compared to those without T2DM (Stamler, Vaccaro, Neaton, & Wentworth, 1993). Compared to persons with CAD only, persons with T2DM and CAD have increased mortality and experience far worse clinical outcomes as a result of CAD events and revascularization (Deaton, et al., 2006; Sobel, Frye, & Detre, 2003). Psychological factors, such as depressive symptom severity, increase CAD risk factors and the risk of adverse cardiovascular events (Rutledge, et al., 2006).

2.1.3 Self-efficacy

The confidence to successfully make change is known as self-efficacy (Bandura, 1977). Patients with both T2DM and CAD must engage in daily regimens in order to make positive changes in their health and decrease their risk of disease-related morbidities. Therefore, self-efficacy is a critical part of disease self-management (Anderson, Funnell, Fitzgerald, & Marrero, 2000).

The concept of "readiness to change" was coined by Bandura (1977) as one construct in his social cognitive theory of human behavior and learning. The foundation of this theory rests on "reciprocal determinism," which states that a person's behavior shapes their environment, which in turn shapes the person's behavior. Social learning occurs when people learn through observing other's behaviors, attitudes, and outcomes due to the behaviors. In order to have effective modeling, the following conditions must be met: 1) attention to the behavior, 2) retention regarding the behavior, 3) reproduction of the behavior, and 4) motivation (a cause to

imitate the behavior). Whether or not one decides if the behaviors should be and can be modeled is strongly based on self-efficacy (Albert Bandura, 1991).

Over time, consensus emerged around the term "self-efficacy" to define a person's confidence in being able to make change (A. Bandura, 1977, 1982). Within the concept of self-efficacy, mastery of a required skill gives one confidence to continue to utilize this skill. Self-efficacy arises from: 1) performance accomplishments (how well they have controlled their T2DM and CAD); 2) vicarious experience (fellow patients' experiences in self-management); 3) verbal persuasion (medical advice); and 4) physiological states (emotional arousal in coping with threatening situations) (A. Bandura, 1977, 1982). Self-efficacy differs from outcome expectancies in that it focuses on the belief in one's skills in performing an act, rather than the outcome of the act itself (**Figure 1**) (A. Bandura, 1977, 1982). A person can believe that an act will produce a desired outcome, but if she or he does not believe the act can be mastered, then the behavior will not be executed. Expectations of self-efficacy determine whether or not the self-management behaviors will commence, how long they will be done, and whether or not they will persist during obstacles and difficult circumstances (A. Bandura, 1977, 1982). This is of importance to the medical field because one's belief that she or he is able to effectively manage his or her health mediates change, and these beliefs are readily stimulated and formed by one's successes with self-management of the diseases (Anderson, et al., 2000; A. Bandura, 1977). Frequently, patients perceive barriers to active self-management of chronic conditions. Depression, difficulty exercising, poor communication with healthcare professionals, low family support, physical pain, and financial problems are the most commonly documented barriers (Jerant, Friederichs-Fitzwater, & Moore, 2005). Furthermore, the lack of drive to fully engage in

the regimens related to chronic conditions can result in poor outcomes and additional utilization of the medical system (Jerant, et al., 2005). The relationship between drive and outcomes is consistent among age groups, literacy levels, and races (Rika Nakahara, et al., 2006; Sarkar, Fisher, & Schillinger, 2006).

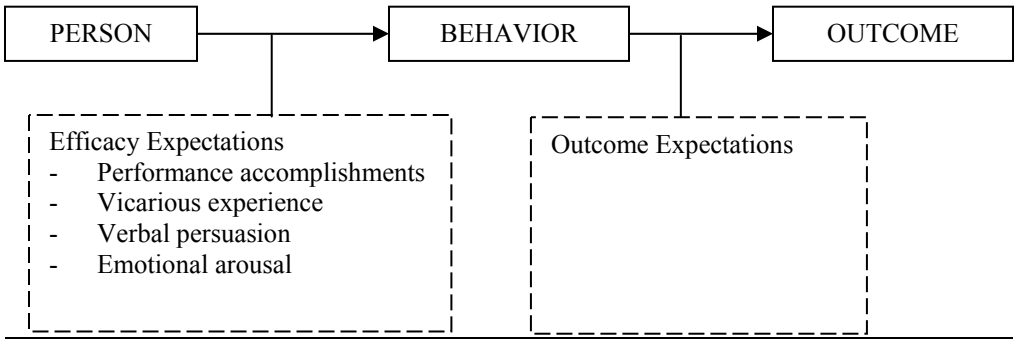


Figure 1. Author's schematic diagram based on Bandura's conceptual model of self-efficacy (A. Bandura, 1977)

Bandura's model was the theoretical context for development of the Chronic Disease Self Management Program launched by researchers at Stanford University (Lorig, 1996). They realized that the effectiveness of chronic disease management is highly contingent upon the self-care behaviors of the patients. This program has been shown to improve self-efficacy, self-management behaviors, and health outcomes, as well as reduce hospitalizations. Therefore, it is important to understand the interaction between chronic conditions such as T2DM and CAD and the patients' self-management behaviors in order to improve their health outcomes (Deaton, et al., 2006; Sansing, 2007).

2.2 LITERATURE REVIEW

The search for appropriate articles regarding T2DM, CAD, and self-efficacy was undertaken using the MEDLINE database through the PubMed database from July 2009 – November 2009. The following guidelines apply to all articles in the literature review. Search results were limited to English publications and human studies in adults aged 19 years and older. Through the evaluation of the abstracts, editorials were removed as well as articles relating to "numeracy," "education tools," and "assessment development."

2.2.1 Self Efficacy and Type 2 Diabetes Management

Multiple studies have shown that self-efficacy may enhance self-management behaviors that in turn influence glycemic control (**Table 1**). The majority of studies reported that self-efficacy was positively associated with better self-care behaviors such as a higher frequency of blood glucose testing and diet and medication adherence, but was not directly associated with glycemic control (Aljasem, Peyrot, Wissow, & Rubin, 2001; Chlebowy & Garvin, 2006b; R. Nakahara, et al., 2006; Nelson, McFarland, & Reiber, 2007; Sousa, Zauszniewski, Musil, Price Lea, & Davis, 2005). One study showed that "[s]elf-efficacy explained 4% to 10% of the variance in diabetes self-care behaviors beyond that accounted for by patient characteristics and health beliefs about barriers [to care]" (Aljasem, et al., 2001). Patients whose self-efficacy was enhanced through self-management skills saw a greater decrease in mean HbA1c (8.08% to 7.40%) after 24 weeks compared to patients without self-management skill training (8.09% to 8.02%), and were more

likely to reach the HbA1c goal of <7% as recommended by the American Diabetes Association (ADA) (ADA, 2004; Chodchoi, Wichit, Linchong, & Sandra, 2007). Part of Bandura's theory states that a positive outcome reinforces self-efficacy, so better glycemic control can serve to improve one's self-efficacy over time. However, Chlebowy et al. (2006a) examined the relationship between psychosocial factors and self-care behaviors and glycemic management in Black and White patients. Outcome expectancy was related to self-care behaviors. Although Black patients reported less satisfaction with social support than did White patients, there were no difference between the races regarding self-efficacy, which was unrelated to self-care behaviors and glycemic control (Chlebowy & Garvin, 2006c).

Non-adherence to oral diabetes medications is one of the leading factors for poor glycemic management (Guillausseau, 2003). In one study, patients on oral medications had higher measures of self-efficacy regarding motivation to change and ability to cope with feelings than patients on insulin (Via & Salyer, 1999). In an additional study, lower self-efficacy was related to the burden of injecting insulin (OR=2.48; 95% confidence interval [CI] 1.27– 4.84) and the burden of adjusting insulin (OR=1.89; 95% CI 1.17– 3.05) (Iris Weijman, et al., 2005).

2.2.1.1 Strengths and Limitations

Despite the variety of assessments used, samples sizes, and populations, most studies centered on the same conclusion: self-efficacy is indeed related to the behaviors that affect glycemic control. The prospective randomized controlled trials were able to assess direction and causality between self-efficacy and glycemic control (Siebolds, Gaedeke, & Schwedes, 2006; Wattana, et al., 2007). Also, the studies were conducted among different races in the US, and in Japan, Germany, and Thailand, extending the generalizability of the results to people of different races and

nationalities (Chlebowy & Garvin, 2006b; R. Nakahara, et al., 2006; Siebolds, et al., 2006; Wattana, et al., 2007). The study by Chlebowy et al. had a methodologically sound study design, but had a small sample size, which could limit its ability to detect statistical differences (N=91). In addition, studies took into consideration the different types of behaviors associated with glycemic control therapy (oral medications versus insulin).

The main limitation was the cross-sectional design of several studies. Therefore, these results could not be used to establish causality or direction of association. The act of glycemic management varies by the use of oral medication or injectable insulin. It is still unclear whether self-efficacy differs by the type of glycemic therapy due to the lack of randomization of glycemic management; therefore, the patients may have differed clinically by the type of insulin therapy prescribed by their physicians prior to entering the study. The self-efficacy assessments were also self-reported. Although this is characteristic of most self-efficacy assessments, it may introduce social desirability bias, in which the respondent reports what she or he believes are the answers that will be desired by the study. Additionally, there is recall bias, in which the respondent's ability to recall positive or negative experiences is skewed by the person's desire to be seen as a good patient, or by poor memory.

Table 1. Self-efficacy and T2DM management

AUTHOR	STUDY DESIGN	SAMPLE SIZE	SELF-EFFICACY ASSESSMENT	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO SELF-EFFICACY)
(Aljasem, et al., 2001)	Cross-sectional, correlational	(N=309)	Modified version of Grossmans Self-Efficacy for Diabetes scale	Greater self-efficacy was associated with a higher frequency of blood glucose testing and better medication adherence and eating habits. SE explained 4% to 10% of the variance in diabetes self-care behaviors
(Chlebowy & Garvin, 2006b)	Two-group, comparative descriptive design	(N=91)	Modified Self-efficacy Questionnaire (SEQ)	Outcome expectancies were related to self-care behaviors, but SE was not related to glycemic control or self-care behaviors
(Chodchio et al. 2007)	Longitudinal, randomized controlled trial	DM management program (N=75) Control (N=72)	DM management program based in Bandura's theory of self-efficacy	DM self-management program based in self-efficacy was associated with better glycemic control.
(R. Nakahara, et al., 2006)	Prospective	(N=256)	Multidimensional Diabetes Questionnaire with a Diabetes-Related Self-Efficacy Scale	SE was related to DM adherence which in turn was related to prospective HbA1c
(Nelson, et al., 2007)	Cross-sectional survey	(N=1,286)	Perceived Competence in Diabetes Scale	Higher self-efficacy was related to better medication and DM meal plan adherence, diet, physical activity, and blood glucose monitoring
(Siebolds, et al., 2006)	Prospective, randomized, controlled, multicenter parallel group comparison	Self-monitoring device (N=113) Control (N=110)	Diabetes counseling algorithm designed to improve, self-perception, self-reflection and self-efficacy	SE and diet counseling plus self-monitoring of blood glucose was more efficient in glycemic control than counseling alone
(Sousa, et al., 2005)	Cross sectional, correlation	(N=141)	Insulin Management Diabetes Self-efficacy Scale (IMDSES)	Greater self-care agency and self-efficacy→ better self-care management → greater glycemic control.Self-care management was not a mediator.
(Via & Salyer, 1999)	Cross-sectional, descriptive, correlation	(N=90)	Diabetes Empowerment Scale (DES)	Patients on oral medications had higher scores in motivation to change and ability to cope with feelings components of the DES than patients on insulin. Baseline HbA1c was not related to SE
(Wattana, et al., 2007)	Randomized controlled trial	Self-management program (N=75) Usual nursing care (N=72)	Self-management program based on Bandura's theory of SE	Patients in the diabetes self-management program showed a better glycemic control and decreased cardiovascular risk factors, and improved quality of life.
(Iris Weijman, et al., 2005)	Cross-sectional, descriptive, correlation	(N=292)	Diabetes Management Self-efficacy Scale	Lower self-efficacy was related to the burden of injecting insulin and the burden of adjusting insulin

Key: DM – diabetes mellitus, SE – self-efficacy

2.2.2 Self-efficacy of Diabetes and Cardiovascular Disease Comorbidity

Deaton et al. (2006) studied symptom distress, self-management, and general and cardiac health status in 1,013 CAD patients with and without T2DM in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial. Self-management was measured by the Self-Management Difficulties Scale (Crohnbach's $\alpha = 0.89$), which was adapted from the Environmental Barriers to Adherence Scale (EBAS) used to measure self-management of diabetes (Irvine, Saunders, Blank, & Carter, 1990).

Researchers found the effects of both CAD and T2DM to be synergistic in hindering self-management. Patients with T2DM and a greater severity of T2DM (HbA1c >7%) had more self-management difficulty regarding medication, exercise, and diet. They also had more physical limitations that promoted the difficulties in self-management. CAD severity was the most important comorbid factor in explaining a poorer risk factor profile for physical disability in patients with T2DM, which was independently associated with increased odds of disability in this patient population. Variables found to be associated with self-management were age, angina status, severity of T2DM, renal disease, symptom distress, and social support ($R^2 = 0.12$; $p = 0.03$) (Deaton, et al., 2006).

2.2.2.1 Strengths and Limitations

The COURAGE Trial is comparable to the BARI 2D study in that it was composed of patients with stable CAD suitable for elective revascularization. The large sample size allowed for higher power to detect differences in self-efficacy between the groups. This study was limited in that it

was cross-sectional and could not establish causality, and used mainly White male patients, thereby limiting the generalizability of the results to females and racial/ethnic minorities.

2.2.3 Self-efficacy and Revascularization

Studies show that self-efficacy improves after revascularization and continues to improve with time; therefore, patients in BARI 2D who are randomized to immediate revascularization are hypothesized to have greater self-efficacy than patients randomized to immediate medical therapy (Table 2). In a study by Aron et al. (2007), quality of life and self-efficacy significantly improved after off-pump and on-pump CABG (Aron, Klinger, & McConnell, 2007). In a population of patients with either PCI and/or MI and patients with the need for revascularization, both self-efficacy and health-related quality of life (HRQoL) increased over time after revascularization (Gardner, et al., 2003). Although men had greater self-efficacy than women, women showed the greatest improvements in self-efficacy over the course of the study. In addition, patients with a history of PCI had the highest mean self-efficacy scores, because their physical limitations were less prohibitive (Gardner, et al., 2003). In a longitudinal study of elderly patients with MI or who had undergone CABG, those patients who experienced MIs had greater mean self-efficacy at week 1 following revascularization ($p<0.001$), while patients who had undergone CABG had greater mean self-efficacy at week 12 ($p<0.001$). Mean self-efficacy expectation scores were moderately high post-procedure (percutaneous transluminal coronary angioplasty [PTCA]) for all self-management behaviors, and all scores increased significantly, except scores for resumption of work-roles, by two weeks post-discharge (Perkins & Jenkins, 1998).

2.2.3.1 Strengths and Limitations

Two of the studies reviewed were longitudinal, and were, therefore, able to assess self-efficacy before and after surgery, and compare the levels of self-efficacy several weeks post-surgery. All studies included not only a variety of quality of life measures, but also physical performance measures, because CAD and revascularization affect physical ability. More specifically, post-event physical disability is an issue in cardiac patients (Perkins & Jenkins, 1998).

Most of the studies reviewed contained selection biases. The study by Aron et al. (2007) was a retrospective study of 295 cardiopulmonary rehabilitation patients who were able to attend at least 80% of the exercise sessions required by the study protocol, thereby possibly resulting in the selection of healthier patients. Also, the study was not designed or powered to detect differences in self-efficacy before and after CABG, because this was not the primary hypothesis. The study by Gardener et al. (2003) was based on a non-randomized sample of convenience; therefore, the clinical and demographic profiles of the patients in each group may have differed. Also, part of the self-efficacy assessment assumed that patients were mobile (introducing selection bias by excluding non-mobile patients), and came with precautions against its generalizability to patients who were older, had lower socioeconomic status, and had greater cardiovascular impairments (Gardner, et al., 2003). The sample size (N=90) and the convenience sample of married White males in the Perkins et al. (1998) study limit the generalizability of their results.

Table 2. Self-efficacy and CAD management

AUTHOR	STUDY DESIGN	SAMPLE SIZE	SELF-EFFICACY ASSESSMENT	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO SELF-EFFICACY)
Aron, Klinger, & McConnell, 2007)	Retrospective	(N=259)	"a self-efficacy tool" for physical performance	Self-efficacy improved in patients post CABG regardless of off-pump or on-pump surgery.
Gardner et al., 2003	Longitudinal	(N=472)	7-item SE questionnaire regarding physical functioning	Self-efficacy improved over time following revascularization Men had higher self-efficacy, but women's self-efficacy improved faster PCI patients' self-efficacy progressed quickly.
Perkins & Jenkins, 1998	Descriptive, correlation	(N=90)	Jenkins Self-Efficacy Expectation Scales	SE scores improved post PTCA

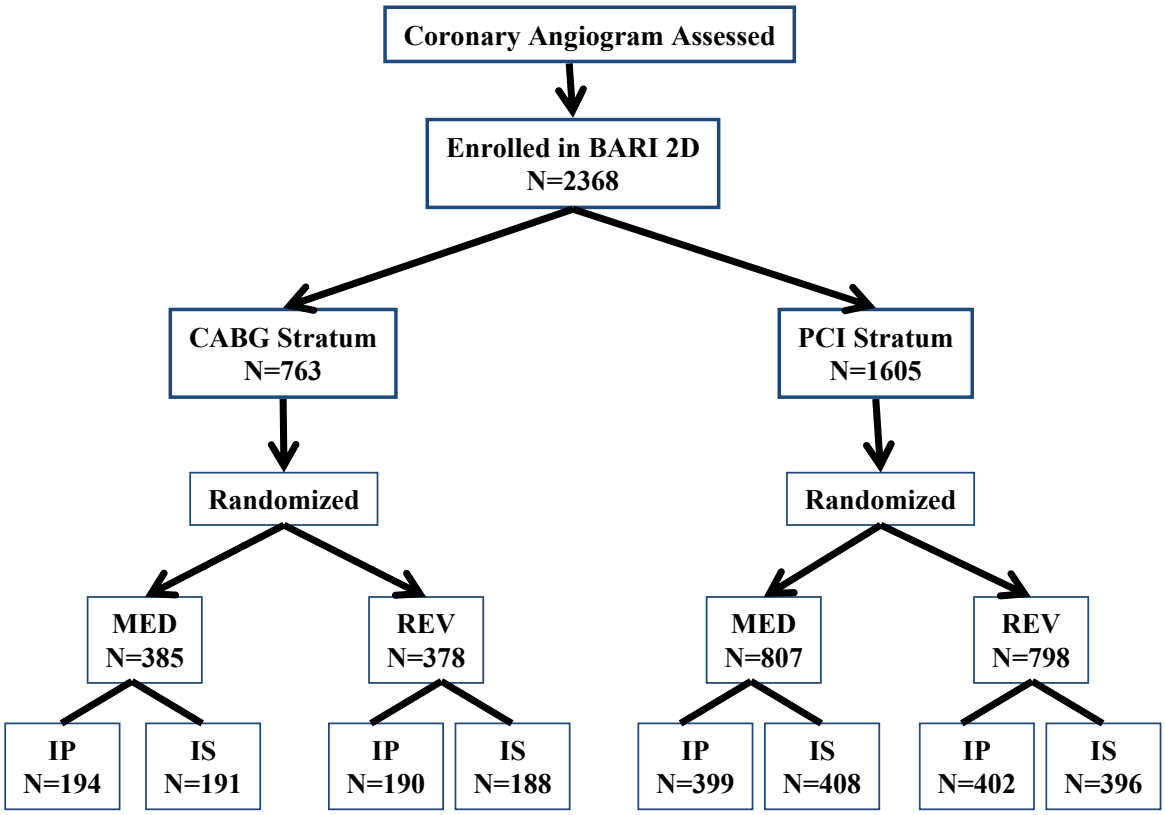
2.3 BARI 2D

2.3.1 Study Design

BARI 2D is a multicenter clinical trial designed to determine optimal treatment strategies for patients with T2DM and documented stable CAD. Using a 2x2 factorial design, BARI 2D compared initial elective revascularization with aggressive medical therapy versus initial aggressive medical therapy and delayed revascularization, while simultaneously studying an insulin-providing versus an insulin-sensitizing strategy of glycemic control to achieve a clinical target of HbA1c <7% (**Figure 2**) (BARI_2D_Study_Group, 2006).

Randomization to either immediate revascularization (REV) or initial medical management (MED) was stratified by BARI 2D site and by intended revascularization to either PCI or CABG as determined by a physician. Patients who were randomized to immediate

revascularization were to receive an intervention by a BARI 2D certified technician within four weeks of randomization. Patients randomized to initial aggressive medical therapy were permitted to receive revascularization if their symptoms worsened or if there were cardiac events. All patients received aggressive medical therapy for cardiac risk factor control, such as dyslipidemia, hypertension, and angina, based on the BARI 2D protocol. The protocol also included a non-pharmacologic Lifestyle Program aimed at smoking cessation, weight loss, foot care, and proper exercise.



Key: IP – insulin providing, IS, insulin sensitizing, MED – medical therapy, REV – immediate revascularization

Figure 2. BARI 2D enrollment and randomization.

Randomization to either insulin-sensitizing drugs or insulin-providing drugs required that patients adopt the assigned form of drug therapy, regardless of the form of therapy prior to study entry. Patients assigned to insulin-sensitizing drug therapy were to be treated with thiazolidinediones or metformin, while patients assigned to insulin-providing drug therapy were treated with sulfonylurea, repaglinide, nateglinide, or insulin (BARI_2D_Study_Group, 2006). If over the course of the study, a patient's HbA1c remained >8%, (s)he was to receive glucose-lowering drugs from the other treatment arm. Additional control of HbA1c was based on an algorithm for optimal glycemic control through combination therapy (Magee & Isley, 2006).

At the baseline visit, extensive clinical, demographic, and psychosocial data were collected including education, employment status, height, weight, HbA1c, duration of T2DM, history of MI, blood pressure, lipid values, and number and type of medications. Study participants also completed a comprehensive battery of self-reported psychosocial measurements including four questions regarding their self-efficacy.

Follow-up visits occurred monthly for the first six months and quarterly thereafter, until the end of the study in 2008. At each follow-up visit, information about clinical risk factors, diabetes complications, clinical events, and medications was collected. The mean follow-up per patient was 5.3 years. The BARI 2D primary endpoint was all-cause mortality. The composite secondary endpoint was death, non-fatal MI, or stroke.

2.3.2 Population

Participants were enrolled between January 1, 2001 and March 31, 2005. There were 49 clinical sites in the United States (US), Canada, Brazil, Mexico, the Czech Republic, and Austria

(N=2,368). Eligible participants had a "diagnosis of T2DM and angiographically documented CAD for which revascularization was not required for prompt control of severe or unstable angina" (BARI_2D_Study_Group, 2006). A physician/investigator at each site determined if the patients were eligible for the study based on the inclusion/exclusion criteria. Inclusion criteria were as follows: diagnosis of T2DM, coronary arteriogram showing one or more vessels amenable to revascularization (≥50% stenosis), objective documentation of ischemia or subjectively documented typical angina with ≥70% stenosis in at least one artery, suitability for coronary revascularization by at least one of the available methods, ability to perform all tasks related to glycemic control and risk factor management, age 25 or older, and informed written consent (BARI_2D_Study_Group, 2006). Exclusion criteria were as follows: definite need for invasive intervention as determined by a cardiologist, any CABG or PCI within the past 12 months, class III or IV CHF, creatinine > 2.0 mg/dl., HbA1c > 13%, need for major vascular surgery concomitant with revascularization (e.g., carotid endarterectomy), left main stenosis ≥ 50%, non-cardiac illness limiting mortality, hepatic disease, fasting triglycerides >1,000 mg/dl in the presence of moderate glycemic control (HbA1c <9.0%), current alcohol abuse, chronic steroid use, known/planned/suspected pregnancy, geographically inaccessible or unable to return for follow-up, enrolled in a competing randomized trial or clinical study, and unable to understand or cooperate with protocol requirements (BARI_2D_Study_Group, 2006).

The recruitment pattern for patients differed according to site. Patients were generally recruited through screenings conducted in the cardiac catheterization laboratory, stress test laboratory, and outpatient clinics both inside and outside of the study sites. Because CAD and T2DM affect minorities disproportionately, there was a strong push to recruit at least 25% minority participants from the sites. Before randomization, it was required that all patients sign

the informed consent document which also contained Health Insurance Portability and Accountability Act (HIPAA) information.

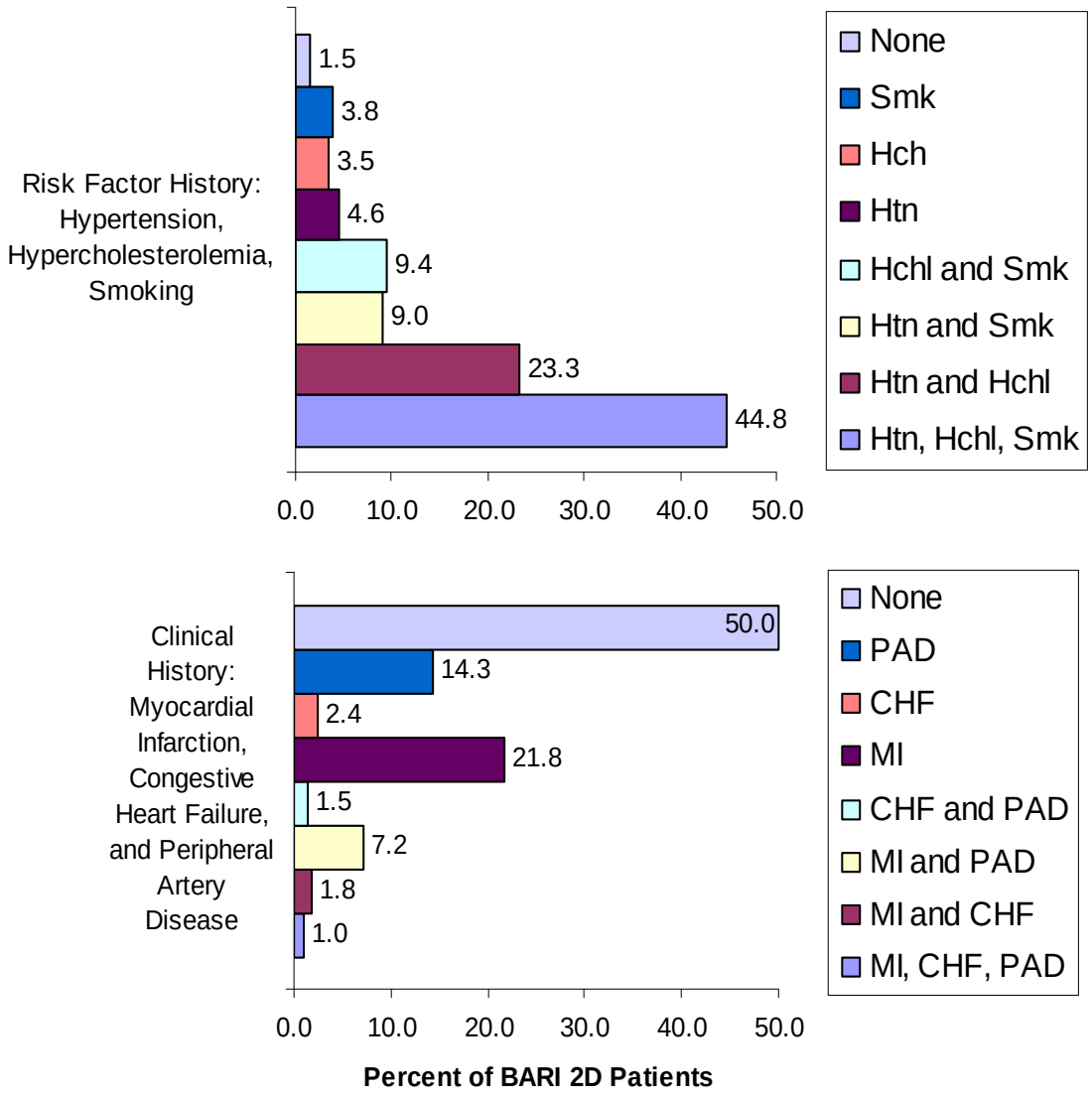
BARI 2D patients were mostly White non-Hispanic (nH) males with a mean age of 62.4±9 (**Table 3**). The majority of the patients were recruited from the U.S. (63%) and Canadian sites (15%). Close to 30% of the patients were racial/ethnic minorities. About a third of the patients (27%) came into the study on insulin. In order to further examine the BARI 2D patient profile, the combination of cardiac risk factors and clinical history is presented in **Figure 3**. Forty five percent of the patients had the combined risk factors of hypertension, hypercholesterolemia, and smoking, nearly a third had a history of clinically documented MI, and seven percent had a history of CHF. Less than a quarter of patients had a prior revascularization.

Of the 2,368 randomized patients, 1,499 patients were from the US sites and 353 patients from the Canadian sites. Of these patients, 1,817 completed a baseline SE assessment (**Figure 4**).

Table 3. Baseline characteristics of BARI 2D population

Baseline Demographic & Clinical Status	(N = 2368)	Baseline Demographic & Clinical Status	(N = 2368)
Age, mean, SD	62.4, 8.9	Hypertension, %	82.5
Male, %	70.4	Hypercholesterolemia, %	81.9
Race, %		Cigarette smoking status, %	
White	70.4	Current	12.5
Black	17	Former	54.4
Asian	4.2	Never	33.1
Indian/Native American	4.3	Myocardial infarction, %	32
Other	4.1	Congestive heart failure, %	6.6
Hispanic ethnicity, %	12.5	Stroke or TIA, %	9.8
Region of World, %		Prior PCI, %	19.6
USA	63.3	Prior CABG, %	6.4
Canada	14.9	Angina status, %	
Brazil	15	None	17.9
Mexico	3.6	Angina equivalents only	21.4
Czech Republic/Austria	3.2	Stable CCS 1	14.3
BMI categories (kg/m^2), %		Stable CCS 2	28.8
Normal or underweight, <25	9.7	Stable CCS 3	7.5
Overweight, 25 to <30	34	Stable CCS 4	1.2
Class 1 obese, 30 to <35	32.1	Unstable angina	9.5
Class 2 obese, 35 to <40	15.3	Duration of DM categories, %	
Class 3 obese, ≥40	9	<5 yrs	33.3
Blood pressure >130/80 mmHg,%	52.4	5 - <10 yrs	23.5
Ankle brachial index ≤0.9	20.1	10 - <20 yrs	29.2
Total cholesterol ≥200 mg/dL, %	19	≥ 20 yrs	14.1
Triglycerides ≥200 mg/dL, %	31	History of insulin use, %	29.3
HDL <40 male <50 female mg/dL, %	72.4	Glycemia measurements, %	
LDL ≥100 mg/dL, %	40.5	$HbA_{1c} \leq 7.0\%$	41.7
Albuminuria		$7.0\% < HbA_{1c} \leq 8.0\%$	25.3
Microalbuminuria (30 < ACR ≤ 300)	22.9	$HbA_{1c} > 8.0\%$	33
Macroalbuminuria (ACR > 300)	9.7	MNSI screening neuropathy score ≥7, %	15.9
		MNSI clinical neuropathy score >2, %	50.3

Key to Table 3: ACR – albumin creatinine ratio, DM – type 2 diabetes mellitus, HbA1c – glycosylated hemoglobin A1c, HDL – high density lipids, LDL – low density lipids, MNSI – Michigan Neuropathy Screening Instrument



Key: CHF – congestive heart failure, Htn – hypertension, Hchl – hypercholesterolemia, MI – myocardial infarction, PAD – peripheral artery disease, Smk – current smoker

Figure 3. Observed combinations of cardiac risk factors and clinical history in the BARI 2D population

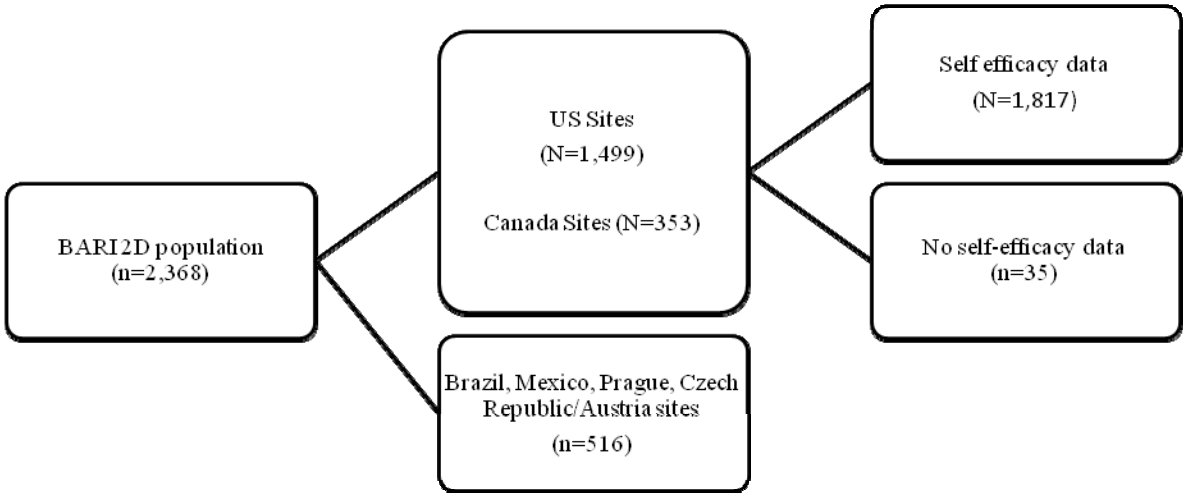


Figure 4. Flowchart for study population

2.3.3 Variables

Self-efficacy is the key measurement of one's self-confidence in medical self-management. Thereby, it serves as the main psychological measure for this proposal. At study entry, BARI 2D participants completed the self-efficacy questionnaire, as well as a comprehensive battery of psychosocial quality of life measures regarding their own health, self-rated health, energy, health distress, and ability to do different activities. Demographic information, clinical history, prescribed pharmaceuticals, and quality of life data were also collected.

2.3.4 Measurements

2.3.4.1 Self-efficacy

Information regarding self-efficacy is part of the Quality of Life section of BARI 2D. The self-efficacy assessment was administered at baseline and annually at Years 1 through 6 and was designed to measure how confident the patient was in his or her ability to do tasks and activities that relate to managing his or her T2DM and CAD in general and specific ways (Appendix A). The ambiguous term "management" may be interpreted as something as simple as trying to monitor glucose regularly or to adhering to a more complex regimen of a specific diet with regular exercise. Patients were encouraged to personally consider what tasks and activities he or she completed on a day-to-day basis, in order to measure confidence in the ability to keep T2DM and CAD "under control."

The self-efficacy assessment was derived from the Chronic Disease Self-management study and was found to have high internal consistency (Crohnbach's $\alpha = 0.92$) (Lorig, 1996). The questions were modified from disease management in general to address heart disease and T2DM specifically. Each question consisted of a 10-point Likert scale with "1 = not at all confident" and "10 = totally confident." Interest lied in the patients' confidence in: 1) doing all day-to-day things necessary to manage their conditions; 2) doing activities for their T2DM and CAD in order to reduce doctor visits; 3) reducing emotional stress associated with their diseases through acts such as prayer, meditation, art, and social contact; and 4) doing activities besides medication adherence, such as exercise, hobbies, and dieting to reduce the impact of the diseases on their daily life.

2.3.4.2 Clinical Risk Factors

HbA1c is used as a measure of diabetic severity, while LDL and systolic blood pressure are used as measures of cardiovascular risk. Resting blood pressure was measured with participants in the seated position. The systolic blood pressure and diastolic blood pressure reported are based on an average of the three sitting blood pressures. Hypertension is defined as a blood pressure level >140/90 mmHg (BARI 2D Coordinating Center, 2002-2005). Fasting total, LDL cholesterol, and high density lipid (HDL) cholesterol, fibrinolytic factors, insulin, and HbA1c levels were measured from blood samples collected at baseline and were analyzed at the BARI 2D core Biochemistry Laboratory. LDL was calculated using the Friedwald equation (Friedwald & Frederickson, 1972). Urine specimens were assayed at the Biochemistry Laboratory for albumin and creatinine in order to diagnose micro- and macroalbuminuria. Medication adherence was not measured in BARI 2D, only the types of medication prescribed. Patients with a history of health

problems may be clinically under control, because of the medications they are using. Therefore, the medications used could serve as a surrogate for a history of the medical problems for which they are taking the medication (e.g., high LDL or high blood pressure).

2.3.4.3 Primary and Secondary Endpoints

The primary endpoint for BARI 2D trial was all-cause death and the secondary composite endpoint was death, nonfatal myocardial infarction, or stroke. Definitions for endpoints and ascertainment methods were provided in the main trial report (BARI 2D Study Group, 2006). Cause of death and stroke were classified and adjudicated by the BARI 2D Mortality and Morbidity committee. The committee was blinded to randomization assignment, treatment received, and additional clinical data. Myocardial infarction was classified by a blinded independent Core Electrocardiography Laboratory.

2.3.4.4 Quality of Life

With self-rated health, patients are asked to rate their general health as either "Excellent," "Very Good," "Good," "Fair," or "Poor" (Ware & Sherbourne, 1992). Health distress and energy were assessed by a 9-item questionnaire in which patients report how they have felt during the past four weeks (Stewart & Ware, 1992). Patients are read five answer options which range from "All of the Time" to "None of the Time." The Duke Activity Status Index (DASI) is a 12-item questionnaire that measures the functionality of the patients in daily and recreational activities (Crohnbach's α=0.67) (Dorian, et al., 2002).

2.4 SUMMARY

Several points are derived from the literature regarding the relationship of psychological factors with T2DM and CAD. Higher self-efficacy is related to lower HbA1c in patients with both CAD and T2DM. However, the direction of this association over time is unknown. T2DM increases the risk for cardiac events, and it also increases the risk for long-term mortality after revascularization. Self-efficacy differs based on the T2DM drug therapies used (insulin versus oral therapy). Self-efficacy is also greater in revascularized patients compared to patients without revascularization, and this difference was seen up to 12 weeks post-procedure.

Future research must be conducted with a more demographically diverse population, because minorities such as Blacks and Native Americans are disproportionately affected by T2DM and CAD (AHA_ASA, 2007; CDC, 2005). Larger sample sizes are also needed in order to increase power, thereby reducing a type II error. A prospective study design would allow for the analysis of causality, compared to cross-sectional studies. Also, research on the association between self-efficacy and CAD/T2DM management is needed over a greater follow-up period. The effects of self-efficacy on cardiac morbidity and mortality in a population with both T2DM and CAD need to be examined given the high rate of comorbidity of the chronic conditions. Therefore, BARI 2D is an ideal study in which these issues can be evaluated.

3.0 PAPER 1: SELF-EFFICACY AND RANDOMIZED TREATMENT THERAPIES FOR TYPE 2 DIABETES MELLITUS AND CORONARY ARTERY DISEASE

3.1 ABSTRACT

OBJECTIVE: The purpose of this study is to examine whether randomized treatment strategies for comorbid Type 2 diabetes and coronary artery disease are associated with patients' confidence in being able to manage their conditions, otherwise known as self-efficacy.

METHODS: Using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, we examined 1,013 patients from the United States (US) and Canada sites. First, elective revascularization by either coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) was selected by a physician as the more appropriate form of revascularization. Patients were then randomized to undergo the recommended revascularization immediately or to receive initial medical therapy with the option of revascularization in the event of worsening cardiac symptoms; patients were also randomized to glycemic therapy by either insulin-sensitizing drugs or insulin-providing drugs. The self-efficacy assessment from the Chronic Disease Self-Management Study was administered at baseline and annually throughout the study. In order to examine how scores could both increase and decrease, analyses were limited to patients whose baseline self-efficacy scores were ≤8 out of 10. Generalized estimating

equations (GEE) were used to determine whether significant associations existed between self-efficacy scores and randomized treatment therapies over time.

RESULTS: There was an average increase in self-efficacy over time, which did not differ by randomized treatment. Over the course of four follow-up years, self-efficacy did not differ significantly between the immediate revascularization and initial medical therapy groups (β=0.04, p=0.65), nor between the insulin-sensitizing and insulin-providing groups (β=0.02, p=0.83).

CONCLUSIONS: Self-efficacy increased over time, but was not associated with treatment strategies for Type 2 diabetes and cardiovascular disease. Confidence in being able to manage one's disease is not hindered or enhanced by the type of therapies, despite differences in therapies.

3.2 INTRODUCTION

Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are highly comorbid conditions that require patients to adapt lifestyle changes and commit to self-management regimens. The optimal treatment strategies for these conditions have been investigated by the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial. Patients were randomly assigned to treatment for both T2DM and CAD; overall, there were no differences in survival rates and cardiovascular events between the treatment groups (BARI_2D_Study_Group, 2009). However, in patients deemed eligible for coronary artery bypass graft (CABG), immediate revascularization was associated with a lower risk of major cardiovascular events

compared to patients with initial treatment by medical therapy (BARI_2D_Study_Group, 2009). Randomization to insulin-sensitizers was associated with better glycemic control and fewer hypoglycemic episodes (low blood sugar) compared to insulin-providers. The effect of these randomized therapies for T2DM and CAD on the patients' confidence in their ability to make the different types of assigned changes necessary for optimal health maintenance, also known as self-efficacy, has not been established.

3.2.1 Coronary Artery Disease and Type 2 Diabetes

Approximately 23.6 million people in the United States (US) have T2DM (17.9 million diagnosed and an estimated 5.7 million undiagnosed), and the lifetime prevalence is 17% (NIDDK, 2007). Complications from T2DM, if left untreated or poorly managed, are blindness, amputations, end stage renal disease, and cardiovascular complications such as myocardial infarction (MI [heart attack]), stroke, and death (NIDDK, 2007). Patients with diabetes have a two- to three-fold increased risk of coronary artery disease (CAD) compared to patients without diabetes, with the risk increasing over time (Kannel & McGee, 1979). In 2004, CAD was the leading cause of death in persons 65 years or older with T2DM, accounting for 68% of the deaths (NIDDK, 2007). In 2005, CAD was the leading cause of death in the US (CDC, 2008). Approximately 80 million adults (approximately 1 in 3) have some form of CAD (CDC, 2008).

3.2.2 Self-efficacy

Patients with both T2DM and CAD must engage in daily regimens in order to make positive changes in their health and decrease their risk of disease-related morbidities. The confidence to successfully make these changes is called self-efficacy and is one component of Albert Bandura's social learning theory (Bandura, 1977). Social learning theory postulates that people learn through observing other's behaviors, personal attitudes, and outcomes of the behaviors. The person then decides if these behaviors should be modeled. Whether or not one decides if the behaviors should be and can be modeled is strongly based on confidence that once can do the behaviors (A. Bandura, 1977, 1982).

3.2.3 Management

The management of T2DM and CAD is not uniform across patients and is a multifaceted process. Universally, all patients must make lifestyle changes that involve diet, exercise, foot care, and medication adherence. The management of these comorbid diseases focuses on the control of HbA1c, blood pressure, and cholesterol levels. There is, however, a diverse range of medication and hospital interventions, each differing in patient-physician involvement, pain, relief of pain, and complexity. The level of difficulty involved in managing one's health can be the pivotal transitioning factor that advances a person from knowing (s)he should do a behavior, to the assessment of his or her ability to carry out the behavior, to the execution and maintenance of that behavior, as described by social learning theory in its application to disease management

(Albert Bandura, 1991). In addition, maintenance/adherence is influenced by both behavior difficulty and outcome satisfaction.

Glycemic control within T2DM involves achieving and maintaining normal levels of HbA1c (<7%) with insulin-sensitizing therapy (oral), insulin-providing therapy (injectable and oral), or a combination therapy. Better self-efficacy enhances self-management behaviors, such as medication adherence, a higher frequency of blood glucose testing, and a healthy diet, that in turn influence glycemic control (Aljasem, et al., 2001; Chlebowy & Garvin, 2006b; R. Nakahara, et al., 2006; Nelson, et al., 2007; Sousa, et al., 2005). Non-adherence to oral diabetes medications is one of the leading factors for poor glycemic management (Guillausseau, 2003). In one study, patients on oral medications had higher measures of self-efficacy regarding motivation to change and ability to cope with feelings than patients on insulin (Via & Salyer, 1999). In an additional study, lower self-efficacy was related to the burden of injecting and adjusting insulin (Iris Weijman, et al., 2005). The cross-sectional designs of most of these studies imply association, but cannot establish causality or direction of association. Insulin is prescribed for more severe T2DM and for T2DM with a long duration; patients in the study were not randomized to the types of glycemic therapy (Moghissi, et al., 2009). It is still unclear whether self-efficacy differs by the type of glycemic therapy due to the lack of randomization of glycemic management; therefore, the patients may have differed clinically by the type of insulin therapy prescribed by their physicians prior to entering the study.

Diabetes therapy also includes control of CAD risk factors such as high levels of low density lipids (>100) and hypertension (>130/80 mmHg) through medications and lifestyle interventions (Gavin, et al., 2003; Ripsin, et al., 2009; Wattana, et al., 2007). Treatment options for CAD include 1) medical management with diet, exercise, and medicine; and/or 2)

revascularization either by coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI). Confidence in self-management may differ according to the treatment prescribed. Health-related quality of life and self-efficacy significantly improve after revascularization by CABG or PCI (Aron, et al., 2007; Gardner, et al., 2003). This improvement in self-efficacy persists over time. In a longitudinal study of elderly patients with MI or who had undergone CABG, patients who had undergone CABG during the study had greater mean self-efficacy at week 12 compared to the MI patients ($p<0.001$). Mean self-efficacy expectation scores were moderately high post-procedure for all self-management behaviors, and the scores increased significantly by two weeks post-discharge. Revascularization by percutaneous transluminal coronary angioplasty (PTCA) and CABG increased self-efficacy over time, especially in patients who have received CABG with no history of MI (Perkins & Jenkins, 1998). These studies were limited by small sample sizes, and all White, physically mobile, and non-randomized samples of convenience, so the clinical profile of the patients varied by treatment assignment. Thus, this increases the Type II error, limits their generalizability, and introduces selection biases.

3.3 RATIONALE

Diabetes therapy by use of insulin drugs and non-insulin drugs places different demands on patients. Insulin is primarily provided in an injectable form and is prescribed for people with more severe forms of T2DM and a longer duration of T2DM (Moghissi, et al., 2009). Insulin secretagouges (part of the insulin-providing drug class) and insulin-sensitizing drugs come in an

oral form. Although the overall concept of taking one's medications remains the same, the physical act of injecting insulin differs greatly from taking an oral insulin-sensitizing medication. Some people find that the injection of insulin is much easier than adhering to healthy dietary habits (I. Weijman, et al., 2005). For others, insulin injections are painful, but necessary, procedures. The pain and the fear of needles brings about anxiety in some patients, resulting in a reduction in medication adherence (Zambanini, Newson, Maisey, & Feher, 1999). Therapies such as these can affect one's self-efficacy in that the patients *know* what they should to do adhere to their injections, but may not *want* or *be able* to adhere to the injections. Therefore, they may lack the self-confidence to carry out the behavior that they know will improve their health.

The outcomes of management must also be considered. Within the BARI 2D trial, insulin-providing drugs, whether injectable or oral, have been associated with poorer glycemic control and increased risk factors compared to patients on insulin-sensitizing drugs (BARI_2D_Study_Group, 2009). Patients who were assigned to insulin-providing therapy were less likely to achieve the target of HbA1c <7.0%, had more hypoglycemia (low blood sugar), had less high density lipids (good cholesterol), and had higher body mass indexes (BMI) throughout the study compared to patients on insulin-sensitizing drugs (BARI_2D_Study_Group, 2009). Poorer performance accomplishments can affect self-efficacy by decreasing confidence in self-management. This lack of self-confidence associated with adherence or the accomplishments may result in decreased health status, leading into a feedback loop (**Figure 5**). This widens the gap between the treatment's efficacy and effectiveness, a public health problem that needs to be addressed. Therefore, patients in BARI 2D who are randomized to insulin-sensitizing therapy are hypothesized to have greater self-efficacy than patients randomized to insulin-providing therapy during the study.

In the context of cardiology, treatments that provide immediate relief from angina, such as revascularization, can in turn improve one's self-confidence in managing their conditions. Angina varies in severity from mild and stable to severe and unstable (Campeau, 1975). If a patient has a relatively severe extent of angina and is revascularized through CABG or PCI, they may experience immediate relief (which some may interpret as a "cure" to their CAD), which in turn improves their self-confidence to manage their health. Studies show that self-efficacy improves after revascularization and continues to improve with time (Aron, et al., 2007; Gardner, et al., 2003). Revascularization in BARI 2D has also been associated with a decreased risk of death and the composite endpoints of death/MI/ stroke among CABG patients compared to medical therapy (BARI_2D_Study_Group, 2009). Therefore, patients in BARI 2D who are randomized to immediate revascularization are hypothesized to have greater self-efficacy than patients randomized to immediate medical therapy during the study.

3.4 SPECIFIC AIMS

Using data from the BARI 2D trial, the purpose of this study was to compare self-efficacy over time by a diabetes treatment strategy of insulin-sensitizing drugs or insulin-providing drugs and a cardiac treatment strategy of initial revascularization or initial medical therapy in patients with comorbid T2DM and stable CAD. In order to examine change in either direction, this analysis will focus on patients on patients whose self-efficacy scores had the ability to decrease and increase over time. Among these patients, the following hypotheses were tested:

1. Patients randomized to insulin-sensitizing therapy will have greater follow-up self-efficacy than patients randomized to insulin-providing therapy.

2. Patients randomized to immediate revascularization will have greater follow-up self-efficacy than patients randomized to initial medical therapy.

3. Within the revascularization strata of PCI and CABG, patients randomized to immediate revascularization will have greater follow-up self-efficacy than patients randomized to initial medical therapy.

3.5 **METHODS**

3.5.1 BARI 2D

BARI 2D is a multicenter clinical trial designed to determine optimal treatment strategies for patients with T2DM and documented stable CAD. Using a 2x2 factorial design, BARI 2D compared initial elective revascularization with aggressive medical therapy (will be referred to as immediate revascularization) versus initial aggressive medical therapy and delayed revascularization if symptoms worsen or are clinically indicated (will be referred to as medical therapy), while simultaneously studying an insulin-providing versus an insulin-sensitizing strategy of glycemic control to achieve a clinical target of HbA1c <7% (**Figure 6**) (BARI_2D_Study_Group, 2006).

Randomization to either immediate revascularization or initial medical therapy was stratified by BARI 2D site and by intended revascularization by either PCI or CABG as

determined by a physician. Follow-up visits occurred monthly for the first six months and quarterly thereafter, until the end of the study in 2008. At each follow-up visit, information about clinical risk factors, diabetes complications, clinical events, and medications was collected. Self-efficacy data were collected annually as part of the quality of life assessments. The mean follow-up per patient was 5.3 years with a range of 3.5 - 6 years. The BARI 2D primary endpoint was all-cause mortality. The composite secondary endpoint was death, non-fatal MI, or stroke.

3.5.2 Population

Participants were enrolled from 49 clinical sites in the US, Canada, Brazil, Mexico, the Czech Republic, and Austria (N=2,368). Eligible participants had a "diagnosis of T2DM and angiographically documented CAD for which revascularization was not required for prompt control of severe or unstable angina" (BARI_2D_Study_Group, 2006). A physician/investigator at each site determined if the patients were eligible for the study based on the inclusion/exclusion criteria. Based on the BARI 2D Manual of Operations (BARI_2D_Coordinating_Center, 2002-2005), inclusion criteria were as follows: diagnosis of T2DM, coronary arteriogram showing one or more vessels amenable to revascularization (≥50% stenosis), objective documentation of ischemia or subjectively documented typical angina with ≥70% stenosis in at least one artery, suitability for coronary revascularization by at least one of the available methods, ability to perform all tasks related to glycemic control and risk factor management, age 25 or older, and informed written consent (BARI_2D_Study_Group, 2006). Exclusion criteria were as follows: definite need for invasive intervention as determined by a cardiologist, any CABG or PCI within the past 12 months, class III or IV CHF, creatinine >2.0 mg/dl., HbA1c >13%, need for major

vascular surgery concomitant with revascularization (e.g., carotid endarterectomy), left main stenosis ≥50%, non-cardiac illness limiting mortality, hepatic disease, fasting triglycerides >1,000 mg/dl in the presence of moderate glycemic control (HbA1c ≤8.0%), current alcohol abuse, chronic steroid use, known/planned/suspected pregnancy, geographically inaccessible or unable to return for follow-up, enrolled in a competing randomized trial or clinical study, and unable to understand or cooperate with protocol requirements (BARI_2D_Study_Group, 2006).

Of all the BARI 2D patients, most were White non-Hispanic males with a mean age of 62.4±9. Of the 2,368 randomized patients, 1,499 patients were from the US sites and 353 patients were from the Canadian sites (**Figure 7**; n=1,852). Given differences in the administration of the self-efficacy assessment (oral versus read), the additional sites from other countries were not included in the analyses. Approximately 30% of all patients were racial/ethnic minorities. About a third of the patients (27%) came into the study on insulin. Forty-five percent of the patients had the combined risk factors of hypertension, hypercholesterolemia, and smoking, nearly a third had a history of clinically documented MI, and seven percent had a history of CHF. Less than a quarter of patients had a prior revascularization. Selection of CABG over PCI as the revascularization method for patients was mainly based on angiographic factors, such as triple vessel disease (odds ratio [OR]=4.43, p<.005), left anterior stenosis ≥70% (OR=2.86, p<.005), and totally occluded lesions (OR=2.35, p<.005). Patients selected for CABG were also more likely to be age 65 and older (OR=1.43, p<0.01) and from non-US sites (OR=2.89, p<0.01) than were those selected for PCI (Kim, et al., 2009).

Because we are interested in examining how the randomized treatment is related to the change in self-efficacy scores, we examined patients whose baseline scores were ≤8 (n=889).

The scores of these selected patients had the ability to increase and decrease over time in contrast to those patients with scores >8 who had limited room to increase.

3.5.3 Data Collection and Measures

3.5.3.1 Self-efficacy

Study participants completed a comprehensive battery of self-reported psychosocial measurements including four questions regarding their self-efficacy. The self-efficacy assessment was administered at baseline and annually at Years 1 through 6 and was designed to measure how confident the patient was in his or her ability to do tasks and activities that relate to managing his or her T2DM and CAD in general and specific ways (Appendix A). The self-efficacy assessment was derived from the Chronic Disease Self-Management Study and was found to have high internal consistency (Crohnbach's α=0.89) (Lorig, 1996). The questions were modified from disease management in general to address heart disease and T2DM specifically. Each question consisted of a 10-point Likert scale with "1 = not at all confident" and "10 = totally confident." Interest lied in the patients' confidence in: 1) doing all day-to-day things necessary to manage their conditions; 2) doing activities for their T2DM and CAD in order to reduce doctor visits; 3) reducing emotional stress associated with their diseases through acts such as prayer, meditation, art, and social contact; and 4) doing activities besides medication adherence, such as exercise, hobbies, and dieting, to reduce the impact of the diseases on their daily life. The final score was an average of the four subscale scores.

3.5.3.2 Randomized Therapies

Prior to randomization, the medical intervention by either CABG or PCI was recommended by a BARI 2D physician. CABG is prescribed for a more severe extent of CAD compared to PCI. Patients randomized to immediate revascularization received their assigned intervention by a BARI 2D certified technician within four weeks of randomization in addition to medical therapy. A proportion of patients randomized to initial medical therapy received revascularization at a later stage in the trial if their symptoms worsened or if there were cardiac events.

Randomization to either insulin-sensitizing drugs or insulin-providing drugs required that patients adopt the assigned form of drug therapy, regardless of insulin use status at baseline. Patients randomized to insulin-sensitizing drug therapy were to be treated with thiazolidinediones or metformin, while patients assigned to insulin-providing drug therapy were treated with sulfonylurea, repaglinide, nateglinide, or insulin (BARI_2D_Study_Group, 2006). If over the course of the study, a patient's HbA1c remained >8%, (s)he was to receive glucose-lowering drugs from the other treatment arm. Initiation of the randomized glycemic therapy and additional control of HbA1c was based on an algorithm for optimal glycemic control through combination therapy (Magee & Isley, 2006).

3.5.3.3 Variables of interest

At the baseline visit, extensive clinical, demographic, and psychosocial data were collected including education, height, weight, HbA1c, duration of T2DM, history of MI, history of hypoglycemia, angina, blood pressure, lipid values, and number and type of medications. Current insulin use at baseline was self-reported by the patient. Duration of diabetes was measured as the time between diagnosis and study entry. Angina was self-reported and measured by the Canadian

Cardiovascular Classification System of Angina Pectoris (CCS), which is measured on a scale from 1 – 4 of increasing severity as measured by activities triggering chest pain (Campeau, 1975).

In order to assess self-rated health, patients were asked to rate their general health as either "Excellent," "Very Good," "Good," "Fair," or "Poor" (Ware & Sherbourne, 1992). Health distress and energy were assessed by a 9-item questionnaire in which patients reported how they felt during the past four weeks (Stewart & Ware, 1992). Patients were given five answer options which ranged from "All of the Time" to "None of the Time." The Duke Activity Status Index (DASI), a 12-item questionnaire that measures the functionality of the patients in daily and recreational activities, was administered (Crohnbach's α=0.67) (Dorian, et al., 2002).

3.5.4 Statistical Methods

The mean follow-up time for patients was 5.3 years. We limited our analyses from baseline to Year 4, due to the large amount of missing data at Years 5 and 6, which was attributable to the extended recruitment phase. In order to examine the change in self-efficacy in patients whose scores had the ability to both increase and decrease over time, analyses were also limited to patients with baseline self-efficacy scores $\leq$8.

Normality of the distribution of the self-efficacy scores was assessed at baseline. Given the large sample size in this analysis (N=1,657), the distribution of the variance can be considered approximately normal (central limit theorem). There was sufficient power to detect small departures from normality based on skewness, kurtosis, and visual inspection.

We compared the difference between the follow-up self-efficacy scores from baseline to Year 1, Year 1 to Year 2, Year 2 to Year 3, and Year 3 to Year 4. The self-efficacy score is the mean of four 10-point subscales. A difference of 0.5, which is based on the effect size seen in the literature that produced a significant difference in self-efficacy scores between diabetes treatment types, was defined as a meaningful change (Via & Salyer, 1999). A difference of ≥0.5 points indicates that at least half of the subscales have either increased or decreased in the same direction by one point. Minimal change was defined as <0.5 difference in follow-up self-efficacy score compared to the baseline score. A decrease or increase was defined as a 0.5-1.5 difference from the baseline score. A large increase and a large decrease were defined as a >1.5 point change from baseline (>1 standard deviation [sd]).

Using intention-to-treat analyses, we analyzed self-efficacy by comparing the following categories of randomized treatment: glycemic therapy (insulin sensitizers versus insulin providers); cardiovascular management (initial revascularization versus initial medical therapy); and cardiovascular management within the intended cardiac revascularization stratum (CABG and PCI). Wilcoxon signed-rank tests were used to compare the mean self-efficacy scores between treatment groups at baseline. Generalized estimating equations (GEE) models were constructed to test the significance of the mean change in self-efficacy scores over time, with all self-efficacy scores included as dependent variables and years in study (including baseline) as the independent variable, controlling for within subject correlation.

In order to estimate the effect of the randomized treatment groups on self-efficacy scores over time, GEE models were constructed. The dependent variable was the follow-up self-efficacy score and the independent variable was the randomized treatment group. Each GEE model controlled for baseline self-efficacy scores, randomized cardiac or glycemic therapy,

follow-up years, and within subject correlation. Time in the study was used as a repeated measure (follow-up years) and as an interaction term with the randomized treatment of interest to measure change from baseline. Separate models were created to examine the effect of randomized cardiac therapy within the revascularization strata (CABG and PCI) stratum. Because patients were required to adopt the randomized form of glycemic therapy despite their current form of therapy upon study entry, separate models were created to examine the effect of randomized diabetes therapy within patients based on baseline insulin use (no or yes).

In the GEE models, the coefficients for the treatment variables represent the estimated difference in self-efficacy for the revascularization group versus the medical therapy group (Models 1-3) and the insulin-sensitizing group versus the insulin providing group (Models 4-6). The coefficients for the time variables show the estimated difference in self-efficacy for each time point compared to Year 4. The coefficients for the treatment*time interaction estimate the difference for each year between the treatment groups. The overall p-values for time and treatment*time interaction test the hypothesis that at least one of the coefficients is equal to zero. For the patients randomized to revascularization, the difference in self-efficacy compared to Year 4 patients randomized to medical therapy is the addition of the coefficients for treatment and treatment*time interaction. Likewise, for the patients on insulin sensitizers, the difference in self-efficacy compared to the Year 4 patients on insulin providers is the addition of the coefficients for treatment and treatment*time interaction.

We expected to see a moderate effect size of approximately 0.5 between treatment groups. Using a sample size analysis based on t-tests, there was >0.84 power (two-sided α=0.05) to detect a 0.4 difference for a small effect size and a 0.6 difference for a large effect size between comparison groups at all time points. After adjusting for multiple comparisons

(Bonferroni α=0.01), there was >0.64 power to detect a 0.4 difference and >0.97 power to detect a 0.6 difference. All analyses were performed using SAS version 9.2; all power analyses were conducted using SAS Power and Sample Size 3.1 (SAS Institute Inc., Cary, NC, 2007).

3.6 RESULTS

In the US and Canadian sites, 1,657 had a baseline self-efficacy score and at least one follow-up score. The baseline self-efficacy score was 7.72±1.81, median=8.0, skewness=-0.85 and kurtosis=0.54 (**Figure 8**). The characteristics of these patients at study entry are shown in the first column of **Table 4.** At study entry, patients were predominately male (71.8%), with an average age of 62.6±8.9 years. The patients were racially and ethnically diverse, with 64.5% White non-Hispanic, 18.3% Black non-Hispanic, 11.5% Hispanic, and 5.7% Other non-Hispanic (including Asian and Native American) patients. The majority of the patients had a high school education and above. There were few smokers (12.9%) and patients with a history of cancer (9.1%). The average duration of diabetes in the BARI 2D patients was 10.6±8.8 years. Patients had a mean HbA1c of 7.5% ±1.5% and probable neuropathy was screened in 15.6% of patients. About a third of patients were using insulin at the time of randomization and the average number of hypertension drugs was 2.3±1. A low percentage of patients (7.4%) had a history of congestive heart failure and a third had a history of MI (28.2%). A large proportion of patients had a clinical history of hypertension and hypercholesterolemia requiring treatment. Just over half of patients reported angina symptoms. Mean systolic blood pressure was 130.7±18.5 mmHg

and the median LDL was 90 mg/dl. The mean self-efficacy score was 7.7±1.8. More than half of the patients rated their health as "Good" to "Excellent" **(Table 5)**. The patients rated their energy and their ability to carry out daily activities as low (DASI). Baseline self-efficacy scores were balanced between randomized treatment groups.

Examining only patients whose baseline scores were ≤8, there were 889 patients at baseline, 873 at Year 1, 827 at Year 2, 788 at Year 3, and 711 at Year 4. The reasons for lost to follow-up are listed in Appendix B. The total numbers of events are not mutually exclusive, so one patient may have several of the listed events. For Years 1 -3, most patients were lost to follow-up due to rescission of consent and death. Towards the end of the study, most patients were lost due to death and study close-out. Time in the study was positively associated with self-efficacy scores overall (β=0.19, p<.001; **Figure 9**). The self-efficacy scores increased significantly from baseline to Year 4 (p<.001; **Figure 10 Figure 11**). However, there were no significant differences between the randomized therapies overall and within either of the treatment strata.

Table 6 shows the mean scores and standard deviation per follow-up period by treatment assignment and strata for those patients with baselines scores ≤8. Although the medical group and the insulin-providing group had lower self-efficacy scores compared to the revascularization group and the insulin-sensitizing group respectively, none of the treatment comparisons were significantly different. The mean self-efficacy scores increased over the years within each of the treatment arms (p-values ≤0.05).

The adjusted GEE models 1 – 3 were created to compare improvement in self-efficacy between patients assigned to revascularization versus medical therapy, overall and within designated patient subgroups (**Table 7**). Self-efficacy scores of patients randomized to initial

revascularization did not significantly differ from scores of patients randomized to medical therapy overall and within revascularization strata. Time was significant overall (p=0.002) and within the PCI stratum (p<.001). The time*treatment interactions were not significant.

The adjusted GEE models 4 - 6 were created to compare improvement in self-efficacy between patients assigned to insulin-sensitizing to insulin-providing treatments (**Table 8**). Patients randomized to insulin-sensitizers did not differ in self-efficacy from those randomized to insulin-providers overall or by insulin use at baseline. Time was significant overall and within patients with no baseline insulin use. Self-efficacy at Year 1 was significantly lower than Year 4 overall and within patients with no insulin use at baseline. The time*treatment interactions were not significant.

The interactions between treatment and time did not reach statistical significance in any of the models, and thus were removed when assessing the main effect of treatment assignment (**Table 9**). There were no significant differences in self-efficacy scores between revascularization versus medical therapy (β=0.03, p=0.76) overall and within the CABG and PCI strata. Additionally, there were no significant differences between insulin sensitizers versus insulin providers (β=0.02, p=0.79) overall and within patients with and without insulin use at baseline.

3.7 DISCUSSION

For those patients with CAD and T2DM who have self-efficacy scores ≤8, there were no differences in follow-up self-efficacy scores based on randomization to treatment with insulin-sensitizing drugs versus insulin-providing drugs, or in randomized treatment to early

revascularization compared to initial medical therapy. Similar to results by Perkins et al. (1989), this study showed that over time, self-efficacy increased or remained stable.

CABG is prescribed for more severe CAD compared to PCI, and immediate revascularization by CABG has been shown to decrease the rates of the clinical endpoints (death and a composite of death/MI/stroke) in BARI 2D patients (BARI_2D_Study_Group, 2009; Kim, et al., 2009). Given that self-efficacy is also associated with better clinical outcomes, we hypothesized that better self-efficacy would be observed in the revascularization group compared to the medical group within patients (Sarkar, Ali, & Whooley, 2009). This would be particularly noticeable in patients with more severe CAD. However, in patients for whom CABG was deemed the appropriate form of revascularization, our study showed there was no difference in self-efficacy between the cardiac therapies.

Insulin use at baseline is indicative of a more severe extent of T2DM and poor glycemic control (Moghissi, et al., 2009). Since insulin use is a marker for more advanced T2DM, it is difficult to distinguish in cross-sectional studies whether the insulin effect is due to treatment or due to the disease. Our study indicates that it is not due to treatment. There was no association between self-efficacy scores and randomization to insulin-sensitizing or insulin-providing therapy overall or by insulin use at baseline. These results are counter to the results of Via and Salyer (1999), whose results showed that patients on oral medication had higher self-efficacy than those on injectable insulin. These null results may reflect drug therapy cross-over and combination drug therapy of insulin-sensitizing and insulin-providing therapy. In addition, insulin-providing drugs are not solely injectable as the insulin secretagouges come in oral form.

Patients whose baseline self-efficacy scores were ≤8 showed an increase in self-efficacy scores over time. With its aggressive medical therapy either via drug therapy, coordinated care,

and/or revascularization, participation in BARI 2D, regardless of treatment type, may have increased the patient's confidence in being able to manage their conditions and provided a sense of empowerment. In BARI 2D, patients have regular contact with health care professionals, including dedicated nurses.

A large clinical trial such as BARI 2D has multiple advantages in studying self-efficacy in patients with comorbid CAD and T2DM. One of the major strengths of the study was the randomization of treatment therapies. This ensured that the patients were demographically and clinically similar between the treatment groups. The patients in the study were demographically diverse, so that the results are generalizable to patients of various races, ethnic groups, education levels, and sexes. The large sample size gave us sufficient power to detect at least a moderate effect size at all time points. BARI 2D also has an extensive database of clinical measures relating to T2DM and CAD so that clinical factors associated with self-efficacy can be studied. In this analysis, self-efficacy improved significantly over time in patients with treatments associated with less severe extent of CAD and T2DM. By Year 4, self-efficacy was higher than it was at Year 1 for patients within the PCI stratum and who had no insulin use at baseline. Future analyses will further investigate the relationship between the clinical measures that are associated with self-efficacy.

There are several limitations that need to be addressed in future analyses. Because the focus of this paper is randomized treatment for T2DM and CAD, the intention-to-treat analyses did not account for the treatment received. Within the first 6 months of study entry, 95% of the initial revascularization group received revascularization and 13% of the medical therapy group received revascularization; by Year 3, 33% of the medical patients had undergone revascularization as clinically indicated (BARI_2D_Study_Group, 2009). Patients whose HbA1c

was not properly managed by their randomized drug therapy (HbA1c ≥8%) crossed over to the other therapy or received combination therapy. By Year 3, nearly 90% of patients were on the assigned diabetes therapy; 43% of the insulin-sensitizing group and 12% of the insulin-providing group received additional medication from the alternative drug class to assist in glycemic control (BARI_2D_Study_Group, 2009). Future analyses will control for the cross-over rates in diabetes therapy and the form of insulin therapy.

In summary, confidence in being able to manage one's disease is not hindered or enhanced by the type of therapies, despite their differences. Self-efficacy was found to increase over time in patients whose self-efficacy was moderately good and who were participating in a medically aggressive program of health care. Clinical measurements, such as HbA1c, lipids, and blood pressure, that are dependent on the type of treatment, must be considered when examining self-efficacy in patients with CAD and T2DM.

3.8 TABLES AND FIGURES FOR PAPER 1

Table 4. Demographics and baseline clinical status by baseline self-efficacy scores

Characteristic	Total (N=1,657)	Baseline SE Score ≤8 (N=889)	Baseline SE Score >8 (N=768)	p-value
Male, %	71.8	69.9	74.1	0.06
Age at study entry, mean, SD	62.6, 8.9	62.4, 8.9	62.8, 8.9	0.46
Race/Ethnicity, %				
White nH	64.5	60.5	69.0	<.0001
Black nH	18.3	18.3	18.4	
Hispanic	11.5	15.1	7.4	
Other nH	5.7	6.1	5.2	
Education, %				
Some high school or less	25.3	28.6	21.6	<.0001
High school diploma	25.8	28.2	23.0	
Post high school education	28.9	27.9	30.1	
Bachelors Degree or higher	19.9	15.3	25.3	
United States Site, %	79.5	78.6	80.6	0.32
Current use of cigarettes or other tobacco product, %	12.9	15.9	9.5	0.00
Malignancy, %	9.1	8.5	9.8	0.39
HbA1c %, mean, SD	7.5, 1.5	7.6, 1.6	7.4, 1.5	0.00
HbA1c ≥8%, %	30.9	33.7	27.6	0.01
Probable neuropathy: screening MNSI ≥7, %	15.6	20.2	10.3	<.0001
Currently taking insulin, %	29.8	34.4	24.5	<.0001
Duration of diabetes (years), mean, SD	10.6, 8.8	11.3, 8.9	9.9, 8.6	0.00
Angina category, %				
No angina	43.2	40.2	46.7	0.02
Angina CCS 1, 2	39.6	41.4	37.6	
Angina CCS 3, 4 or unstable	17.1	18.4	15.6	
History of treated congestive heart failure, %	7.4	9.3	5.2	0.00
History of myocardial infarction, %	28.2	28.7	27.7	0.67
Number of hypertension drugs, mean, SD	2.3, 1.0	2.4, 1.0	2.2, 1.0	<.0001
Hypercholesterolemia requiring treatment, %	82.9	85.3	80.1	0.01
Sitting systolic blood pressure (mmHg), mean, SD	130.7, 18.5	131.4, 19.0	129.9, 17.9	0.11
Systolic blood pressure >140 mmHg, %	25.1	25.9	24.2	0.44
Low density lipids mg/dl, median (interquartile range)	90 (72-112)	91 (72-113)	88 (72-112)	0.16
Low density lipids ≥ 100 mg/dl, %	35.1	36.2	33.7	0.29

Table 5. Baseline quality of life measures and randomized treatment and strata by baseline self-efficacy scores

Characteristic	Total (N=1,657)	Baseline SE Score ≤8 (N=889)	Baseline SE Score >8 (N=768)	p-value
QUALITY OF LIFE				
Self efficacy score (0-10), mean, SD	7.7, 1.8	6.4, 1.5	9.3, 0.6	<.0001
Self rated health category (1-Excellent 5 - Poor), %				
Excellent	1.6	0.4	2.9	<.0001
Very good	10.7	5.3	16.9	
Good	41.5	35.0	49.1	
Fair	33.7	41.1	25.1	
Poor	12.6	18.2	6.0	
Duke Activity Status Index (DASI) (0-58.2), mean, SD	19.8, 14.2	15.6, 12.4	24.6, 14.7	<.001
Energy score (0-100), mean, SD	47.3, 21.5	41.4, 19.9	54.3, 21.3	<.001
Health distress score (0-100), mean, SD	43.0, 25.3	50.7, 23.7	34.1, 24.1	<.001
RANDOMIZED TREATMENT AND STRATA				
Glycemic treatment, %				
Insulin sensitizing	50.0	48.8	51.3	0.32
Insulin providing	50.0	51.2	48.7	
Cardiovascular treatment, %				
Medical therapy	51.2	52.4	49.7	0.28
Initial revascularization	48.8	47.6	50.3	
Cardiac revascularization strata, %				
CABG	24.3	24.3	24.4	0.98
PCI	75.7	75.7	75.6	

Key: CABG – coronary artery bypass graft, CCS 1–CCS 4 - Cardiovascular Classification System 1 - 4, CHF – congestive heart failure, HbA1c – glycosylated hemoglobin, HS – high school, LDL – low density lipids, MI – myocardial infarction, nH – non-Hispanic, PCI – percutaneous coronary intervention, SD – standard deviation

Table 6. Self-efficacy scores (mean, SD) by randomized treatment assignment over time among patients with baseline scores ≤8

	Time	N	All	IP	IS	Treatment p-value
Glycemic Therapy	Baseline	889	6.4, 1.5	6.4, 1.4	6.5, 1.5	0.36
	Year 1	873	6.9, 1.9	6.9, 1.8	6.9, 1.9	0.79
	Year 2	827	7.0, 1.8	7.0, 1.9	7.1, 1.8	1.00
	Year 3	788	7.2, 1.8	7.1, 1.9	7.2, 1.7	0.51
	Year 4	711	7.2, 1.8	7.1, 1.8	7.2, 1.8	0.54
	Time p-value		<.001	<.001	<.001	
	Time	**N**	**All**	**REV**	**MED**	**Treatment p-value**
Cardiac Therapy: All	Baseline	889	6.4, 1.5	6.4, 1.4	6.4, 1.5	0.88
	Year 1	873	6.9, 1.9	6.9, 1.9	6.9, 1.9	0.65
	Year 2	827	7.0, 1.8	7.1, 1.8	7.0, 1.8	0.38
	Year 3	788	7.2, 1.8	7.2, 1.9	7.1, 1.8	0.36
	Year 4	711	7.2, 1.8	7.2, 1.8	7.2, 1.8	0.82
	Time p-value		<.001	<.001	<.001	
Cardiac Therapy: CABG Stratum	Baseline	216	6.6, 1.3	6.7, 1.3	6.5, 1.4	0.12
	Year 1	212	7.2, 1.9	7.2, 2.0	7.1, 1.9	0.76
	Year 2	202	7.2, 1.8	7.2, 1.6	7.2, 1.9	0.74
	Year 3	193	7.3, 1.8	7.3, 1.7	7.3, 1.9	0.89
	Year 4	179	7.2, 1.7	7.4, 1.7	7.0, 1.7	0.14
	Time p-value		<.001	0.02	<.001	
Cardiac Therapy: PCI Stratum	Baseline	673	6.4, 1.5	6.3, 1.5	6.4, 1.5	0.28
	Year 1	661	6.8, 1.9	6.7, 1.9	6.9, 1.8	0.42
	Year 2	625	7.0, 1.8	7.1, 1.9	6.9, 1.8	0.26
	Year 3	595	7.1, 1.9	7.2, 2.0	7.1, 1.8	0.30
	Year 4	532	7.2, 1.8	7.1, 1.9	7.2, 1.8	0.55
	Time p-value		<.001	<.001	<.001	

Key: IP – insulin-providing therapy, IS – insulin-sensitizing therapy, MED – initial medical therapy with delayed revascularization, REV – initial revascularization with medical therapy
Analysis is limited to patients with baseline scores ≤8.

Table 7. Separate GEE models of treatment, time, and treatment* time interaction on self-efficacy scores

Revascularization vs. medical therapy	Follow-up Years	Coefficient Estimate	Standard Error	p-value	Overall p-value
MODEL 1: OVERALL (N=889)					
Treatment		0.06	0.13	0.66	
Time	1	-0.18	0.10	0.08	0.002
	2	-0.13	0.10	0.19	
	3	0.02	0.10	0.87	
	4	ref=0			
Treatment * Time	1	-0.13	0.15	0.39	0.67
	2	0.04	0.14	0.76	
	3	0.00	0.14	0.99	
	4	ref=0			
MODEL 2: CABG (N=216)					
Treatment		0.32	0.25	0.20	
Time	1	0.18	0.19	0.34	0.85
	2	0.17	0.20	0.41	
	3	0.26	0.19	0.17	
	4	ref=0			
Treatment*Time	1	-0.33	0.27	0.23	0.55
	2	-0.30	0.29	0.30	
	3	-0.31	0.27	0.25	
	4	ref=0			
MODEL 3: PCI (N=673)					
Treatment		-0.03	0.16	0.85	
Time	1	-0.30	0.12	0.01	<.001
	2	-0.22	0.11	0.05	
	3	-0.06	0.11	0.57	
	4	ref=0			
Treatment * Time	1	-0.06	0.18	0.73	0.50
	2	0.16	0.17	0.33	
	3	0.11	0.16	0.52	
	4	ref=0			

Each model is adjusted for baseline self-efficacy score, randomized diabetes therapy, follow-up years, and the interaction between randomized cardiac therapy and follow-up years.
Analysis is limited to patients with baseline scores ≤8.

Table 8. Separate GEE models of treatment, time, and treatment* time interaction on self-efficacy scores

Insulin sensitizers vs. insulin providers	Follow-up Years	Coefficient Estimate	Standard Error	p-value	Overall p-value
MODEL 4: OVERALL (N=889)					
Treatment		0.06	0.13	0.65	
Time	1	-0.30	0.11	0.01	0.002
	2	-0.12	0.10	0.24	
	3	0.03	0.10	0.73	
	4	ref=0			
Treatment * Time	1	-0.11	0.15	0.46	0.78
	2	-0.02	0.14	0.88	
	3	0.04	0.14	0.79	
	4	ref=0			
MODEL 5: NO BASELINE INSULIN USE (N=583)					
Treatment		0.05	0.16	0.75	
Time	1	-0.34	0.13	0.01	0.001
	2	-0.11	0.12	0.34	
	3	0.11	0.11	0.31	
	4	ref=0			
Treatment*Time	1	-0.16	0.18	0.37	0.58
	2	-0.11	0.17	0.51	
	3	0.05	0.16	0.76	
	4	ref=0			
MODEL 6: BASELINE INSULIN USE (N=306)					
Treatment		0.04	0.25	0.86	
Time	1	-0.19	0.20	0.35	0.45
	2	-0.14	0.20	0.50	
	3	-0.17	0.20	0.41	
	4	ref=0			
Treatment*Time	1	0.01	0.27	0.97	0.90
	2	0.13	0.27	0.62	
	3	-0.05	0.27	0.86	
	4	ref=0			

Each model is adjusted for baseline self-efficacy score, randomized cardiac therapy, follow-up years, and the interaction between randomized diabetes therapy and follow-up years.
Analysis is limited to patients with baseline scores ≤8.

Table 9. Separate GEE models with randomized treatment as the main effect on self-efficacy

Treatment Groups (Main effect)	Estimate	Standard Error	P-value
Revascularization vs. medical therapy			
Model 1: Overall (N=889)	0.03	0.09	0.76
Model 2: CABG (n=216)	0.07	0.19	0.72
Model 3: PCI (n=673)	0.01	0.10	0.95
Insulin sensitizers vs. insulin providers			
Model 4: Overall (n=889)	0.02	0.09	0.79
Model 5: No baseline insulin use (n=583)	-0.02	0.11	0.88
Model 6: Baseline insulin use (n=306)	0.08	0.17	0.65

Models 1-3 are adjusted for baseline self-efficacy score, randomized diabetes therapy, and follow-up years.
Models 4-6 are adjusted for baseline self-efficacy score, randomized cardiac therapy, and follow-up years.
Analysis is limited to patients with baseline scores ≤8.

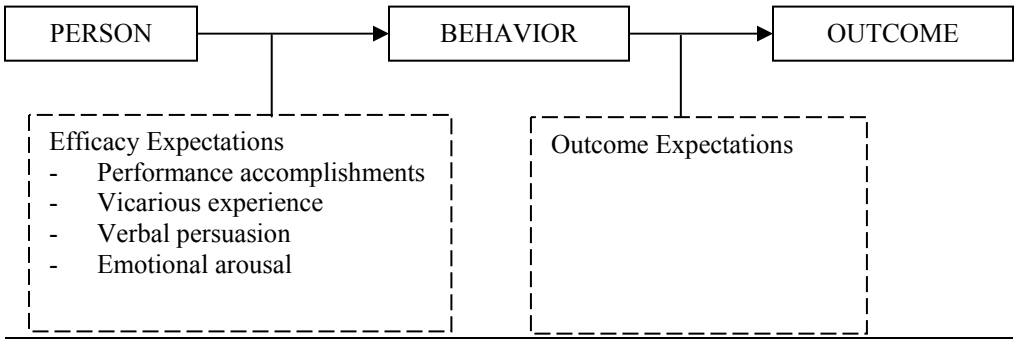
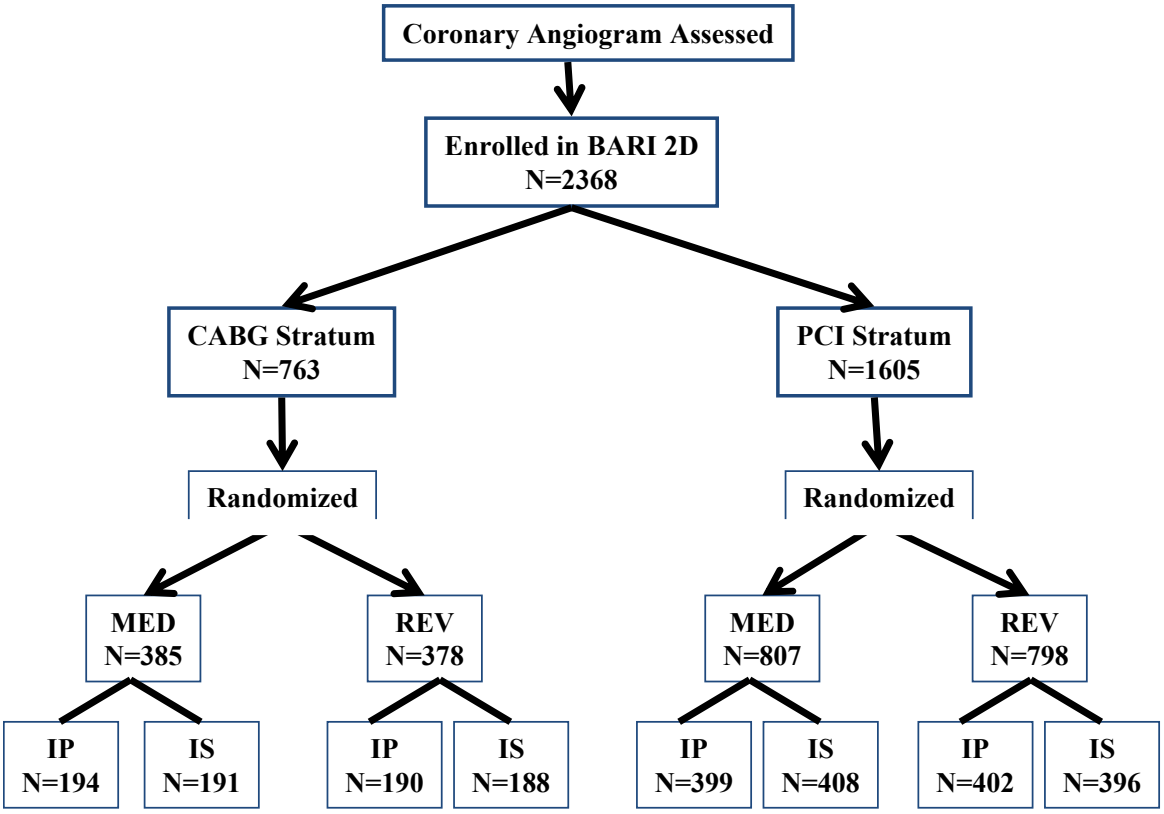


Figure 5. Author's schematic diagram based on Bandura's conceptual model of self-efficacy (A. Bandura, 1977)



Key: IP – insulin providing, IS, insulin sensitizing, MED – medical therapy, REV – immediate revascularization

Figure 6 BARI 2D enrollment and randomization.

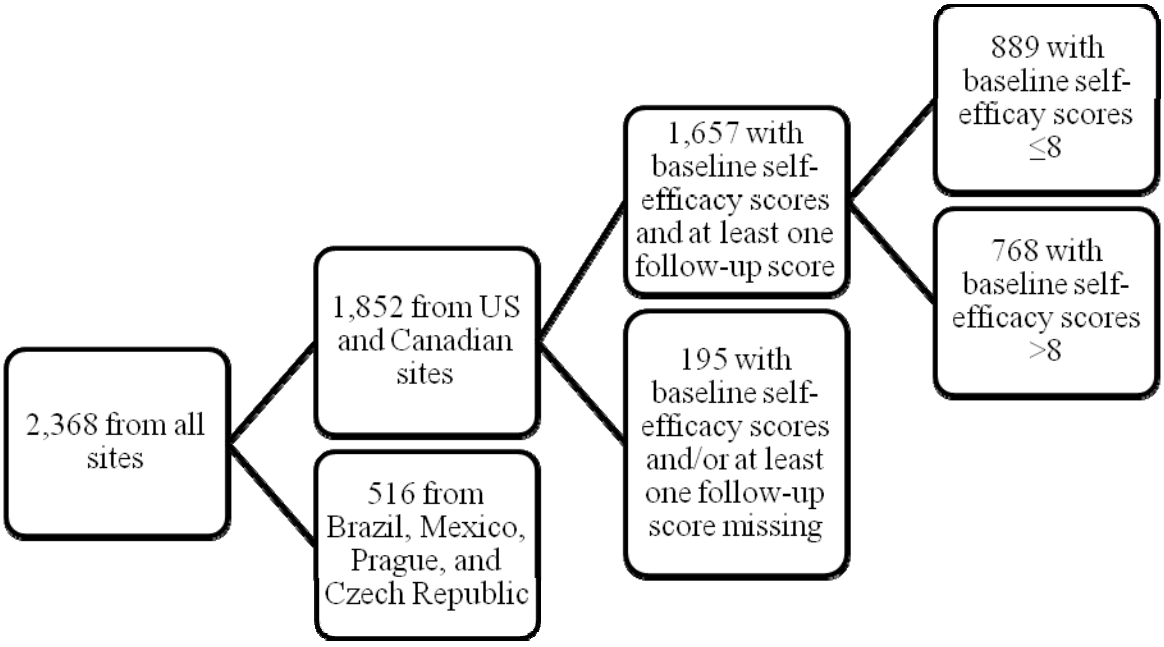


Figure 7. Population flowchart for Aim 1

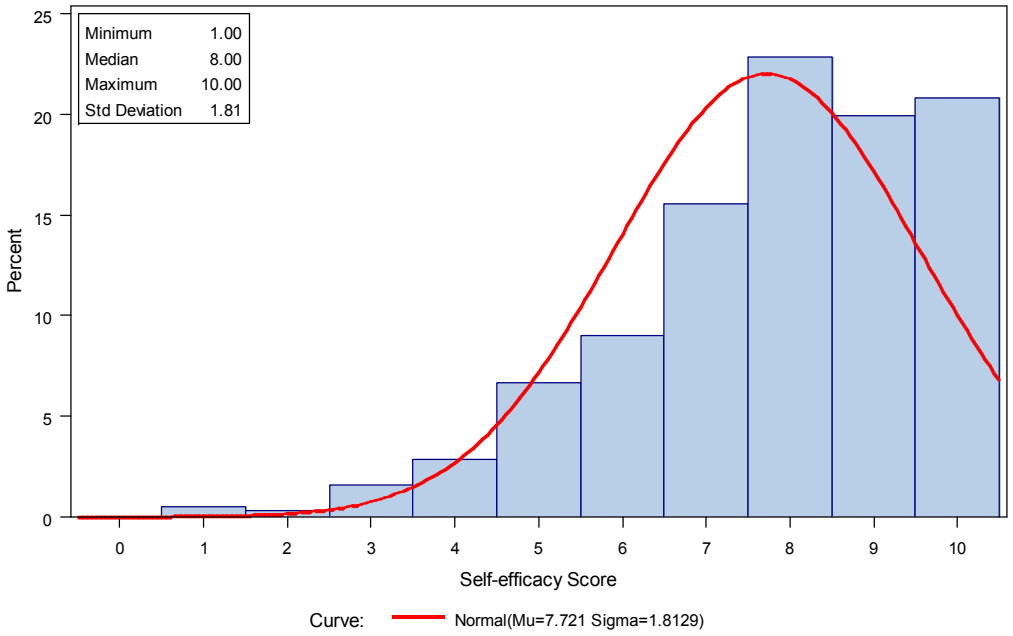


Figure 8. Histograms of baseline self-efficacy scores

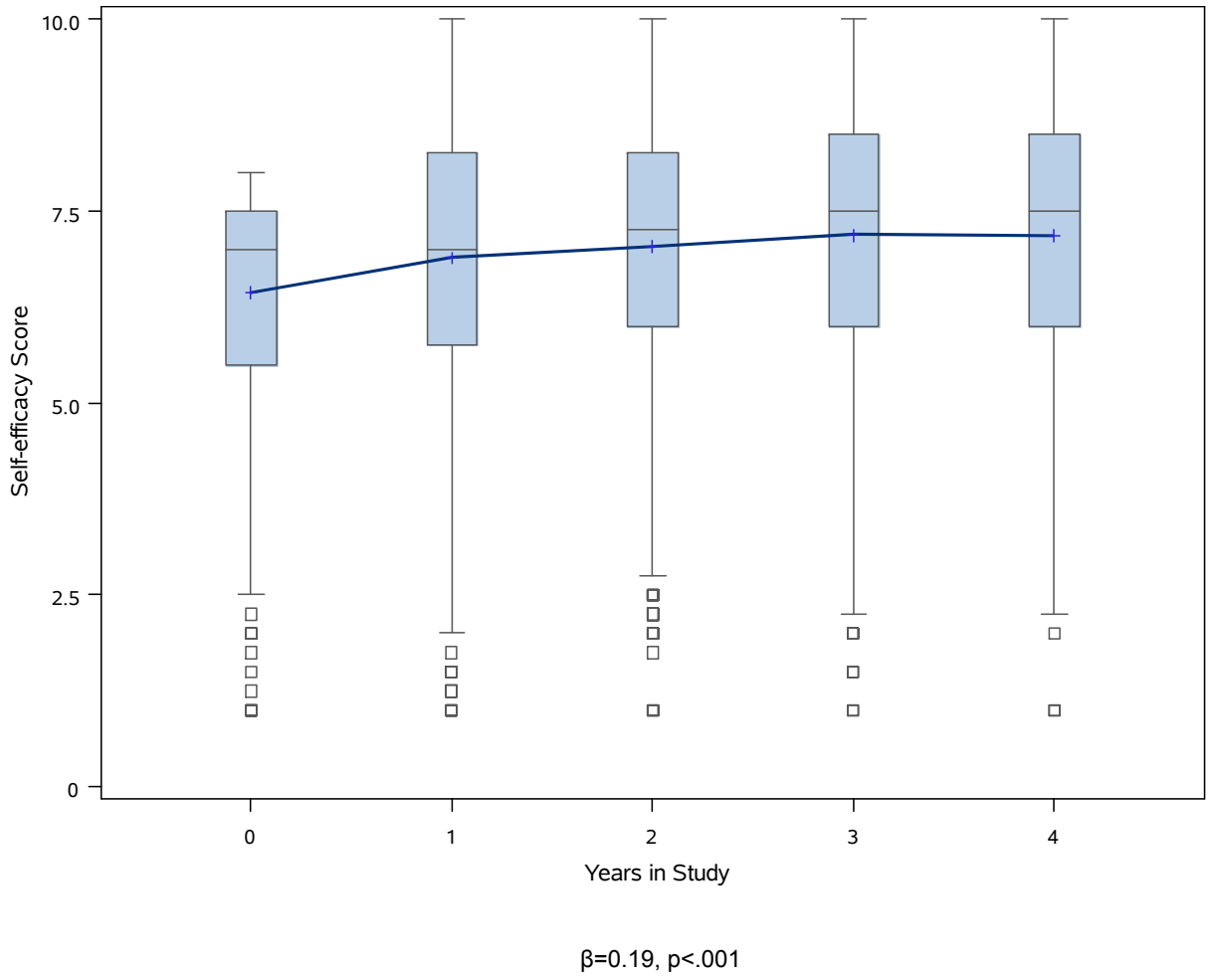
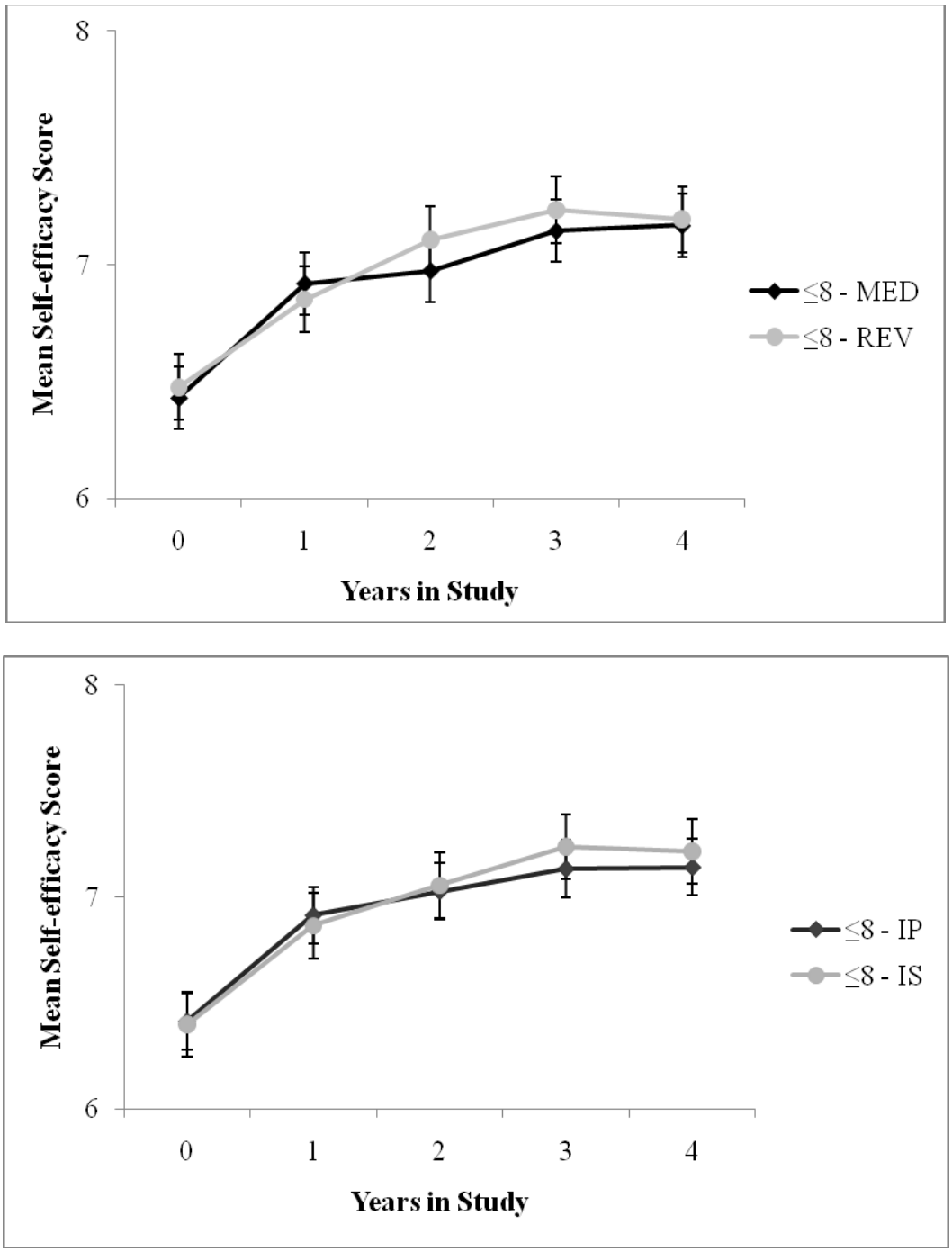
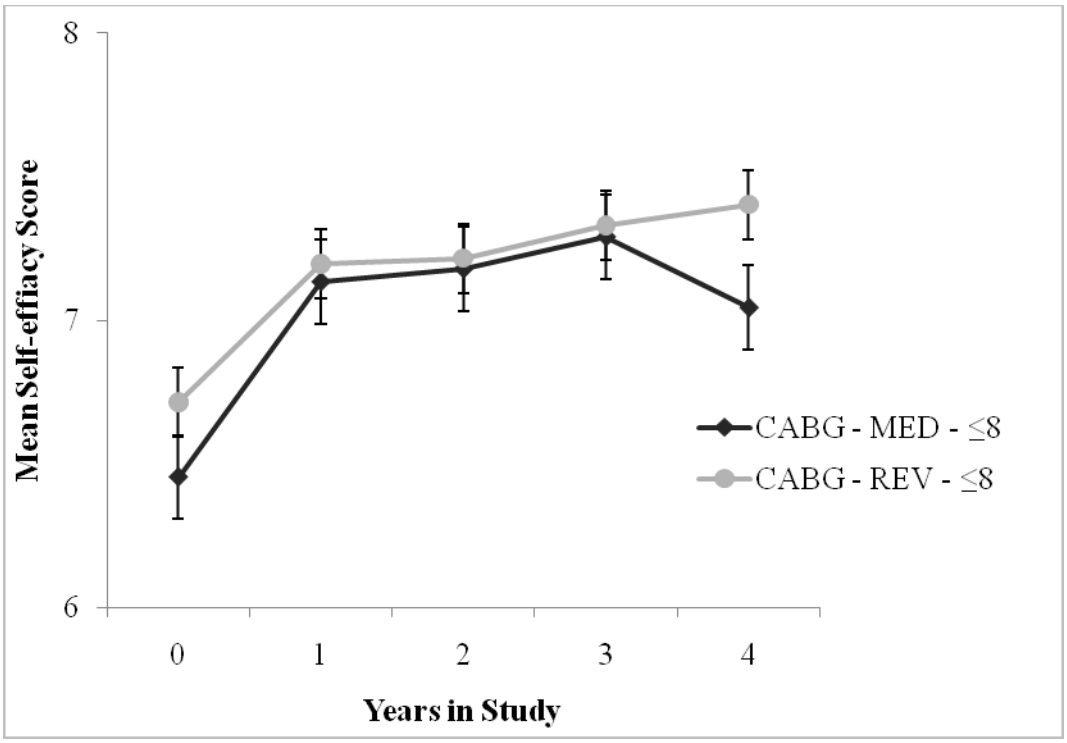


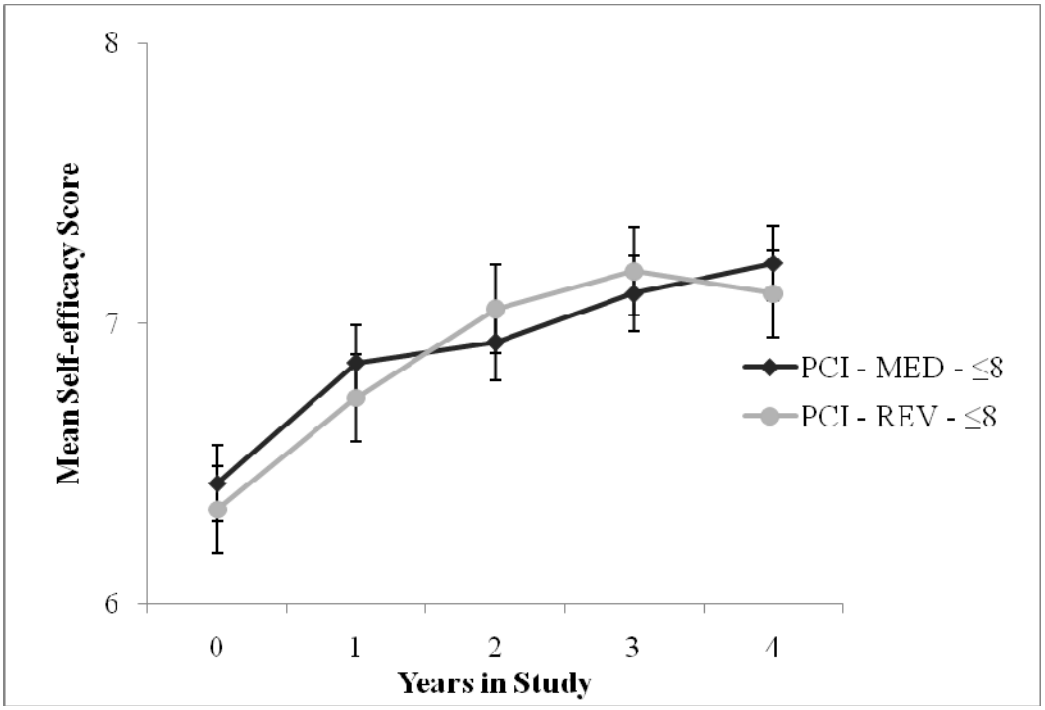
Figure 9. Boxplots of efficacy scores and years within patients whose baseline scores ≤8 with line connecting mean values



Key: IP – insulin providers, IS – insulin sensitizers, MED – medical therapy, REV - revascularization

Figure 10. Mean self efficacy score over time by randomized treatment and baseline self-efficacy score





Key: CABG – coronary artery bypass graft, PCI – percutaneous coronary intervention, MED – medical therapy, REV – revascularization

Figure 11. Mean self efficacy score over time by randomized treatment and baseline self-efficacy score within revascularization strata

4.0 PAPER 2: THE RELATIONSHIP BETWEEN SELF-EFFICACY AND RISK FACTOR CONTROL OVER TIME AND THE MODERATING EFFECT OF RACE/ETHNICITY

4.1 ABSTRACT

OBJECTIVE: The purpose of this study was to examine the temporal relationship between self-efficacy and risk factors of HbA1c, body mass index (BMI), and physical functioning over time in patients with comorbid Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD). The secondary aim was to examine race/ethnicity as an effect modifier.

METHODS: Using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, we examined 1,562 patients from the United States (US) and Canada sites. Patients were randomized to receive treatment for both T2DM (insulin sensitizing drugs vs. insulin providing drugs) and CAD (immediate revascularization vs. medical therapy). The self-efficacy assessment from the Chronic Disease Self-Management Study was administered at baseline and annually throughout the study. Subject-specific mixed models and year lag models were used to assess the relationship between self-efficacy and the risk factors over time.

RESULTS: Higher self-efficacy at study entry was significantly associated with greater reductions in HbA1c (β=-0.03, $p<.001$) and larger improvements in physical function during the trial, although the magnitude of the association between baseline self-efficacy and physical function declined over time (interaction $p=0.02$). These associations did not depend on

race/ethnicity. A feedback loop was shown between self-efficacy and all three risk factors over time. The feedback association between HbA1c and self-efficacy was stronger for Whites than for Blacks and Hispanics.

CONCLUSIONS: Better self-efficacy was related to improved glycemic control and physical functioning. Furthermore, self-efficacy was positively associated with control of risk factors up to the following year; and risk factor control was predictive of self-efficacy in the following year. This is of public health relevance because it shows how self-efficacy can be used as a marker of past health and a predictor of future health.

4.2 INTRODUCTION

Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are highly comorbid conditions that share the same modifiable risk factors, such as being overweight and having a low level of physical activity. The ability to manage health risk factors is thought to be influenced by the patients' confidence in their ability to manage their conditions (Lorig, 1996). Self-efficacy, the belief that one is able to make changes necessary for self-management, has been found to be associated with glycemic control and cardiac symptom burden (A. Bandura, 1977; Chlebowy & Garvin, 2006b; Sarkar, Ali, & Whooley, 2007; Sullivan, et al., 1996). In addition, it is well documented that cardiac risk factors and glycemic control are less well managed in racial/ethnic minority populations, such as Blacks, Hispanics, and Native Americans, compared to Whites (Abate & Chandalia, 2003; AHA, 2009a; Colleran, Richards, & Shafer, 2007). The disparities within these racial/ethnic groups also apply to self-efficacy related to medical management, as racial ethnic minorities report feeling less confident in being able to carry out the necessary behaviors for proper health care (Duru, et al., 2009). Therefore, using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, we sought to examine the association between self-efficacy and cardiovascular and diabetes risk factor control over time, and how race/ethnicity modifies this association. First, we will examine the epidemiology of CAD and T2DM. Then we will examine self-efficacy and how it relates to clinical and physical risk factors, namely HbA1c, physical functioning, and body mass index (BMI

4.2.1 Type 2 diabetes mellitus

Racial/ethnic minorities are 1.5 to 20 times more likely to develop T2DM than their White non-Hispanic (nH) counterparts, with prevalence rates of 6.6% in White nHs, 7.5% in Asian Americans, 11.8% in Black nHs, and 10.4% in Hispanics (ADA, 2007). Based on 20 years of surveillance data, the Framingham Heart Study found that patients with diabetes had a two- to three-fold increased risk of CAD compared to patients without diabetes (Kannel & McGee, 1979).

Modifiable risk factors include being overweight (BMI≥25), having a sedentary lifestyle, and poor diet (ADA, 2009). Non-modifiable risk factors for T2DM include having a family history of diabetes, being of racial/ethnic minority status, and older age (ADA, 2004, 2009; Engelgau, et al., 2004). Minorities present worse diabetes control, receive different treatment regimens, are more likely to receive insulin, and have higher rates of complications (HHS, 2001).

4.2.2 Cardiovascular disease

Approximately 80 million adults in America (approximately 1 in 3) have some form of CAD. Blacks and Hispanics have higher rates of CAD compared to Whites, and the prevalence rate of Hispanics is 25% higher than that of Blacks (AHA, 2009a). CAD was the leading cause of death in 2005, accounting for 36.2% of deaths in White nH, 33.6% in Black nH, and 39.6% in Hispanics (CDC, 2008).

Modifiable risk factors are smoking/smoke exposure, high cholesterol, T2DM, sedentary lifestyle, high body mass index, unhealthy diet, hypertension, and alcohol consumption (AHA,

2009b). Non-modifiable risk factors for CAD include being of racial/ethnic minority status, male sex, older age, and having a family history of CAD (especially before the age of 60). In 2010, the American Heart Association (AHA) added psychosocial indices to the list of risk factors as listed by the INTERHEART study (AHA, 2009b).

4.2.3 Self-efficacy

4.2.3.1 Self-efficacy and HbA1c

Glycemic control is key in maintaining healthy levels of glucose in the blood, thereby reducing the risk of cardiovascular and diabetes complications (ADA, 2009). The literature presents mixed results regarding the relationship between glycemic control and self-efficacy, with some studies documenting no association and others showing a strong association. Duru et al. (2009) used a case-control design to examine how the associations between depression, self-efficacy, and medication adherence and modifiable risk factors (HbA1c, LDL, and systolic blood pressure) differed between Black and White patients (n=764). Cases were patients with poor control of two of the three measures, as measured by HbA1c ≥8.0%, LDL ≥100, and systolic blood pressure >130 mmHg. Controls were patients whose three measures were in good control. Self-efficacy was measured by two questions assessing the patients' acknowledgement of risk and their belief in their ability to lower risk. The association between self-efficacy and good risk factor control was not significant in either race. However, depression and low medication adherence increased the odds of poor risk factor control in Black patients (Duru, et al., 2009).

A study by Chlebowy and Garvin (2006) utilized a two-group comparative descriptive design to examine the relationships between social support, self-efficacy, and outcome

expectations to T2DM self-care behaviors and glycemic control in White and Black participants (N=91). Self-efficacy was measured by the Self-Efficacy Questionnaire (α coefficient for overall score=0.92) (Chlebowy & Garvin, 2006c). Self-efficacy was not significantly related to glycemic control for either race, while higher outcome expectation was significantly related to better glycemic control in both races.

Sarkar et al. (2006) examined the relationship between self-efficacy and T2DM management in a racially diverse, low-income population of 408 participants with limited ability to read and comprehend written health materials (poor health literacy). Self-efficacy was significantly associated with diet, exercise, self-monitoring of blood glucose, and foot care, even after controlling for T2DM factors, race, and health literacy. In an additional study, Sarkar et al. (2007) showed that the associations between self-efficacy and self-management (exercise, blood glucose monitoring, and foot care) were consistent within White, Black, Latino, and Asian /Pacific Islander patients.

There are several issues one must consider when examining self-efficacy and glycemic control as measured by HbA1c. One, although different assessments of self-efficacy were used in each study, results tended to show that self-efficacy was positively associated with behaviors related to glycemic management. Two, glycemic management may be based on the participant's exposure to T2DM education. Patients with T2DM education may be more likely to perform the needed daily tasks regarding health maintenance, and they may also be of higher socioeconomic status, thereby having a more positive T2DM profile (Chlebowy & Garvin, 2006a). Additionally, few studies have reported their patient's cardiac status. Patients with a comorbid cardiac condition have poorer self-efficacy than those without (Deaton, et al., 2006). Three, given the disparities in the control of risk factors between racial/ethnic minority groups, self-efficacy and

its relation to risk factor control needs to be studied in a setting where treatment is randomized, thereby eliminating the differences in treatment due to race/ethnicity.

4.2.3.2 Self-efficacy and physical functioning

There is evidence for a positive relationship between self-efficacy and physical functioning. Self-efficacy has been shown to be associated with physical functioning in patients with CAD. A study by Sullivan et al. (1998) prospectively examined the role of self-efficacy in patients with CAD (N=198), controlling for anxiety and depression. Like the BARI 2D study (Brooks et al., 2006), patients were eligible for elective surgery. Instruments used were the 13-item Cardiac Self-Efficacy Scale, which looked at function, maintenance, and symptom control, the SF-36 (physical functioning), and the Sheehan Family/Home and Social Interface Scales (Sheehan, Harnett-Sheehan, & Raj, 1996; Sullivan MD. Andrea Z, 1998; Ware & Sherbourne, 1992). Self-efficacy was found to be a good predictor of physical function and role function after controlling for CAD severity, anxiety, and depression. This study is limited in that the validity of the self-efficacy assessment scale used has not been determined.

The goal of a study by Sarkar et al. (2007) was to examine the relationship between cardiac self-efficacy and health status in 1,024 patients with congestive heart disease in the Heart and Soul Study, controlling for severity of congestive heart disease and depression. Cardiac self-efficacy was measured using Sullivan's 5-item scale (Crohnbach's $\alpha = 0.80$) (Sullivan et al., 1998). Lower self-efficacy was found to be independently associated with greater cardiac symptom burden, greater physical limitations, worse quality of life, and worse overall health. Because the study was cross-sectional, directionality and causality cannot be established.

Furthermore, the majority of the patients were older, low-income White males, limiting the generalizability of the results.

In a longitudinal study of a Turkish cohort, 60 cardiac patients were randomized to a home-based cardiac exercise program (grounded in the theory of self-efficacy) or no intervention (control) in order to study each group's lipids, exercise tolerance, and self-efficacy (Senuzun, Fadiloglu, Burke, & Payzin, 2006). Self-efficacy was measured by the Cardiac Self-Efficacy Index (CESEI), whose test-retest reliability was 0.97 (Crohnbach's α=0.87) (Hickey, Owen, & Froman, 1992). At the end of the 12 weeks, the home-based cardiac exercise group's clinical risk factor profile significantly improved in comparison to the control group. Senuzun et al. (2006) concluded that exercise along with enhanced self-efficacy might have improved the patients' exercise capacity, thereby improving their clinical outcomes. However, this conclusion may be premature because the control group should have an intervention that was not grounded in the self-efficacy theory.

4.2.3.3 Self-efficacy and weight

Sol et al. (2006) studied the effects of baseline self-efficacy on vascular risk factors, including physical activity, BMI and glucose levels in patients at high risk for developing additional vascular complications (Sol, van der Graaf, van der Bijl, Goessens, & Visseren, 2006). In a randomized trial of 153 patients with vascular disease, patients were randomized to receive either usual care or nursing care with self-efficacy promotion and medical therapy for one year. Self-efficacy was measured by the adapted Type 2 Diabetes Mellitus Self-efficacy Scale (Crohnbach's α=0.69) (Bijl, Poelgeest-Eeltink, & Shortridge-Baggett, 1999). Baseline and composite self-efficacy were related to dietary choices and an increase in physical activity, but

were not related to changes in BMI or other vascular risk factors. However, BMI was related to self-efficacy in a study that examined the mediating effects of adherence, BMI, and self-efficacy in the relationship between depression and worsening T2DM (Sacco, et al., 2005). Adherence and BMI were independent mediators of self-efficacy and T2DM control.

In a sample of 274 patients at risk for T2DM, self-efficacy was found to be related to weight loss and long-term weight maintenance in the Diabetes Prevention Program (Delahanty, Meigs, Hayden, Williamson, & Nathan, 2002). Delahanty et al. (2002) also showed that the strength of the correlations between BMI and self-efficacy regarding weight loss differed as a function of race/ethnicity; with a stronger association between weight loss and high self-efficacy in White nH compared to minorities. In a sample of 106 overweight to obese Black women, high self-efficacy was not associated with weight loss, but greater weight loss was seen in patients with lower self-efficacy (Martin, Dutton, & Brantley, 2004). The authors proposed that the patients with lower self-efficacy were more accepting of the assistance provided by the program, and therefore complied with the weight-loss regimens, whereas the patients with higher self-efficacy were either satisfied with their weight or less compliant with the weight loss regimens. However, in a community sample of Appalachian patients who were mainly at risk for T2DM from being overweight and having low physical activity, self-efficacy was not related to being overweight, nor to having low physical activity (Serrano, Leiferman, & Dauber, 2007).

4.2.3.4 Self-efficacy in patients with T2DM and CAD

In order to keep T2DM and CAD under control, patients must make a number of daily decisions regarding medication, glucose monitoring, nutrition, physical activity, and stress management

(Anderson, et al., 2000). Self-efficacy is highly related to T2DM self-management, such as glycemic management (HbA1c), dieting (BMI), and physical activity, which are strongly related to the control of risk factors (Evenson, et al., 1999; Franz, et al., 2002).

Although prior research has shown that self-efficacy is associated with better clinical outcomes for T2DM and CAD separately, little research has examined the role of self-efficacy in patients with both T2DM and CAD and has been conducted longitudinally in diverse populations. A cross-sectional analysis of baseline health status in the BARI 2D study examined the association between self-efficacy and HbA1c, systolic blood pressure, and low-density lipids, as well as demographic and clinical factors associated with self-efficacy (Sansing, 2007). The study population was composed of 1,447 patients with comorbid CAD and T2DM. Better HbA1c was positively associated with self-efficacy, even after adjusting for race/ethnicity, age, sex, and education. Hispanic ethnicity, history of congestive heart failure, number of hypertension drugs, probable neuropathy, and insulin use were negatively associated with self-efficacy (Sansing, 2007). However, because the analyses were cross-sectional, the direction of association could not be established. In addition, because Hispanic ethnicity was highly associated with self-efficacy, there is a need to examine further the role of race/ethnicity in the control of risk factors.

4.3 RATIONALE

The control of the risk factors associated with T2DM and CAD is not solely a result of the prescribed healthcare regimens as given by one's physician (Jerant, et al., 2005). Psychosocial factors play a considerable role in the management of these comorbid diseases, as indicated by

the American Heart Association (AHA, 2009b). Risk factors for CAD and T2DM vary by race, with minorities carrying an unequal burden compared to Whites. Winkleby et al. (1994) found that Hispanic ethnicity and low self-efficacy were associated with less positive change in cardiovascular risk factors. In addition, Hispanic ethnicity has been associated with lower self-efficacy compared to non-Hispanics (Sansing, 2007). Thus, there is a need to examine self-efficacy and risk factors in a racially/ethnically diverse population. Self-efficacy is conceptualized as a state (transient and situational), as opposed to a trait (inherent and permanent), that may change over time, increasing or decreasing based on the successes and failures in goal attainment (Gist & Mitchell, 1992). If a person fails to achieve their risk factor goals, despite their efforts, they are less likely to adhere properly to medical advice compared to someone who succeeds at controlling their risk factors. Therefore, temporal analyses are needed to understand how self-efficacy relates to the outcomes of T2DM and CAD management over time in a diverse population.

4.4 SPECIFIC AIMS

The objective of the proposed study is to examine how baseline self-efficacy is associated with the control of risk factors over time in persons with both T2DM and CAD, and to examine race/ethnicity as an effect modifier. Data from the BARI 2D trial, a National Institutes of Health (NIH)-sponsored, multi-center, randomized clinical trial of patients with T2DM and angiographically-documented stable CAD was used to test the following hypotheses:

1. There will be a positive association between baseline self-efficacy (predictor) and follow-up glycemic control (HbA1c) and lifestyle risk factor (BMI and physical functioning) outcomes over time.
2. There will be a time-lag effect between self-efficacy and risk factor control.
    a. Higher self-efficacy (predictor) will be associated with better glycemic and lifestyle risk factor control the following year (outcomes).
    b. Better glycemic and lifestyle risk factor control (predictors) will be associated with higher self-efficacy the following year (outcome).
3. Race/ethnicity will serve as an effect modifier for the association between self-efficacy and glycemic control, BMI, and physical functioning over time in hypotheses 1 and 2.

Results of these analyses may provide a better understanding of the relationships and disparities among clinical, demographic, and psychosocial factors shaping health outcomes. This research is of importance to the public health field because it examines how differences in the confidence of minorities, who are disproportionately affected by T2DM and CAD, may affect their clinical prognosis.

4.5 METHODS

4.5.1 BARI 2D

BARI 2D is a multicenter clinical trial designed to determine optimal treatment strategies for patients with T2DM and documented stable CAD. Using a 2x2 factorial design, BARI 2D compared initial elective revascularization with aggressive medical therapy (will be referred to as immediate revascularization) versus initial aggressive medical therapy and delayed revascularization if symptoms worsen or are clinically indicated (will be referred to as medical therapy), while simultaneously studying an insulin-providing versus an insulin-sensitizing strategy of glycemic control to achieve a clinical target of HbA1c <7% (**Figure 12**) (BARI_2D_Study_Group, 2006).

Randomization to either immediate revascularization or initial medical therapy was stratified by BARI 2D site and by intended revascularization to either PCI or CABG as determined by a physician. Follow-up visits occurred monthly for the first six months and quarterly thereafter, until the end of the study in 2008. At each follow-up visit, information about clinical risk factors, diabetes complications, clinical events, and medications was collected. Self-efficacy data were collected annually as part of the quality of life assessments. The mean follow-up per patient was 5.3 years with a range of 3.5 - 6 years. The BARI 2D primary endpoint was all-cause mortality. The composite secondary endpoint was death, non-fatal MI, or stroke.

4.5.2 Population

Participants were enrolled from 49 clinical sites in the US, Canada, Brazil, Mexico, the Czech Republic, and Austria (N=2,368). Eligible participants had a "diagnosis of T2DM and angiographically documented CAD for which revascularization was not required for prompt control of severe or unstable angina" (BARI_2D_Study_Group, 2006). A physician/investigator at each site determined if the patients were eligible for the study based on the inclusion/exclusion criteria. Based on the BARI 2D Manual of Operations (BARI_2D_Coordinating_Center, 2002-2005), inclusion criteria were as follows: diagnosis of T2DM, coronary arteriogram showing one or more vessels amenable to revascularization (≥50% stenosis), objective documentation of ischemia or subjectively documented typical angina with ≥70% stenosis in at least one artery, suitability for coronary revascularization by at least one of the available methods, ability to perform all tasks related to glycemic control and risk factor management, age 25 or older, and informed written consent (BARI_2D_Study_Group, 2006). Exclusion criteria were as follows: definite need for invasive intervention as determined by a cardiologist, any CABG or PCI within the past 12 months, class III or IV CHF, creatinine >2.0 mg/dl., HbA1c >13%, need for major vascular surgery concomitant with revascularization (e.g., carotid endarterectomy), left main stenosis ≥50%, non-cardiac illness limiting mortality, hepatic disease, fasting triglycerides >1,000 mg/dl in the presence of moderate glycemic control (HbA1c ≤8.0%), current alcohol abuse, chronic steroid use, known/planned/suspected pregnancy, geographically inaccessible or unable to return for follow-up, enrolled in a competing randomized trial or clinical study, and unable to understand or cooperate with protocol requirements (BARI_2D_Study_Group, 2006).

For this analysis, patients were limited to US and Canadian sites due to global differences in the definition of race/ethnicity and the administration of the self-efficacy assessment (oral versus written) (**Figure 13**). Due to the sample sizes, we examined only White non-Hispanic, Black non-Hispanic, and Hispanic patients. Patients in the analyses must have a baseline measurement and at least one follow-up measurement for all of the following variables: self-efficacy, race/ethnicity, HbA1c, DASI, height, and weight (N=1,562).

4.5.3 Data Collection and Measures

4.5.3.1 Self-efficacy

Study participants completed a comprehensive battery of self-reported psychosocial measurements including four questions regarding their self-efficacy. The self-efficacy assessment was administered at baseline and annually at Years 1 through 6 and was designed to measure how confident the patient was in his or her ability to do tasks and activities that relate to managing his or her T2DM and CAD in general and specific ways (Appendix A). The self-efficacy assessment was derived from the Chronic Disease Self-Management Study and was found to have high internal consistency (Crohnbach's α=0.89) (Lorig, 1996). The questions were modified from disease management in general to address heart disease and T2DM specifically. Each question consisted of a 10-point Likert scale with "1 = not at all confident" and "10 = totally confident." Interest lied in the patients' confidence in: 1) doing all day-to-day things necessary to manage their conditions; 2) doing activities for their T2DM and CAD in order to reduce doctor visits; 3) reducing emotional stress associated with their diseases through acts such as prayer, meditation, art, and social contact; and 4) doing activities besides medication

adherence, such as exercise, hobbies, and dieting, to reduce the impact of the diseases on their daily life. The final score was an average of the four subscale scores.

4.5.3.2 Risk factors of interest

Race was self-reported based on the US Census Classification System as either 1) American Indian/Alaskan Native, 2) Asian, 3) Black/African American, 4) Native Hawaiian/Pacific Islander, 5) White, or 6) Other (including those of multiple races). Hispanic ethnicity (Latino or Spanish origin) was to be indicated regardless of race. HbA1c levels were measured from blood samples collected at baseline, and were analyzed at the BARI 2D core Biochemistry Laboratory. Physical status was measured by the Duke Activity Status Index (DASI), a 12-item self-reported quality of life questionnaire that measures functional capacity or activities of daily living. It ranges from 0 (poor) to 58.2 (best) and uses physical work capacity to estimate peak metabolic equivalents (Crohnbach's α=0.67) (Dorian, et al., 2002; Hlatky, et al., 1989). Body mass index (kg/m^2) was calculated by clinical measurements of weight and height.

4.5.3.3 Additional variables

Sex, age, education, cigarette use, history of cancer and cardiovascular complications, probable neuropathy, current insulin use at baseline, duration of diabetes, and angina status were self-reported. Fasting total, low-density lipid cholesterol (LDL), and high-density lipid cholesterol were measured from blood samples collected at baseline and were analyzed at the BARI 2D core Biochemistry Laboratory. While BARI 2D has data regarding the types of medication prescribed, there is no information regarding adherence. With the self-rated health assessment, patients are asked to rate their general health as either "Excellent," "Very Good," "Good," "Fair," or "Poor"

(Lorig, 1996; Ware & Sherbourne, 1992). Health distress and energy are assessed by a 9-item questionnaire in which patients report how they have felt during the past four weeks (Stewart & Ware, 1992). Patients are read five answer options that range from "All of the Time" to "None of the Time."

4.6 STATISTICAL METHODS

The mean follow-up time for patients was 5.3 years. However, clinical sites joined BARI 2D and began recruitment at different time points throughout the study, and the average follow-up time for patients varied by site. Therefore, analyses were limited from baseline to follow-up Year 4. Missing baseline data were replaced by the mean baseline values for variables with ≤5% missing data.

Normality of the distribution of the self-efficacy scores, HbA1c values, DASI scores, and BMI were assessed at baseline. Given the large sample size in this analysis, the distribution of baseline self-efficacy score could be considered approximately normal (central limit theorem). HbA1c, DASI, and BMI were analyzed using parametric statistics. Differences in baseline characteristics of patients were compared by race/ethnicity using chi-square, t-tests, and Wilcoxon signed rank tests to identify confounders which are used in the lag models.

In modeling the relationship between baseline self-efficacy and follow-up risk factor status (Aim 1), we used subject-specific mixed models with fixed (i.e., race and sex) and random effects (i.e., person-specific intercept and follow-up time variables) to assess within-person change over time. All models included the study treatment assignment and randomization strata,

follow-up time, as well as the baseline values for the risk factor outcome in order to model follow-up risk factor status adjusting for baseline level. Interaction terms between self-efficacy and race/ethnicity and between self-efficacy and time were included in the models to test for effect modification (Aim 3). The final sets of models were adjusted for demographic and clinical confounders.

In modeling the direction of the association between self-efficacy and follow-up risk factor status (Aim 2), time-lag models were created (Equation 1) (Twisk, 2003). Y_{it} is the observation for patient i at year t, βo is the random intercept, β_{1j} is the regression coefficient for the predictor variable, X_{ijt-1} is the predictor variable j for patient i at year $t-1$, and J is the number of predictor variables. In order to examine the cyclic association between self-efficacy and risk factors, models were created with 1) self-efficacy (lag) as the predictor and risk factors as the outcomes and 2) risk factors (lag) as the predictors and self-efficacy as the outcomes.

$$(1) \qquad Y_{it}=\beta_o+\sum_{j=1}^{J}\beta_{1j}X_{ijt-1}+\ldots$$

Within the construct of these models, we adjusted for demographic and clinical confounders and tested for interactions between race/ethnicity and self-efficacy and between race/ethnicity and the risk factor covariate. Therefore, interaction terms between self-efficacy and race/ethnicity were included with the purpose of testing for effect modification (Aim 3).

In order to understand which baseline variables were associated with follow-up self-efficacy scores, subject-specific mixed models were constructed with follow-up self-efficacy scores included as dependent variables and years in study and baseline demographics and clinical variables as the independent variables, controlling for within subject correlation. The model controlled for assigned treatment, randomization strata, age, sex, race/ethnicity, and baseline

self-efficacy. The variable with the highest p-value was removed from the full model, and the model was run again until the most parsimonious model was created.

All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, 2007). The α-levels of significance were 0.05 and 0.01.

4.7 RESULTS

4.7.1 Baseline status

In the US and Canadian sites, 1,562 patients had an assessment at baseline and at one (not necessarily at Year 1) or more follow-up time points: 1,533 at Year 1, 1,442 at Year 2, 1,390 at Year 3, and 1,184 at Year 4 (Table 10). About a third of the patients were racial/ethnic minorities. The main reasons for the decreasing number of patients throughout the duration of the study were study close-out and death. Analyses were not conducted with Year 5 (n=948 including those with no follow-up). The distribution of baseline self-efficacy, HbA1c, DASI, and BMI overall and by race/ethnicity are shown in **Figures 14-17**, and show the same distribution for all races/ethnicities. The mean baseline self-efficacy score was 7.76±1.81, median = 8.0, skewness = -0.86, kurtosis=0.56, and Kolmogorov-Smirnov p=0.01. The mean baseline HbA1c was 7.2%±1.5, the mean baseline DASI score was 16.2%±14.1, and the mean BMI was 32.7±6.0. Baseline self-efficacy was highly negatively correlated with baseline HbA1c (r=-0.088, p=0.001) and positively correlated with physical functioning (r=0.37, p<.001), but not BMI (r=-0.03, p=0.12) (**Table 11**). **Figure 18** shows mean self-efficacy, HbA1c, DASI, and

BMI over time by race/ethnicity. Self-efficacy and HbA1c both decrease in White nH and Black nH patients and increase in Hispanic patients over time. For all patients, DASI increases from baseline to Year 1 and decreases from Year 1 – 4, and BMI increases over the years.

The characteristics of the patients in the analyses are presented in **Table 12** overall and stratified by race/ethnicity. Overall, the majority of the patients were male (71.4%), and patients were approximately 62.8 years of age, completed high school, and were from the United States sites (81.5%). Few patients smoked (13.4%) or had cancer (7.2%). Patients' diabetes control was very good, as indicated by an HbA1c of approximately 7.5%. Few patients had self-screened probable neuropathy (16.1%) or clinically screened neuropathy (0.8%). Less than a third (30.2%) of patients used insulin at baseline. The average duration of T2DM was 10.6 years. Patients were on average obese (mean BMI=32.8). The majority of patients had no angina or mild angina (Canadian Cardiovascular Classification System [CCS] 1, 2). Regarding the patients' clinical histories, 7.7% had a history of congestive heart failure, 28.7% had a history of MI, and 25.9% had a history of peripheral artery disease (Campeau, 1975). The average number of hypertension drugs was 2.3±1.0. A large proportion of the patients had a clinical history of hypertension and hypercholesterolemia requiring treatment. The mean systolic blood pressure was 130.7±18.6 mmHg and the median LDL was 92 mg/dl. The mean self-efficacy score was 7.8±1.8. Approximately 53.7% of patients rated their health as "Good" to "Excellent." The mean physical functioning scores was 19.5 (DASI range=0-58.2). Randomization was successful in providing a balanced distribution of patients between the cardiovascular and diabetes treatment arms; three quarters of the patients were assigned to the PCI revascularization stratum.

The race/ethnicities differed by sex, age, education, United States sites, cigarette use, cancer history, HbA1c, neuropathy, insulin use, body mass index, angina status, number of hypertension drugs, systolic blood pressure, LDL, and all quality of life measures.

4.7.2 Baseline self-efficacy and risk factors

We first examined how baseline self-efficacy was related to follow-up risk factors and if this effect was modified by race/ethnicity. The models in **Table 13** include the baseline value for the risk factor of interest (HbA1c, DASI, or BMI), time (years of follow-up), race/ethnicity (Models 4-15 only), randomization arms, revascularization strata, baseline self-efficacy, and interaction terms between baseline self-efficacy and either time or race/ethnicity (Models 7-15 only). The estimated coefficients for self-efficacy and self-efficacy interaction terms are listed for each of the follow-up risk factors (outcomes). Baseline self-efficacy was associated with significantly lower HbA1c (β=-0.05, p<.001) and higher DASI scores (β=2.23, p<.001), but not with BMI, compared to baseline (Models 1-3). Adjusting for race/ethnicity, baseline self-efficacy was associated with significantly lower HbA1c (β=-0.04, p=0.009) and higher DASI scores during follow-up (β=2.23, p<.001), but not with BMI (Models 4-6). The interaction between baseline self-efficacy and time (follow-up years) was not significant; therefore, the effect of self-efficacy on HbA1c and BMI did not differ over the follow-up period (Models 7 and 9). However, the interaction between baseline self-efficacy and time was significant in the association with DASI (p=0.02) indicating that the effect of baseline self-efficacy on physical functioning diminished over time (Model 8), and the interaction term was retained in the model. Race/ethnicity was not a significant modifier of the association between baseline self-efficacy and HbA1c (2 degrees of

freedom [d.f.] p=0.70), physical functioning (2 d.f. p=0.68), and BMI (2 d.f. p=0.30) (Models 10-12). After adjusting for baseline confounders, higher baseline self-efficacy remained a significant predictor of better HbA1c and higher DASI scores, but not with BMI (Models 13-15). Three-way tests of time*race*self-efficacy interactions were non-significant (p's >0.74).

4.7.3 Baseline factors related to follow-up self-efficacy

At baseline, Whites nH had the highest self-efficacy scores followed by Black nH and Hispanic patients (**Table 14**). After adjusting for baseline self-efficacy, Blacks had significant improvements in self-efficacy scores over the course of the study compared to Whites (β=0.24, p=0.004), and Hispanics had less improvements over time than Whites though not significant. Older age (β=0.02, p<.001), greater physical function (β=0.02, p<.001), and lower weight (β=-0.01, p=0.02) were associated with higher self-efficacy during follow-up relative to baseline levels. Baseline angina CCS 1 and 2 were also positively associated with improvement in self-efficacy.

4.7.4 Time-lag associations between self-efficacy and risk factors

Next, we examined how self-efficacy was associated with risk factor control in the subsequent year, and how risk factor control was associated with self-efficacy in the subsequent year. **Table 15** presents multivariate time-lag models. Models 1-3 include self-efficacy (lag) as a predictor and the risk factors as the outcomes. Self-efficacy was associated with a decrease in HbA1c (β= -0.020, p=0.01) and an increase in DASI (β=0.373, p<.001) (Models 1 and 2). The interaction

between race/ethnicity and self-efficacy was significant for HbA1c (2 d.f p=0.03); Black nH patients showed a significant increase in HbA1c compared to White nH patients. The interaction was no longer significant after adjusting for confounders (2 d.f. p=0.06). Models 10-18 present the coefficient estimate for risk factors (predictors) and self-efficacy (outcome). HbA1c and BMI were both associated with a decrease in self-efficacy (β=-0.082, p<.001 and β=-0.026, p<.001, respectively). DASI was associated with an increase in self-efficacy (β=0.021, p<.001). The interaction between HbA1c and race/ethnicity was significant (2 d.f. p=0.03, adjusted p=0.02), therefore indicating that the association between HbA1c and subsequent self-efficacy is less strong in Black nH and Hispanics patients compared with White nH patients.

4.8 DISCUSSION

The primary goal of the current study was to examine how self-efficacy relates to risk factors (HbA1c, physical functioning, and BMI) and how race/ethnicity modified this association. The main findings from these analyses is that 1) self-efficacy is associated with risk factor control, namely glycemic control and physical functioning; and 2) the association between baseline self-efficacy and risk factors is not dependent on race, but when we look examine the associations over time, race/ethnicity is important in the feedback loop.

First, we demonstrated that higher baseline self-efficacy was associated with better follow-up glycemic control and physical functioning in all patients. This is similar to the findings from previous research, whose results suggested that self-efficacy could aid in glycemic control by increasing adherence to medical regimens (Jerant, et al., 2005; R. Nakahara, et al., 2006;

Robertson & Keller, 1992). Similar to the study by Martin et al. (2004), self-efficacy was associated with improved physical functioning in people whose self-efficacy was able to increase. In patients with higher baseline self-efficacy scores, physical functioning declined at a greater rate compared to patients with lower baseline scores. In the current study, it is possible that patients who entered the study with high self-efficacy may have felt their physical functioning was good, and therefore did not contribute much effort in trying to increase their physical functioning. This may partially account for the greater decline in their DASI scores over time as compared to patients with lower self-efficacy. Baseline self-efficacy was not associated with follow-up BMI. Only 9.7% of the BARI 2D patients were normal or underweight at baseline, and the average BMI increased throughout the study. Therefore, despite increasing or decreasing self-efficacy scores, the patients' BMIs continued to increase.

Race/ethnicity did not moderate the effect between baseline self-efficacy and the selected risk factors, and these associations remained even after adjusting for factors that varied between the races such as age, sex, education, and clinical status. Although Black nH patients reported being less confident than White nH patients in their ability to manage their health, Blacks patients were still able to improve their HbA1c. In addition, the magnitude of the direction of change in physical functioning in Black nH patients was similar to Whites. These findings may indicate a form of health pessimism, in which Blacks are more likely to rate their health as fair or poor compared to Whites despite their actual health status (Boardman, 2004; Thomas, et al., 2010). Here, we have observed that Black nH patients rated their self-efficacy lower than White nH despite improvements in glycemic control in Black nH patients.

Second, the current study revealed that self-efficacy was associated with subsequent risk factor control for HbA1c, physical functioning, and less strongly for BMI; and these risk factors were associated with subsequent self-efficacy. The evidence points to a cyclic effect (feedback loop) as indicated by Bandura's model of self-efficacy (A. Bandura, 1977). The theory states that self-efficacy is associated with outcomes that are associated with future self-efficacy. Race/ethnicity moderated the effect between HbA1c and subsequent self-efficacy, with the strongest association between self-efficacy and subsequent HbA1c observed in White nH patients. As glycemic control improved, self-efficacy increased less in Black nH and Hispanic patients compared with Whites. So, in the presence of good glycemic control, Blacks and Hispanic patients rated their self-efficacy as low compared to Whites. Again, this is evidence of a form of health pessimism in Black patients as it relates to their confidence in being able to manage their conditions.

In previous studies, it was suggested that self-efficacy was associated with medical adherence. However, the current study did not measure adherence. We were primarily able to measure the clinical and physical outcomes, which is an indicator of the level of adherence to medications, diet, and exercise. This study was also limited by the time intervals in which self-efficacy and the risk factors were measured. One possibility is that self-efficacy may be better associated with risk factors at a time span of less than one year. However, for this research, the values and measurements were taken annually. Risk factor data for HbA1c and BMI were collected more frequently, but annual visits were used in order to provide the same number of observations per patient.

In conclusion, in patients with comorbid T2DM and CAD, self-efficacy was related to HbA1c and physical functioning, and self-efficacy predicted outcomes, which in turn predicted self-efficacy. This is in line with the feedback loop associated with Bandura's models of self-efficacy and outcomes. In addition, the associations between self-efficacy and glycemic control were more apparent in White nH patients compared to Black nH and Hispanic patients. Efforts to improve cardiovascular and diabetes outcomes in patients with both T2DM and CAD should focus on improving the patients' confidence in glycemic management, as well as providing guidance to increase their daily physical activity to the best of their ability. Positive outcomes should be internalized by the patient in order to boost their confidence in continuing proper health care management, as well improve their overall quality of life.

4.9 TABLES AND FIGURES FOR PAPER 2

Table 10. Frequency and percentage of patients by year by race/ethnicity and study status at time of study

n *%*	Years in Study				
	Baseline (n=1,562)	**1** (n=1,533)	**2** (n=1,442)	**3** (n=1,390)	**4** (n=1,184)
Race/Ethnicity					
White nH	1067	1052	997	957	817
	68.31	68.62	69.14	68.85	69
Black nH	304	295	275	266	220
	19.46	19.24	19.07	19.14	18.58
Hispanic	191	186	170	167	147
	12.23	12.13	11.79	12.01	12.42
Study Status					
Vital status - alive	1056	1041	1003	986	842
	67.61	67.91	69.56	70.94	71.11
Vital status - unknown	34	32	23	15	11
	2.18	2.09	1.6	1.08	0.93
Close out – end of study	204	200	190	190	183
	13.06	13.05	13.18	13.67	15.46
Other	104	98	97	96	86
	6.66	6.39	6.73	6.91	7.26
Death	164	162	129	103	62
	10.5	10.57	8.95	7.41	5.24

Key: nH – non Hispanic

Table 11. Correlation of baseline self-efficacy and baseline risk factors

Pearson Correlation Coefficients, N = 1,562 Probability > |r| under H0: Rho=0				
	Self efficacy score	**HbA1c**	**DASI**	**BMI**
Self-efficacy score	1.000	-0.082 0.001	0.370 <.0001	-0.038 0.133
HbA1c	-0.082 0.001	1.000	-0.050 0.050	0.050 0.051
DASI	0.370 <.0001	-0.050 0.050	1.000	-0.182 <.0001
BMI	-0.038 0.133	0.050 0.051	-0.182 <.0001	1.000

Table 12. Baseline table by race/ethnicity

Characteristic	Total (N=1562)	White nH (N=1067)	Black nH (N=304)	Hispanic (N=191)	Overall p-value
Male, %	71.4	78.1	49.7	69.1	<.001
Age at study entry, mean, SD	62.8, 8.8	63.4, 8.7	61.6, 9.3	61.2, 8.4	<.001
Education level, %					
Some high school or less	24.9	20	29.6	45	<.001
High school diploma	26.6	26.6	28.6	23.6	
Post high school education	29.5	30.3	30.9	23	
Bachelors degree or higher	19	23.1	10.9	8.4	
United States sites, %	81.5	73.9	97	99	<.001
Current cigarette smoker, %	13.4	12.1	18.1	13.1	0.03
Malignancy (cancer), %	7.2	8.4	4.3	5.2	0.02
HbA1c %, mean, SD	7.5, 1.5	7.3, 1.4	8.0, 1.7	7.7, 1.6	<.001
HbA1c ≥ 8%, %	30.5	26.6	40.5	36.6	<.001
Probable neuropathy: screening MNSI ≥7, %	16.1	14.8	13.8	26.7	<.001
MNSI clinical score, mean, SD	0.8, 0.4	0.8, 0.4	0.9, 0.3	0.9, 0.3	0.05
Currently taking insulin, %	30.2	26.3	42.1	33	<.001
Duration of T2DM, mean, SD	10.6, 8.8	10.3, 8.6	11.9, 9.4	10.8, 8.4	0.02
Body mass index, mean, SD	32.8, 6.0	32.8, 5.8	33.4, 6.9	31.6, 5.3	<.001
Angina status, %					
No Angina	43	44.6	36.5	44.5	<.001
Angina 1, 2	39.3	40.6	36.8	36.1	
Angina 3, 4	17.7	14.8	26.6	19.4	
History of congestive heart failure, %	7.7	6.9	9.5	8.9	0.26
History of myocardial infarction, %	28.7	30.2	26	24.6	0.15
Peripheral artery disease (PAD), %	25.9	24.6	27.6	30.4	0.19
Number of hypertension drugs, mean, SD	2.3, 1.0	2.2, 1.0	2.6, 1.0	2.1, 0.9	<.001
Hypercholesterolemia requiring treatment, %	83.9	83.35	85.95	84.04	0.56
Systolic blood pressure average, mean, SD	130.7, 18.6	128.9, 17.5	136.7, 20.0	131.4, 19.9	<.001
Systolic blood pressure > 140, %	24.8	21.5	36.5	25.1	<.001
LDL mg/dl, median (Q1-Q3)	92 (73-111)	89 (71-107)	101 (82-127)	94 (71-110)	<.001
LDL ≥100 mg/dl, %	35.1	30.5	49.7	37.7	<.001
Self efficacy score (0-10), mean, SD	7.8, 1.8	7.9, 1.7	7.7, 1.9	7.0, 2.0	<.001
Self rated health category, %					<.001
Excellent	1.34	1.59	0.99	0.52	
Very good	10.95	12.09	7.57	9.95	
Good	41.42	46.49	32.57	27.23	
Fair	33.8	29.62	44.41	40.31	
Poor	12.48	10.22	14.47	21.99	
DASI (0-58.2), mean, SD	19.5, 14.1	20.9, 14.2	17.9, 13.2	14.1, 13.3	<.001
Energy score (0-100), mean, SD	47.0, 21.6	47.2, 21.8	49.1, 20.0	42.6, 22.2	0.00
Health distress score (0-100), mean, SD	43.0, 25.4	41.6, 24.8	43.0, 25.9	51.0, 26.4	<.001
Glycemic arm treatment, %	50.4	50.9	47.4	52.9	0.43
Cardiovascular treatment, %	48.7	48.1	48.7	52.4	0.55
Revascularization strata, %					<.001
CABG	24.0	26.1	14.8	26.7	
PCI	76.0	73.9	85.2	73.3	

Key: DASI – Duke Activity Status Index, MI – myocardial infarction, LDL – low density lipids, MNSI – Michigan Neuropathy Screening Instrument, Q1-Q3 – first and third quartile

Table 13. Multivariate mixed models of baseline self-efficacy (predictor) and risk factors (outcome)

		Separate outcomes					
		HbA1c		DASI		BMI	
Models *	**Predictors and Interaction Terms**	**Est.**	**P-value**	**Est.**	**P-value**	**Est.**	**P-value**
1-3	Baseline self-efficacy (race/ethnicity not in model)	-0.05	<.001	2.23	<.001	-0.14	0.11
4-6	Baseline self-efficacy	-0.03	0.009	2.23	<.001	-0.13	0.15
7-9	Baseline self-efficacy	-0.06	0.008	0.84	<.001	-0.007	0.84
	Baseline self-efficacy*Time (interaction)	-0.001	0.90	-0.14	0.02	0.01	0.40
10-12	Baseline self-efficacy	-0.03	0.07	0.62	<.001	0.04	0.28
	Baseline self-efficacy*Race/ethnicity (2 d.f. test)		0.70		0.68		0.30
	Baseline self-efficacy*Black nH (interaction)	-0.006	0.86	-0.30	0.38	-0.11	0.13
	Baseline-self-efficacy*Hispanic (interaction)	-0.03	0.40	-0.08	0.84	-0.06	0.46
13-15**	Baseline self-efficacy	-0.03	<.001	0.87	<.001	0.03	0.32
	Time	0.02	0.04	0.15	0.76	0.14	<.001
	Baseline self-efficacy*Time (interaction)			-0.14	0.02		

Note: Tests of time*race*self-efficacy interactions were non-significant (p's >0.74).

* All models include race/ethnicity (with the exception of models 1-3), the baseline value for the risk factor of interest, time in follow-up years, randomized diabetes (insulin sensitizers versus insulin providers) and cardiovascular (medical therapy versus immediate revascularization) treatment assignment, and revascularization strata (coronary artery bypass graft versus percutaneous coronary intervention).

** Models 13-15 additionally adjust for baseline values of race/ethnicity, HbA1c, BMI, DASI, age, post high school education, USA sites, malignancy (cancer), clinical neuropathy, insulin use, duration of diabetes, angina status, number of hypertension drugs, systolic blood pressure, and low density lipids.

Table 14. Multivariate model of baseline variables associated with follow-up self-efficacy

Effect	Estimate	p-value
Black nH vs. White nH	0.24	0.004
Hispanic vs. White nH	-0.17	0.11
Age (per year)	0.02	<.001
Body mass index	-0.01	0.02
Duke Activity Status Index	0.02	<.001
Clinical neuropathy	-0.06	0.004
Angina 3, 4, Unstable vs. none	0.14	0.13
Angina 1, 2 vs. none	0.28	0.003
Insulin Providing vs. Insulin Sensitizing	-0.07	0.31
Revascularization vs. Medical Therapy	0.05	0.49
CABG vs. PCI	0.12	0.13
Baseline self-efficacy	0.31	<.001

Key: CABG – coronary artery bypass graft, PCI – percutaneous coronary intervention

Table 15. Time-lag models of self-efficacy and risk factors

Predictor: Self-efficacy (Lag), Outcome: Risk Factor		HbA1c		DASI		BMI	
Models	**Predictor**	**Est.**	**P-value**	**Est.**	**P-value**	**Est.**	**P-value**
1-3	Self-efficacy	-0.020	0.01	0.373	<.001	-0.025	0.09
4-6	Self-efficacy	-0.029	0.002	0.346	<.001	-0.032	0.08
	Self-efficacy*Race/ethnicity (2 d.f. test)		0.03		0.38		0.87
	Self-efficacy*Black nH	0.050	0.01	-0.075	0.72	0.019	0.64
	Self-efficacy*Hispanic	-0.005	0.82	0.299	0.21	-0.0001	0.99
7-9**	Self-efficacy	-0.024	0.01	0.302	<.001	-0.022	0.22
	Self-efficacy*Race/ethnicity (2 d.f. test)		0.06		0.41		0.73
	Self-efficacy*Black nH	0.044	0.03	-0.070	0.73	0.024	0.53
	Self-efficacy*Hispanic	-0.005	0.84	0.285	0.23	0.016	0.72

Predictor: Risk Factor (Lag), Outcome: Self-efficacy		HbA1c Self-efficacy		DASI Self-efficacy		BMI Self-efficacy	
Models	**Predictor**	**Est.**	**P-value**	**Est.**	**P-value**	**Est.**	**P-value**
10-12	Risk factor	-0.082	<.001	0.021	<.001	-0.026	<.001
13-15	Risk factor	-0.123	<.001	0.018	<.001	-0.029	<.001
	Risk factor*Race/ethnicity (2 d.f. test)		0.03		0.05		0.66
	Risk factor*Black nH	0.090	0.04	0.012	0.02	0.008	0.50
	Risk factor*Hispanic	0.113	0.03	0.006	0.34	0.013	0.47
16-18**	Risk factor	-0.101	<.001	0.016	<.001	-0.013	0.06
	Risk factor*Race/ethnicity (2 d.f. test)		0.02		0.09		0.97
	Risk factor*Black nH	0.083	0.05	0.011	0.03	0.001	0.93
	Risk factor*Hispanic	0.125	0.02	0.004	0.53	0.003	0.85

Three way tests of lag variable*race/ethnicity*time were non-significant (2 d.f. p's>0.15).

Key: BMI – body mass index, DASI – Duke Activity Status, d.f. – degrees of freedom, Est. - coefficient estimate, nH – non Hispanic,

* All models include race/ethnicity, the baseline value for the risk factor of interest, time in follow-up years, randomized diabetes (insulin sensitizers versus insulin providers) and cardiovascular (medical therapy versus immediate revascularization) treatment assignment, and revascularization strata (coronary artery bypass graft versus percutaneous coronary intervention).
** Models 7-9 and 16-18 additionally adjust for baseline values of HbA1c, BMI, DASI, age, post high school education, USA sites, malignancy (cancer), clinical neuropathy, insulin use, duration of diabetes, angina status, number of hypertension drugs, systolic blood pressure, and low density lipids.

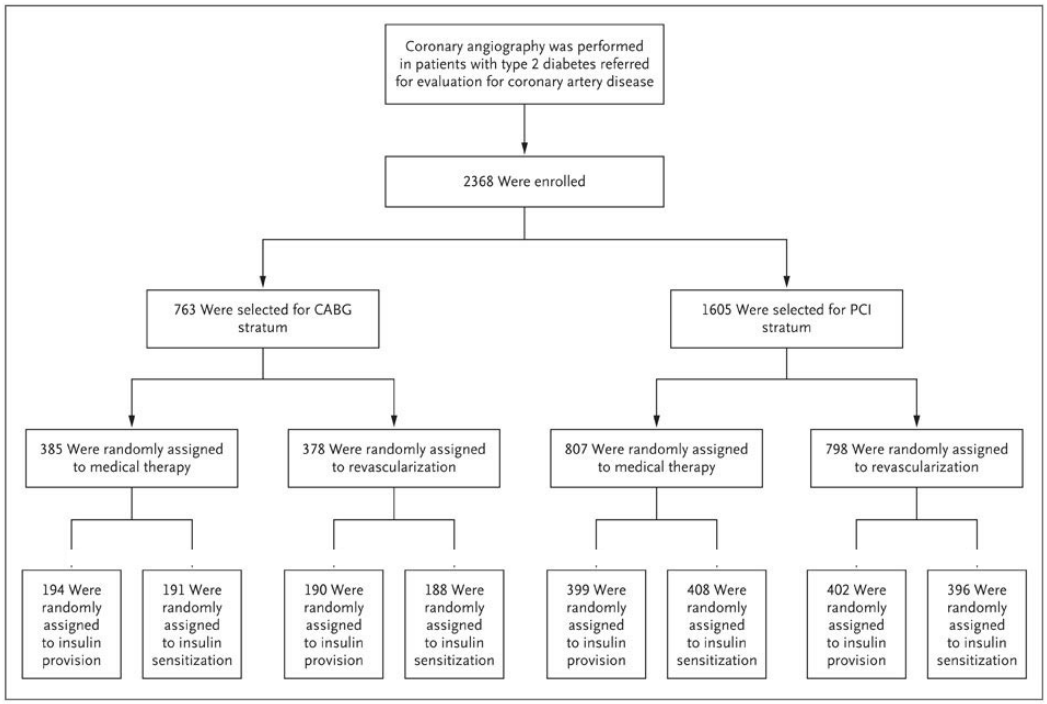
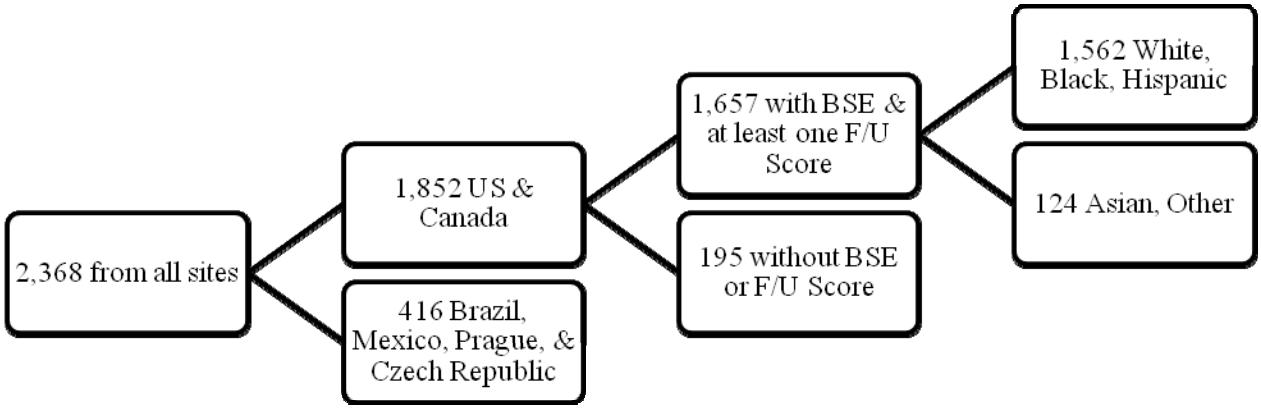


Figure 12. BARI 2D enrollment and randomization.
Modified from BARI_2D_Study_Group. (2009). A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med, 360(24), 2503-2515.



Key: BSE – Baseline self-efficacy, F/U – follow-up

Figure 13. Population flowchart for Aim 2

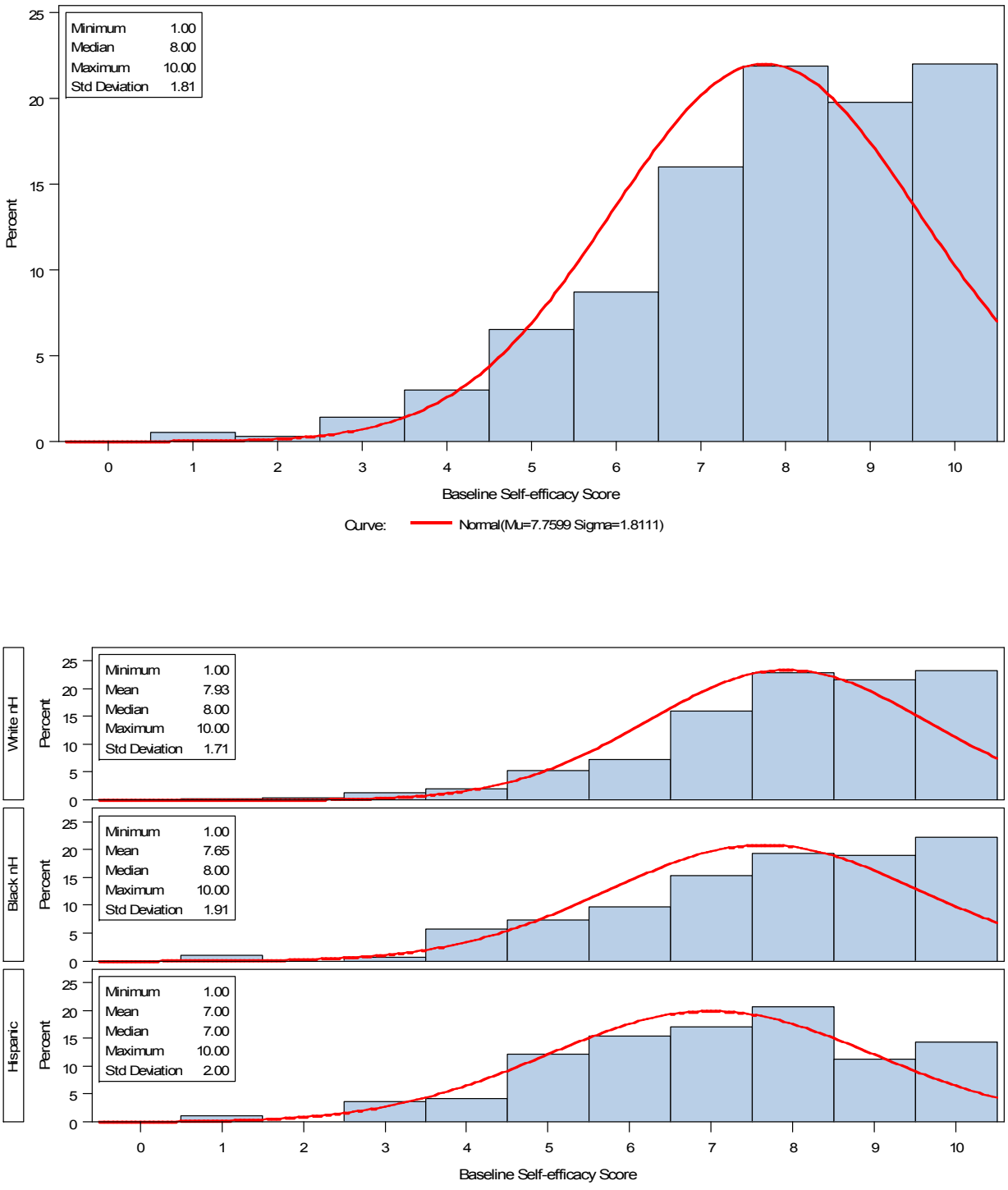


Figure 14. Distribution of baseline self-efficacy scores overall and by race/ethnicity

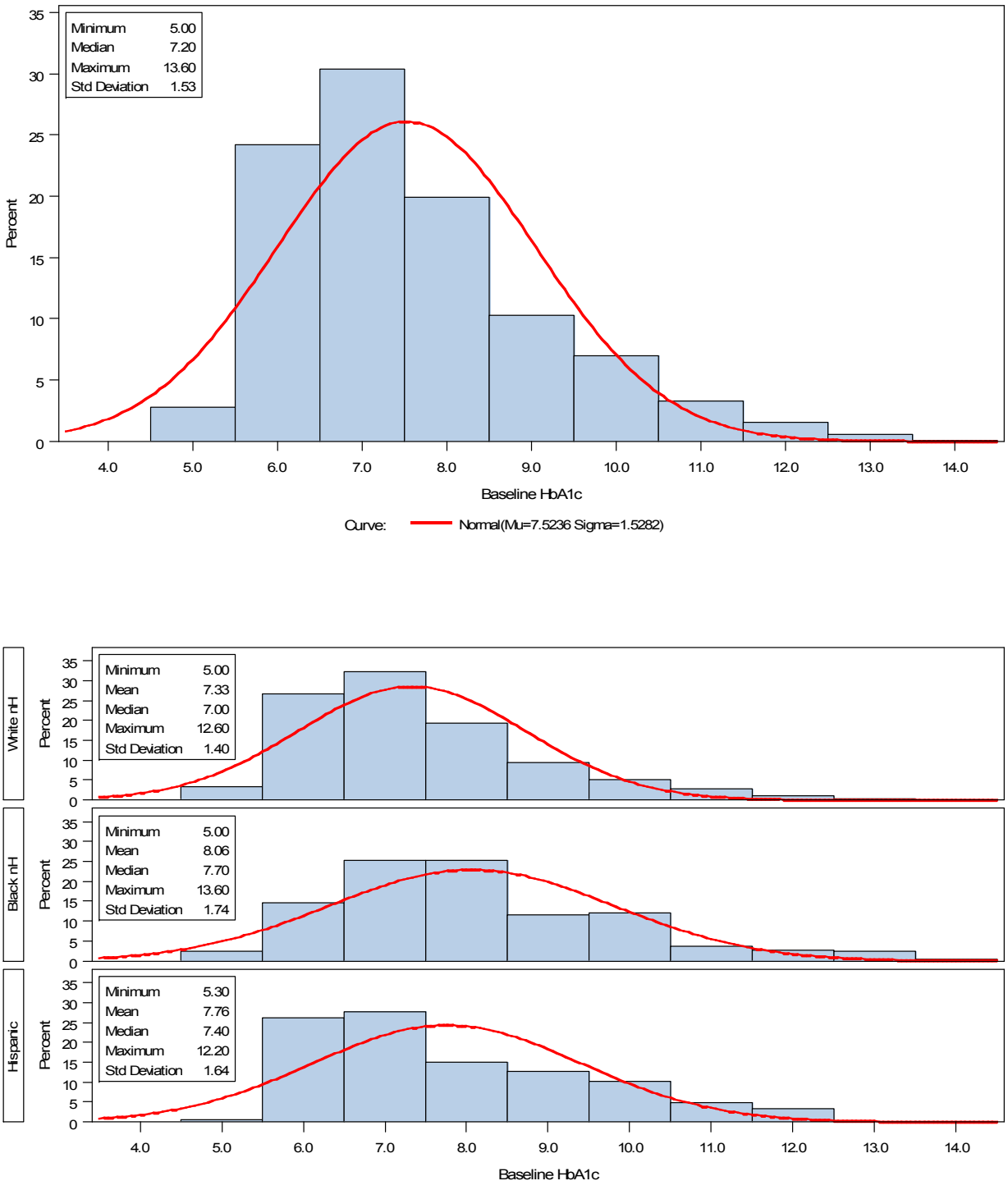


Figure 15. Distribution of baseline HbA1c overall and by race/ethnicity

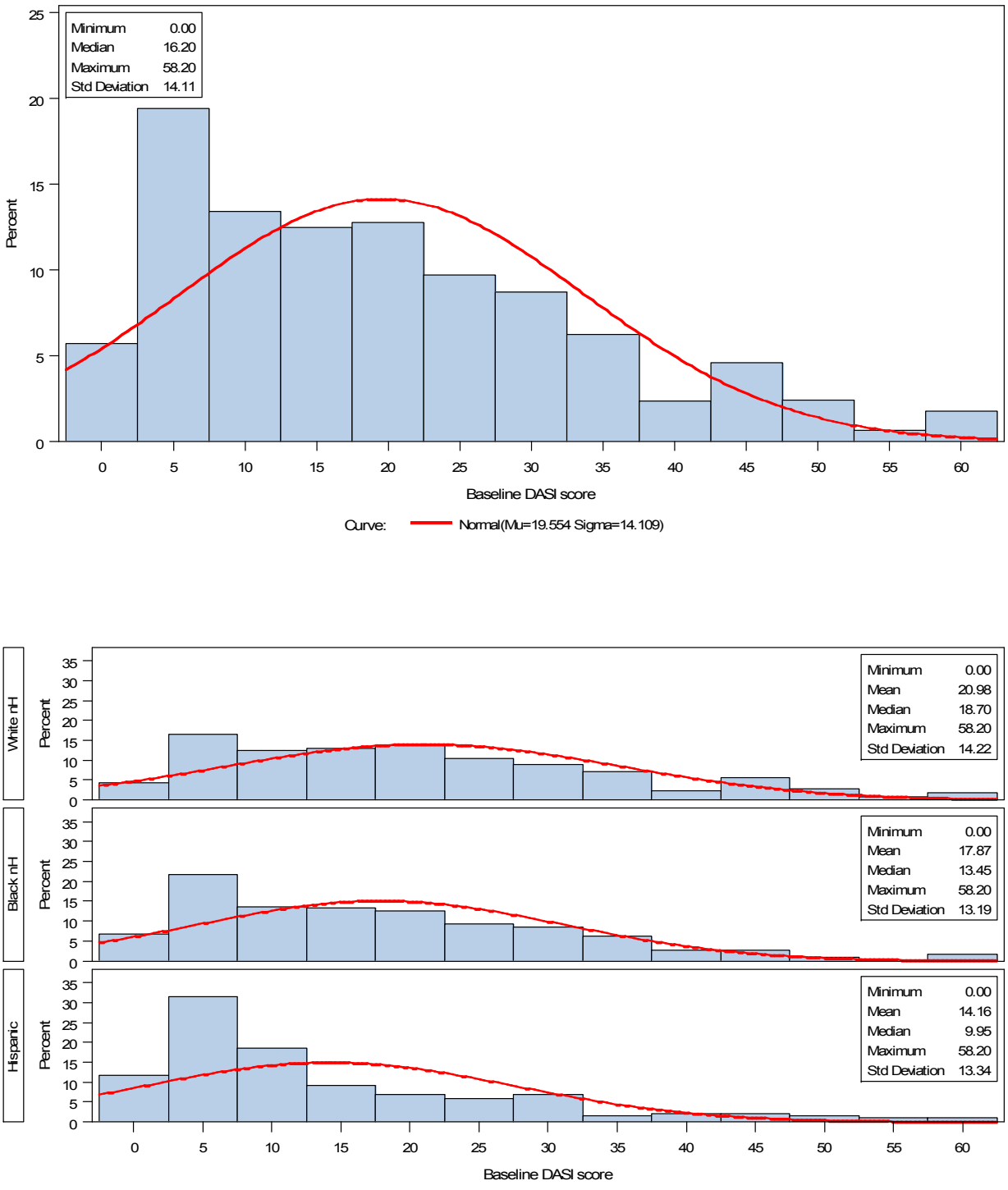


Figure 16. Distribution of baseline DASI scores overall and by race/ethnicity

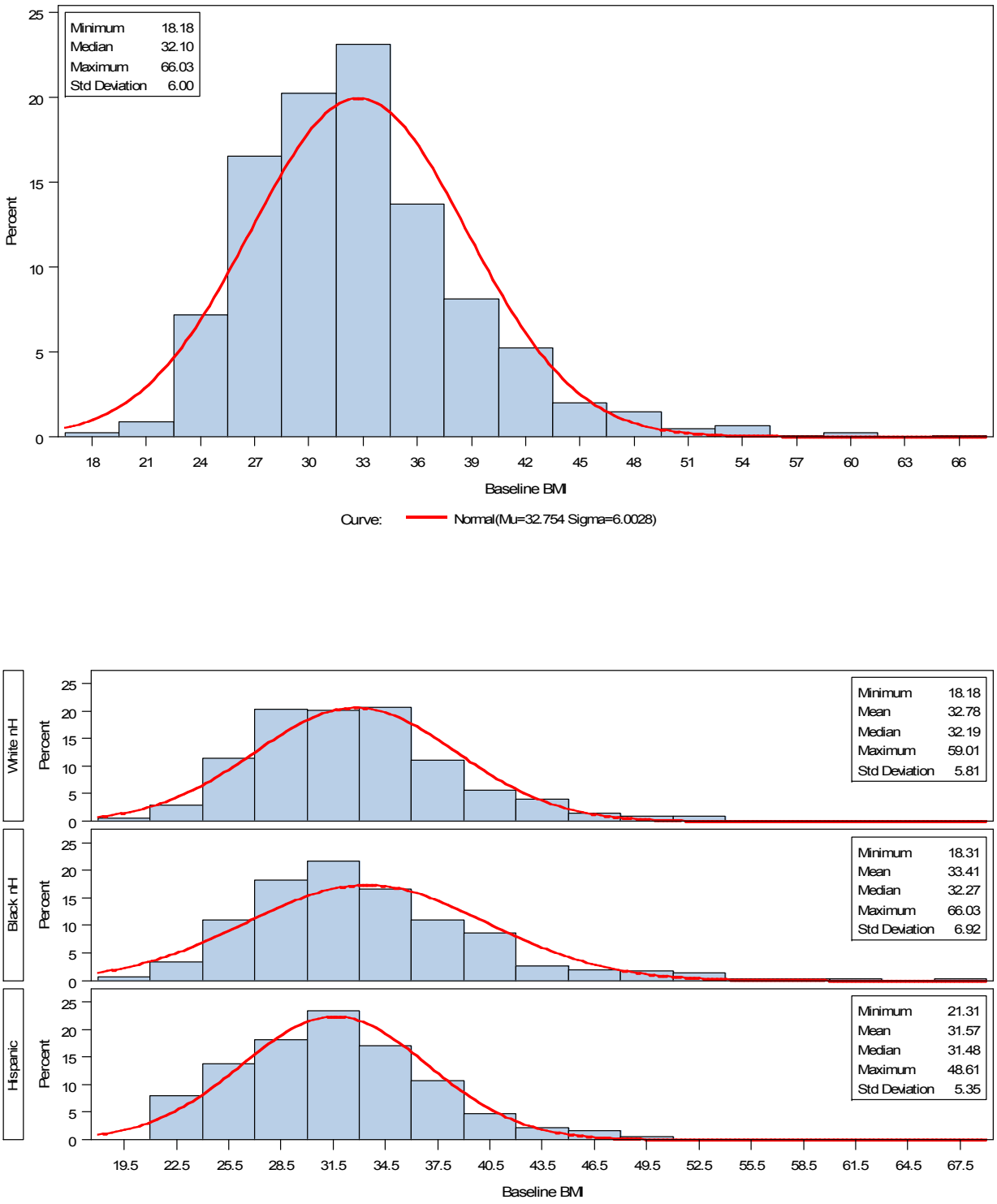
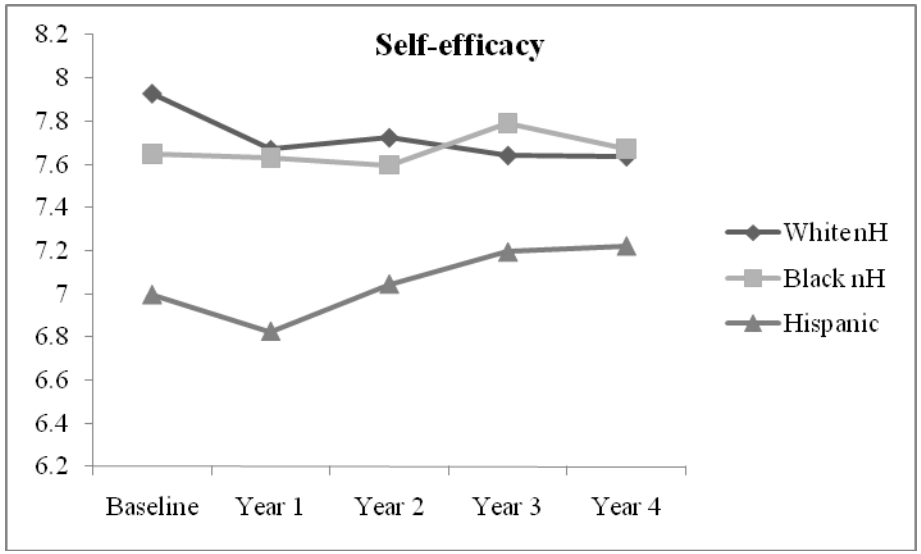
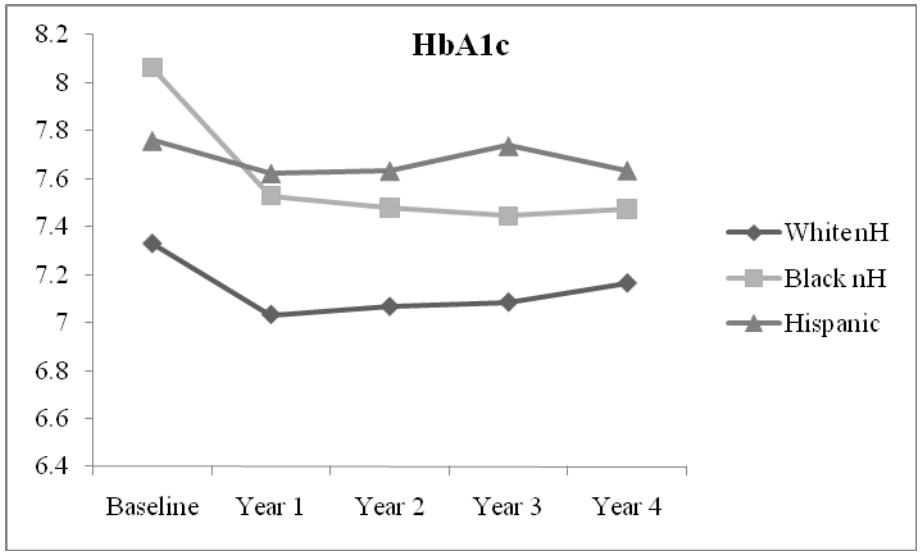
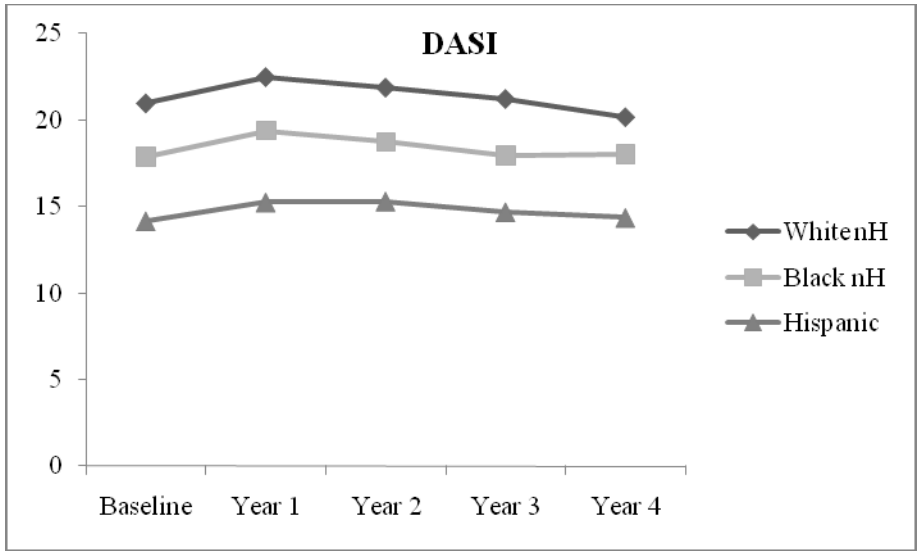


Figure 17. Distribution of baseline BMI overall and by race/ethnicity







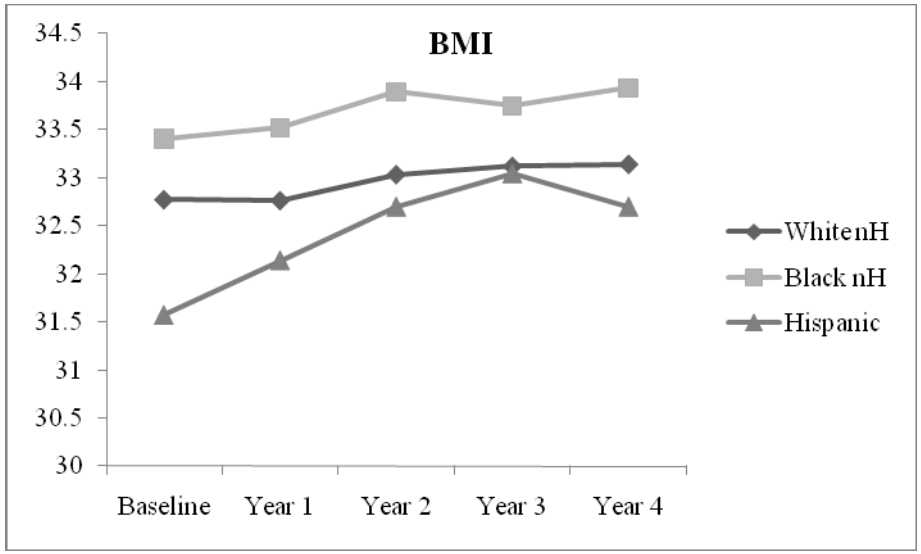


Figure 18. Line graphs of mean self-efficacy scores, HbA1c, DASI scores, and BMI by race/ethnicity over time

5.0 PAPER 3: SELF-EFFICACY AND CARDIOVASCULAR ENDPOINTS

5.1 ABSTRACT

OBJECTIVE: The purpose of this study was to examine the association between self-efficacy and the cardiovascular outcomes death, death/myocardial infarction (MI)/stroke, subsequent revascularization procedures, and angina.

METHODS: Using data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial, we examined 1,817 patients from the United States (US) and Canada sites. Patients were randomized to receive treatment for Type 2 diabetes mellitus (T2DM) by either insulin sensitizing drugs or insulin providing drugs, and for coronary artery disease (CAD) by either immediate revascularization or medical therapy. The self-efficacy assessment from the Chronic Disease Self-Management Study was administered at baseline and annually throughout the study. Kaplan-Meier rates were used to examine all of the outcomes, except for angina. Mixed models were used to examine the presence of angina over time. We tested for interactions between self-efficacy and cardiac treatment.

RESULTS: Compared to fair-excellent self-efficacy, poor baseline self-efficacy was associated with an increased risk of a composite endpoint of death/MI/stroke (hazard ratio [HR]=1.34, p=0.01), subsequent revascularizations (HR=1.30, p=0.004), subsequent PCIs (HR=1.43, p<.001), and angina (odds ratio [OR]=1.11, p<.001). These associations were not significant after adjusting for baseline demographic and clinical covariates. A decrease in self-efficacy from

baseline to Year 1 was a powerful predictor of death (adjusted HR=2.32, p<.001) and death/MI/stroke (HR=1.79, p<.001).

CONCLUSIONS: Although poor baseline self-efficacy was associated with an increased risk of death/MI/stroke, subsequent revascularization procedures and angina, these associations were primarily explained by differences in baseline risk factors. The negative change in self-efficacy was a more powerful predictor of BARI 2D's primary and secondary endpoints.

5.2 INTRODUCTION

Type 2 diabetes mellitus (T2DM) is associated with an increased risk of cardiovascular events in patients with coronary artery disease (CAD) (Stamler, Vaccaro, Neaton, & Wentworth, 1993). There are multiple methods to treat these conditions, namely medical therapy and cardiac revascularization. However, the psychological predictors of cardiac morbidity and mortality are gaining more attention from researchers as, "The first step toward targeted prevention measures" (Sarkar 2009, page 1). Poor self-efficacy is associated with poor health status and cardiac severity, increased physiological stress, and poor patient behaviors such as insufficient adherence to prescribed medications (Sarkar, 2007; Murray et al., 2007; Tu et al., 2005). Yet, the extent to which cardiac morbidity/mortality is associated with self-efficacy is unclear.

The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial was a randomized clinical trial that compared therapies for patients with T2DM and CAD. There was no significant difference between five-year survival rates of patients randomized to immediate revascularization or medical management (88.3% vs. 87.8%, respectively; p=0.97); nor, did freedom from the composite of death/myocardial infarction (MI)/stroke differ between the two

groups (77.2% vs. 75.9%, respectively; p=0.70). However, in patients who were selected for coronary artery bypass graft (CABG), as opposed to percutaneous coronary intervention (PCI) procedures, the cardiovascular event rate was significantly lower in the revascularization group as compared to the medical therapy group (22.4% vs. 30.5%, respectively; p=0.01) (BARI_2D_Study_Group, 2009). Quality of life indices, such as self-efficacy, were collected in order to examine additional risk factors for cardiac events. It is unknown how self-efficacy may affect the survival and freedom from cardiac events in this patient population, and whether this varies by treatment regimen.

Using data from the BARI 2D trial, the primary aim of this paper is to examine how self-efficacy is associated with the adverse cardiac events of death, myocardial infarction, stroke, subsequent revascularization, and angina. The secondary aim is to examine how these associations differ by the types of randomized cardiovascular therapy: either medical therapy or revascularization. The definitions and epidemiology of the adverse clinical events associated with CAD (death, MI, stroke, angina, and subsequent revascularizations), cardiovascular therapies, and self-efficacy, will be presented first. Then we will examine clinical event rates by self-efficacy level, and determine whether revascularization treatment interacts with this psychological risk factor. This analysis is novel in two respects: 1) this study involves a cardiac patient population with Type 2 diabetes mellitus (T2DM) – a risk factor for adverse cardiovascular morbidity and mortality; and 2) it is the first study to examine how self-efficacy is associated with mortality with respect to the *type* of cardiovascular therapy.

5.2.1 Cardiac events

5.2.1.1 Coronary artery disease

Coronary artery disease (CAD) is characterized by atherosclerotic plaque build-up in the arteries, resulting in inadequate circulation of blood to the heart, brain, and surrounding tissues. Approximately 81.1 million adults in America (36.9%) have some form of CAD, which was the leading cause of death in 2006, accounting for 831,100 deaths (NHLBI, 2009). Black non-Hispanics (nH) have higher rates of CAD compared to Whites and Hispanics (AHA, 2010). CAD was also the leading cause of death in 2005 accounting for 36.2% of deaths in White nHs, 33.6% in Black nHs, and 39.6% in Hispanics (CDC, 2008).

A major clinical risk factor for CAD is T2DM. If untreated or poorly managed, T2DM can result in blindness, amputations, end stage renal disease (ESRD), and cardiovascular complications such as MI (heart attack) and stroke (NIDDK, 2007). In 2004, CAD disease accounted for 68% of the deaths in people with T2DM aged 65 years or older (NIDDK, 2007). Based on 20 years of surveillance data, the Framingham Heart Study found that patients with diabetes had a two- to three-fold increased risk of CAD compared to patients without diabetes (Kannel & McGee, 1979).

5.2.1.2 Myocardial infarction

MI is a rapid necrosis of the myocardium due to interrupted blood flow from the arteries. In 2006, 8.5 million (3.6%) people in the US experienced a MI; and MI accounted for 141,500 deaths (AHA, 2010). The prevalence rates in White nH males and females were 5.1% and 2.6%, respectively. In Black nH males and females, the rates were 3.6% and 2.9%, respectively, and in Mexican American males and females, they were 2.6% and 2.0%, respectively (AHA, 2010).

5.2.1.3 Stroke

A stroke (cerebrovascular accident) is developing brain damage caused by interrupted blood flow to the brain due to a hemorrhage (bleeding in the brain) or ischemia (restricted blood flow). In 2006, the US prevalence of strokes was 6.4 million (2.9%) and the incidence of new and recurrent strokes was 795,000. Strokes accounted for 137,000 deaths in the US (AHA, 2010). The prevalence of stroke differs by gender and race/ethnicity, with higher rates reported in females and racial/ethnic minorities. In 2006, the prevalence rate in White nH males and females was 2.3 and 3.1%, respectively, and in Black nHs, 3.8% and 4.3%, respectively. In Hispanics and Mexican Americans, the rates ranged from 2.6 – 3.1%.

5.2.1.4 Angina

Angina is a treatable cardiovascular complication marked by intermittent chest pain due to reduced oxygen to the heart (Campeau, 1975). Classic angina, as defined by the Canadian Cardiovascular Society (CCS) Functional Classification of Angina, is based on the activity that evokes pain and physical limitations (Campeau, 1975). The classification system ranges from Class 1 to Class 4, with Class 1 being evoked by strenuous activities and Class 4 evoked by less strenuous activities:

- Class I: Prolonged exertion with no physical limitations
- Class II: Walking more than two blocks or more than one flight of stairs with slight physical limitations
- Class III: Walking more than two blocks or more than one flight of stairs with marked physical limitations
- Class IV: Minimal activity or at rest with severe physical limitations

5.2.2 CAD Treatment

Treatment options for CAD include a) medical management with diet, exercise, and medicine; or b) revascularization either by CABG or PCI. CABG is an invasive procedure in which a healthy blood vessel is grafted onto the heart to bypass the blocked part of the coronary artery. Due to the invasive nature of the procedure, it is not common to be revascularized by CABG more than once. PCI is a less invasive procedure in which a balloon–tipped catheter is placed into the diseased arteries of the heart (AHA, 2009). In the event of a subacute (coagulated) stent or worsening CAD, subsequent revascularizations by PCI can be performed.

5.2.3 Self-efficacy

The patient's self-confidence plays a crucial role in the ability to manage potentially harmful and fatal chronic conditions (Lorig, 1996). Self-efficacy, the belief that one is able to make changes necessary for self-management, has been found to be associated with glycemic control and cardiac symptom burden (A. Bandura, 1977; Chlebowy & Garvin, 2006b; Sarkar, et al., 2007; Sullivan, et al., 1996). The idea of self-efficacy originates from Albert Bandura's social learning theory, which proposes that behaviors are learned from observing and analyzing the behaviors of others (A. Bandura, 1977).

Joekes et al. (2007) hypothesized that patients with low self-efficacy are prone to poorer clinical outcomes as a result of MI, because their low self-efficacy impairs their ability to seek clinical help in an optimal time window. Only 20% of people who have an acute MI reach medical care within an optimal time window; 75% of this delay is attributed to the patient's decision to seek help. Joekes found that during an MI, low self-efficacy combined with negative

outcome expectancies were associated with an increased delay in reaching the hospital promptly (Joekes, Van Elderen, & Schreurs, 2007).

Self-efficacy has also been studied extensively in CAD patients after a non-fatal MI. Findings show that self-efficacy was one of the most relevant psychological constructs in cardiac rehabilitation. Moore et al. (2007) revealed that in a sample of 248 participants treated for CAD or an MI, self-efficacy was the most salient psychological mediator in the prediction of health status. Self-efficacy predicted MI patients' self-management behaviors during the three months following the events (Joekes, et al., 2007).

In Paper 2, an inverse cross-sectional relationship was demonstrated between baseline self-efficacy and angina in patients with both T2DM and CAD. Patients who began the study with self-efficacy scores >8 (on a 1 [poor] -10 [best] point scale) were more likely to be absent of classic angina compared to patients with self-efficacy scores ≤8 (46.2% vs. 39.8%, p=0.02). Sarkar et al. (2007) have shown a negative association between cardiac symptom burden and self-efficacy; however, no direct association between self-efficacy and angina was demonstrated.

Measuring the patients' self-efficacy about their cardiac management provides a quick and powerful assessment of cardiac symptom burden, function, and outcomes in patients with CAD (Sarkar et al., 2007 & 2009). In an observational cohort study of ambulatory patients with stable coronary heart disease, Sarkar et al. (2007) showed that even after controlling for cardiac risk factors and symptoms, self-efficacy was a strong predictor of cardiac health status. For each standard deviation decrease in the self-efficacy score, the odds for cardiac symptom burden more than doubled (adjusted odds ratio [OR] = 2.1, p = .001). In the same cohort of patients, Sarkar et al. (2009) evaluated the association between self-efficacy and objective measures of cardiac

function, heart failure hospitalization, and all-cause mortality (Sarkar, et al., 2009). Self-efficacy was measured using the 5-item Sullivan Self-Efficacy to Maintain Function Scale. Among 1,024 patients with CAD, self-efficacy was an effective proxy for clinical risk factors in predicting heart failure hospitalizations (OR per standard deviation [sd] decrease = 1.4, $p = 0.0006$) and all-cause mortality (OR per SD decrease = 1.4, $p < 0.0001$) (Sarkar, et al., 2009). The interaction between self-efficacy and depressive symptoms was not significant. After adjusting for demographics, medical history, medication use, depressive symptoms, and social support, the association of cardiac self-efficacy with both heart failure hospitalization and mortality was explained by worse baseline cardiac function. However, one of the main limitations of this study was the use of a predominately older, lower-income male population which 1) limits the generalizability of the results; and 2) is a population at risk for T2DM – a clinical risk factor not documented in this study.

In a sub-study of BARI 2D by Sansing et al. (Paper 2), self-efficacy was examined in patients with both CAD and T2DM. Patients with lower baseline self-efficacy scores carried a greater burden of cardiac risk factors compared to patients with baseline self-efficacy scores >8. Compared to patients with baseline self-efficacy scores >8, those patients with poorer baseline self-efficacy scores (≤8) were more likely to be female, Hispanic, and have a lower education. These patients also had significantly worse clinical profiles, including higher HbA1c, greater neuropathy, more severe angina, a history of congestive heart failure, and higher number of hypertension drugs. There were no differences in age, distribution of US sites, malignancy (cancer), history of MI, systolic blood pressure, and low density lipids between those with scores <8 and ≥8. In a longitudinal analysis of the BARI 2D study, results showed a feedback loop between increased self-efficacy and better risk factor control. It was also noted that patients

randomized to an initial strategy of revascularization, by PCI or CABG, and a strategy of medical therapy had similar self-efficacy over the subsequent four years of follow-up.

5.2.4 Psychological factors and cardiac therapies

For patients with coronary disease, revascularization has been shown to be associated with better quality of life compared to no revascularization. In a report by Eagle et al. (2004) in the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for Coronary Artery Bypass Graft Surgery, both CABG and PCI were related to greater health-related quality of life (HRQoL) compared to traditional medical therapy (Committee, et al., 2002). PCI provided improvements in HRQoL in the earlier post-procedure compared to CABG, while CABG improved health-related quality of life better than traditional medical therapy for up to five years post-surgery (Hofer, Doering, Rumpold, Oldridge, & Benzer, 2006).

5.3 RATIONALE

The primary aim of this analysis was to examine the relationship between self-efficacy and the cardiovascular clinical endpoints of the BARI 2D study, all-cause mortality, a composite of death, MI, and stroke, subsequent revascularization (any revascularization, PCI and CABG), and angina. The secondary aim was to examine how these relationships vary by cardiac treatment (initial revascularization or medical therapy). This goal is important because it examines how the confidence of a person with chronic conditions can affect serious adverse events and mortality. These conditions are sometimes physically painful, limit the patients' mobility, significantly

decrease their lifespan, can include large medical costs, and involve lifestyle changes for them, as well as for their caregivers and families.

Self-efficacy is needed to adapt to these lifestyle changes, and poor self-efficacy has been associated with poorer cardiac status, which results in increased cardiac events and complications (Sarkar, et al., 2009). This literature has shown that patients with poor self-efficacy have greater cardiac symptom burden compared to patients with high self-efficacy. Given that many risk factors are associated with poorer self-efficacy, one can hypothesize that poor self-efficacy is associated with worse clinical outcomes. The majority of the literature regarding self-efficacy and cardiovascular symptoms and outcomes was based on observational data from the Heart and Soul Study resulting in potential confounders between the types of treatments used and the clinical and demographic profile of the recipients (Sarkar, et al., 2007; Sarkar, et al., 2009; Sarkar, et al., 2006). For instance, patients who were revascularized may have had worse cardiac clinical status compared to patients who were not revascularized at all.

In the BARI 2D clinical trial, the randomized cardiac therapy (prompt revascularization vs. medical therapy) was not associated with patient self-efficacy during follow-up. Moreover, the cardiac treatment was not associated with the primary and principal secondary BARI 2D endpoints of death and the composite of death, MI and stroke, respectively (BARI_2D_Study_Group, 2009). However, the rate of subsequent revascularization and the prevalence of angina were significantly higher among patients randomized to initial medical therapy compared to patients randomized to revascularization. Using prospective data from a randomized clinical trial, we will examine the relationship between self-efficacy and cardiovascular outcomes overall, and with respect to the cardiac treatment.

5.4 SPECIFIC AIMS

In order to further examine if self-efficacy is related to clinical outcomes of death, death/myocardial infarction/stroke, subsequent revascularization, and angina in patients with comorbid T2DM and CAD, the hypotheses are as follows:

H1: Lower self-efficacy at baseline will be associated with an increased risk of each of the clinical endpoints.

H2: Lower self-efficacy at baseline will be associated with an increased risk of each of the clinical endpoints among patients randomized to medical therapy and revascularization.

5.5 METHODS

5.5.1 BARI 2D Study design

BARI 2D is a multicenter clinical trial designed to determine optimal treatment strategies for patients with T2DM and documented stable CAD. Using a 2x2 factorial design, BARI 2D compared initial revascularization with intensive medical therapy (will be referred to as prompt revascularization) versus initial intensive medical therapy and delayed revascularization if symptoms worsen or are clinically indicated (will be referred to as medical therapy), while simultaneously studying an insulin-providing versus an insulin-sensitizing strategy of glycemic control to achieve a clinical target of HbA1c <7% (BARI_2D_Study_Group, 2006).

Randomization was stratified by BARI 2D site and by the intended revascularization, PCI or CABG, as determined by a physician. Follow-up visits occurred monthly for the first six months and quarterly thereafter, until the end of the study in 2008. At each follow-up visit, information about clinical risk factors, diabetes complications, clinical events, and medications was collected. Self-efficacy data were collected annually as part of the quality of life assessments. The mean follow-up per patient was 5.3 years with a range of 3.5 to 6 years. The BARI 2D primary endpoint was all-cause mortality. The composite secondary endpoint was death, non-fatal MI, or stroke.

5.5.2 Population

Participants were enrolled from 49 clinical sites in the US, Canada, Brazil, Mexico, the Czech Republic, and Austria (N=2,368). Eligible participants had T2DM and had angiographically documented CAD that did not require immediate revascularization for control of symptoms (BARI_2D_Study_Group, 2006). Inclusion criteria were as follows: diagnosis of T2DM, coronary arteriogram showing one or more vessels amenable to revascularization (≥50% stenosis), documentation of ischemia or documented classic angina with ≥70% stenosis in at least one artery, suitability for coronary revascularization by at least one of the available methods, ability to perform all tasks related to glycemic control and risk factor management, age 25 or older, and informed written consent (BARI_2D_Study_Group, 2006). Patients were excluded if there was a definite need for invasive intervention as determined by a cardiologist, any CABG or PCI within the past 12 months, class III or IV CHF, creatinine >2.0 mg/dl, HbA1c >13%, need for major vascular surgery concomitant with revascularization (e.g., carotid endarterectomy), left main stenosis ≥50%, non-cardiac illness limiting mortality, hepatic disease,

fasting triglycerides >1,000 mg/dl in the presence of moderate glycemic control (HbA1c ≤8.0%), current alcohol abuse, chronic steroid use, known/planned/suspected pregnancy, geographically inaccessible or inability to return for follow-up, enrolled in a competing randomized trial or clinical study, and inability to understand or cooperate with protocol requirements (BARI_2D_Study_Group, 2006).

5.5.3 Data Collection and Measures

5.5.3.1 Self-efficacy

The self-efficacy assessment was administered at baseline and annually at Years 1 through 6. The instrument was designed to measure how confident the patient was in his or her ability to do tasks and activities that relate to managing his or her T2DM and CAD in general and specific ways (Appendix A). The term "management" may be interpreted as something as simple as trying to monitor glucose regularly or to adhering to a more complex regimen of a specific diet with regular exercise. Patients were encouraged to personally consider what tasks and activities he or she completed on a day-to-day basis, in order to measure confidence in the ability to keep T2DM and CAD "under control." The self-efficacy assessment was derived from the Chronic Disease Self-Management Study (Lorig, 1996). The questions were modified from general disease management to heart disease and T2DM specifically. Each question consisted of a 10-point Likert scale with "1 = not at all confident" and "10 = totally confident." Interest lied in the patients' confidence in: 1) doing all day-to-day things necessary to manage their conditions; 2) doing activities for their T2DM and CAD in order to reduce doctor visits; 3) reducing emotional stress associated with their diseases through acts such as prayer, meditation, art, and social contact; and 4) doing activities besides medication adherence, such as exercise, hobbies, and

dieting to reduce the impact of the diseases on their daily life. The individual items in the self-efficacy score had high internal consistency (Cronbach's $\alpha = 0.92$).

5.5.3.2 Endpoints

The primary endpoint for the BARI 2D trial was all-cause mortality and the secondary composite endpoint was death, nonfatal myocardial infarction, or stroke. Definitions for endpoints and ascertainment methods were provided in the main trial report (BARI 2D Study Group, 2006). Cause of death and stroke were classified and adjudicated by the BARI 2D Mortality and Morbidity Committee. The committee was blinded to randomization assignment, treatment received, and additional clinical data. MI was classified by a blinded independent Core Electrocardiography Laboratory. The definition of a subsequent revascularization was based on the randomization arm. For patients randomized to medical therapy, a subsequent revascularization was the first revascularization in BARI 2D. For patients randomized to the prompt revascularization arm, the subsequent revascularization was the first one following their initial protocol-driven revascularization. Angina was assessed at the BARI 2D annual clinic visits and was categorized using the Canadian Cardiovascular Society (CCS) classification system (Campeau, 1976).

5.5.3.3 Demographic and Clinical variables

Race was self-reported based on the US Census Classification System as: 1) American Indian/Alaskan Native; 2) Asian; 3) Black/African American; 4) Native Hawaiian/Pacific Islander; 5) White; or 6) Other (including those of multiple races). Hispanic ethnicity (Latino or Spanish origin) was indicated regardless of race. A detailed clinical history was recorded at study entry including smoking status, history of cancer and cardiovascular complications, duration of

diabetes, neuropathy symptoms, and diabetes medication use. Body mass index (BMI) (kg/m2) was calculated by clinical measurements of weight and height. HbA1c levels, fasting total, low-density lipid cholesterol (LDL), and high-density lipid cholesterol (HDL) were measured from blood samples collected at baseline and were analyzed at the BARI 2D Core Biochemistry Laboratory. BARI 2D collected data regarding medications prescribed, but there is no information regarding patient adherence in this study.

5.5.3.4 Statistical Methods

Analyses were restricted to patients with a self-efficacy score at baseline. Moreover, due to language barriers and method of administration, only patients from US and Canadian sites were included in this analysis. Normality of the distribution of the self-efficacy scores was assessed to be approximately normal. Baseline self-efficacy was categorized into quartiles, and then, based on the left skewed distribution, was dichotomized as Poor (score 1-6.7) vs. Fair/Good/Excellent (6.75-10). Change is calculated as the Year 1 self-efficacy score minus the baseline self-efficacy score. Change from baseline to Year 1 was examined categorically as: ≥1.5 decrease, moderate change between -1.5 and 1.5 (reference group), and ≥1.5 increase. The value of 1.5 was chosen based on the standard deviation of the change between baseline and Year 1 (Paper 1).

Baseline demographics and clinical characteristics were compared to baseline self-efficacy categories. Differences in baseline characteristics were compared using chi-square, t-tests, and Wilcoxon signed-rank tests. Five year Kaplan-Meier (KM) rates of all cause mortality, death/MI/stroke, subsequent procedure, subsequent PCI, and subsequent CABG were calculated according to the baseline self-efficacy scores (Poor vs. Fair-Excellent), and compared using log-

rank statistics. The KM event rates were examined overall and within each cardiac randomization arm (prompt revascularization and medical therapy).

Hazard ratios for baseline self-efficacy were estimated for the endpoints of death, death/MI/stroke, and subsequent procedures, subsequent PCIs, and subsequent CABGs based on Cox proportional hazards regression models. Baseline self-efficacy was coded as a dichotomous predictor and the clinical outcomes over a period of five years were included. In order to estimate the effect of changing self-efficacy over time within the BARI 2D trial, the self-efficacy change scores from baseline to Year 1 were used as a predictor variable for cardiovascular outcomes occurring over the subsequent four years of follow-up. Each model was adjusted for the study design variables, assigned prompt revascularization (vs. medical therapy), assigned insulin providing drugs (vs. insulin sensitizing drugs), and the randomization stratification of intended CABG (vs. PCI). The first set of models only adjusted for the study design variables. The second set of models adjusted for the study design variables, as well as demographic and clinical confounding variables. Cox models were created for the overall population and for each cardiac treatment arm individually.

Mixed models were conducted with the presence of angina symptoms as the outcome variable and time (follow-up years) as repeated measures. The models controlled for revascularization strata (CABG vs. PCI), cardiovascular treatment (prompt revascularization vs. medical therapy), and glycemic therapy (insulin providing vs. insulin sensitizing), where appropriate. There were tests for interactions between the self-efficacy predictor variable and cardiac treatment.

5.6 RESULTS

There were 1,817 patients with a self-efficacy assessment at baseline and 1,526 of these patients had measures at Year 1 (Figure 19). The mean baseline self-efficacy score was 7.71±1.83; however, the distribution was skewed and not normally distributed. The mean change in self-efficacy score from baseline to Year 1 was -0.175±1.93 (Figure 20), and the change score distribution was approximately normal. Missing baseline covariate data (with the exception of self-efficacy) were replaced by the mean value, when the percent missing did not exceed 5% (**Table 16**).

Self-efficacy was categorized by quartiles (**Table 17**). The ranges of the four quartiles varied greatly. Upon examination of the quartiles of self-efficacy, a consistent pattern emerged such that the Poor group contrasted markedly with the Fair-Excellent groups. Therefore, self-efficacy was analyzed as a dichotomous variable (Poor vs. Fair/Good/Excellent). All analyses were also conducted using self-efficacy as a continuous variable. Abiding by the direction of the self-efficacy assessment's author, the self-efficacy variable was not transformed (Lorig, 1996) (personal communication between Sansing and Lorig via e-mail, 2007). In addition, in order to account for the effect of participation in BARI 2D on the patients' self-efficacy, we examined change in self-efficacy from baseline to Year 1 as a predictor variable.

Patients with Poor self-efficacy and those with higher self-efficacy had significantly different demographic and clinical profiles at baseline (**Table 18**). Patients with Poor self-efficacy were less likely to be male, White nH, to complete a post high school education, and had a lower history of cancer. They had higher mean HbA1c, were more likely to have neuropathy symptoms, had a longer duration of T2DM, increased use of insulin, had a higher rate of

peripheral artery disease, used more hypertension drugs, and had high LDL, a high albumin creatinine ratio (renal impairment), and an increased history of congestive heart failure requiring treatment. There were no differences in self-efficacy in randomized treatment and assignment to CABG, which indicates a balanced study design.

Baseline self-efficacy was not related to all-cause mortality and subsequent CABG (**Table 19**). Higher self-efficacy was associated with lower rates of death/MI/stroke (five year Kaplan Meier event rates: 20.9% vs. 27.3%, p=0.01; **Figure 21a**), fewer subsequent procedures (35.1% vs. 42.7%, p=0.003), and fewer PCI procedures (23.6% vs. 33.6%, p<.001) in the overall BARI 2D population. The difference in the death/MI/stroke rate by self-efficacy group was significant among patients randomized to medical therapy (p=0.01), but not among those randomized to revascularization (p=0.27). The interaction between treatment groups and baseline self-efficacy was not significant (p=0.39). In both the medical and the revascularization groups, patients with Poor self-efficacy had higher rates of subsequent procedures compared to those with higher self-efficacy, but the subsequent revascularization rates were consistently higher in the medical therapy randomized treatment group (**Figure 21b**). The Kaplan-Meier curves for death/MI/stroke and subsequent procedures for patients with Poor and Fair-Excellent self-efficacy show that the difference in the cumulative event rates for these outcomes between the baseline self-efficacy groups continue to separate over the five year follow-up.

Poor baseline self-efficacy, when adjusted for change in self-efficacy, was not significantly associated with death in this population (**Table 20**). Poor self-efficacy at baseline was associated with an increased risk of death/MI/stroke (hazard ratio [HR]=1.34, p=0.01), subsequent procedures (HR=1.30, p=0.004), and subsequent PCIs (HR=1.43, p<.001) over a 5 year period. These associations were attenuated after adjusting for baseline variables; and self-

efficacy was independently associated with subsequent PCI (HR=1.32, p=0.02), but not death/MI/stroke or subsequent procedures.

When adjusting for self-efficacy, several study design variables were related to an increased risk of subsequent revascularization procedures (**Table 20**). Immediate revascularization and randomization to the CABG stratum were associated with a decreased risk of subsequent procedure and subsequent PCI compared to medical therapy and PCI stratum. When adjusted for baseline covariates, the association between the CABG stratum and subsequent PCI was no longer significant. CABG was associated with approximately 3 times the risk for subsequent CABG.

Mixed models were created to estimate the effect of self-efficacy on angina over time (**Table 21**). The models in Set 1 adjust for time only, and the models in Set 2 adjust for time, study treatment, and baseline variables (see Methods). Poor self-efficacy is the main predictor variable in the top half of the tables, and change in self-efficacy is the main predictor in the bottom half. Better baseline self-efficacy was associated with an 11% (p<.001) decrease in the risk of angina; however, this association did not persist after adjusting for treatment and baseline covariates. A decrease in self-efficacy from baseline to Year 1 was associated with a 9% increased risk of angina (p<.001), but this association did not remain significant after adjustment for treatment and baseline confounders. The association between self-efficacy and angina did not vary by randomization to medical therapy or revascularization (i.e., none of the interaction p-values for self-efficacy and cardiac treatment were significant; all p-values >0.40). Time was associated with a decreased risk of angina when controlling for baseline self-efficacy (OR=0.91 per year, p<.001) and change in self-efficacy (OR=0.87, p<.001). Study design variables were not related to an increased risk of angina in these models.

5.7 DISCUSSION

The primary goal of this study was to examine the association between baseline self-efficacy and cardiovascular outcomes in patients with both T2DM and CAD. Poor self-efficacy and a decrease in self-efficacy from baseline to Year 1 were associated with several cardiac outcomes. Although no association between baseline self-efficacy and the primary endpoint of all-cause mortality was established in multivariate analyses, we did observe several critical associations with secondary outcomes. First, Poor baseline self-efficacy was associated with higher 5-year cardiac event rates compared to Fair/Good/Excellent self-efficacy. Second, a decrease in self-efficacy from baseline to Year 1 was associated with greater adverse outcomes. Compared to moderate change, this decrease was associated with a more than two-fold risk of death, a greater risk of death/MI/stroke after adjustments for baseline covariates, and a greater risk of angina when adjusted for time only.

Overall and within patients randomized to medical therapy, poor baseline self-efficacy was independently associated with higher 5-year rates of death/MI/stroke, subsequent procedures, subsequent PCI's, and angina than Fair-Excellent self-efficacy. The primary findings are similar to those of Sarkar et al. (2009), who showed that lower self-efficacy was a powerful predictor of increased cardiac burden, including heart failure and all cause mortality. After adjustments, the increase in heart failure and mortality were mainly attributed to poorer baseline cardiac function. In BARI 2D, only when change in self-efficacy (from baseline to Year 1) was incorporated into the model did self-efficacy become associated with all-cause mortality. Because self-efficacy is a state as opposed to a trait, and changes over time are based on successes and failures, a cross-sectional observation of self-efficacy is an inadequate predictor of

death. It is more important to capture evidence of improvement, stability, and decline in one's confidence. This variable of "change" is valuable because it shows the effect of participation in BARI 2D and the direction of the state. For instance, two people may enter the study with a baseline self-efficacy score of 8 and similar baseline profiles. By using these baseline scores as the predictor, it would be premature to conclude that these patients have a similar risk of death. Further, consider that by Year 1, one patient's self-efficacy increases to 10 and the other patient's score may decrease to 6. Here, the "change" in scores over time has proven to be a stronger predictor of death as the second patient is at higher risk for death.

In line with the findings by Sarkar et al. (2009), poor baseline self-efficacy was associated with greater cardiac symptoms and burden, as defined by death/MI/stroke, angina, subsequent revascularization procedures, and subsequent PCI. When factoring in serious non-fatal adverse events of MI and stroke as outcomes, baseline self-efficacy became a strong predictor. The association between self-efficacy and death/MI/stroke persisted after adjustments for randomized treatment groups and baseline covariates. This demonstrates the strength of a person's self-confidence in the management and prevention of serious cardiac outcomes that are potentially debilitating and fatal. In addition, Joekes et al. (2007) stated that low self-efficacy was a barrier to seeking punctual treatment for an MI, thereby increasing the risk for associated adverse prognoses. This further emphasizes the serious nature of poor self-confidence in a patient population at increased risk for adverse events and why these patients are at an increased risk of death. It also appeared that patients with poor baseline self-efficacy and a decrease in score from baseline to Year 1 were at higher risk for angina. However these associations were primarily explained by baseline covariates.

In BARI 2D, poor self-confidence combined with poorer baseline function lead to a greater risk of having a subsequent procedure. This was especially significant in the patients randomized to medical therapy in which a subsequent procedure was defined as their very *first* procedure in BARI 2D. Patients randomized to medical therapy were only revascularized in the event of worsening cardiac conditions, as opposed to patients randomized to prompt revascularization who received a procedure shortly after enrollment into the study. Therefore, patients in medical therapy were more likely to have subsequent procedures. In the medical therapy arm, more than half of the patients with poor self-efficacy received a subsequent procedure compared to 47% of patients with better self-efficacy. In addition, subsequent procedures included both CABG and PCI. PCI is a revascularization procedure that can be performed multiple times, as opposed to CABG which is infrequently performed more than once. Therefore, the association between self-efficacy and subsequent procedures is primarily explained by the PCI. This may explain why there was no association between self-efficacy and subsequent CABG.

In conclusion, in patients with comorbid T2DM and CAD, poor baseline self-efficacy was associated with an increased risk of death/MI/stroke, subsequent revascularization procedures, and subsequent PCIs. In addition, a decrease in self-efficacy from baseline to Year 1 was associated with death and death/MI/stroke. These results must be seen in light of several limitations. First, the patient population is one that is eligible for elective revascularization. Therefore, their clinical status is less severe than patients who must undergo immediate revascularization. The patients in the study may have had better self-efficacy than the aforementioned set of patients. Second, the self-efficacy assessment did not specifically distinguish between the management of T2DM and CAD. It generalized the management of the

diseases, therefore we were not able to study self-efficacy regarding each disease separately. Third, the effects of self-efficacy may have been due to depressive symptoms, which are clearly established as risk factors for CAD morbidity, diabetes, and mortality (Rutledge, et al., 2006). We could not adjust for depressive symptoms in our analyses because the assessment of depressive symptoms (CES-D) was incorporated into the BARI 2D protocol in February 2006, after the study began. These data were collected annually at Years 3-6.

These limitations are balanced by several important strengths. First, this study was a prospective, randomized, controlled clinical trial with a large study population. We were able to prospectively observe self-efficacy and other variables at baseline and follow their change throughout the study. Second, because the treatment for T2DM and CAD was randomized, allocation of the patient population to treatment groups was not biased by demographic or clinical status. Third, the study population was demographically diverse, which increased the generalizability of the results. Fourth and most importantly, this study is the first non-observational study to examine the association between self-efficacy and mortality. This study demonstrated that a decrease in self-efficacy more than doubles one's risk for death.

This research is of great public health significance because it provides evidence of another psychosocial factor that can impact mortality. The increase in subsequent procedures associated with poor self-efficacy can impose a significant financial burden on the currently fiscally exhausted medical field. There is no research published to date that measures the effect of self-efficacy improvement programs on mortality. Because we have examined the impact of change in self-efficacy on mortality, the next steps for research in this field should focus on addressing the change in clinical variables over time in conjunction with the change in self-

efficacy. This would allow one to assess how the feedback loop is associated with the cardiac outcomes.

5.8 TABLES AND FIGURES FOR PAPER 3

Table 16. Missing values and replaced means

Variable	Mean	Missing	N	Action
Education	4.50	24	2344	Replaced with mean
Current cigarette smoker	0.13	8	2360	Replaced with mean
Malignancy	0.08	3	2365	Replaced with mean
HbA1c %	7.66	6	2362	Replaced with mean
HbA1c ≥ 8%	0.35	72	2296	Replaced with mean
Probable neuropathy: screening MNSI ≥ 7	0.16	29	2339	Replaced with mean
Neuropathy: clinical MNSI > 2	0.50	26	2342	Replaced with mean
Insulin use at baseline	0.28	4	2364	Replaced with mean
Duration of Type 2 diabetes mellitus	10.44	23	2345	Replaced with mean
Angina category within 6 weeks	4.00	4	2364	Replaced with mean
History of CHF requiring treatment	0.07	20	2348	Replaced with mean
History of MI	0.32	40	2328	Replaced with mean
Hypercholesterolemia requiring treatment	0.82	32	2336	Replaced with mean
Sitting systolic blood pressure average	131.70	35	2333	Replaced with mean
Sitting systolic blood pressure > 140	0.27	35	2333	Replaced with mean
Sitting diastolic blood pressure average	74.51	36	2332	Replaced with mean
Low density lipids mg/dl	96.20	131	2237	Replaced with mean
Body mass index	31.74	28	2340	Replaced with mean

Key: Hba1c – hemoglobin A1c, MNSI – Michigan neuropathy screening instrument

Table 17. Quartiles of baseline self-efficacy

Baseline Self efficacy score (0-10), N=1817					
Category: Baseline self-efficacy scores	**N**	**Mean**	**Standard Deviation**	**Minimum**	**Maximum**
1) Poor: 1.0-6.7	449	5.15	1.23	1.00	6.67
2) Fair: 6.75-8.0	529	7.47	0.43	6.75	8.00
3) Good: 8.25-9.0	402	8.66	0.28	8.25	9.00
4) Excellent: 9.25-10.0	437	9.80	0.28	9.25	10.00

Table 18. Baseline demographics and clinical status by baseline self-efficacy scores

	Total (N=1,817)	Poor SE: Score 1 - 6.7 (N=449)	Fair - Excellent SE: Score 6.75-10 (N=1,368)	p-value
Male, %	71.6	66.4	73.3	0.005
Race/Ethnicity, %				
White nH	64.1	53.2	67.6	<.001
Black nH	18.9	20.7	18.3	
Hispanic	11.5	18.9	9.1	
Asian nH	4.8	5.8	4.5	
Other nH	0.7	1.3	0.5	
Age at study entry, mean, SD	62.6, 9.0	62.0, 8.8	62.9, 9.0	0.08
Body mass index, mean, SD	32.5, 6.1	32.8, 6.6	32.4, 5.9	0.30
United States site, %	80.6	79.5	80.9	0.51
Current cigarette smoker, %	13.1	14.3	12.7	0.41
Post high school education, %	48.4	33.2	53.4	<.001
History of malignancy, %	9.6	7.1	10.5	0.04
HbA1c %: mean, SD	7.6, 1.5	7.7, 1.6	7.5, 1.5	0.003
HbA1c ≥ 8%, %	32	36.3	30.5	0.02
MNSI clinical score, mean, SD	2.5, 1.7	2.7, 1.7	2.4, 1.7	0.005
Probable neuropathy: screening MNSI ≥ 7, %	15.9	24.7	13	<.001
Duration of T2DM, mean, SD	10.7, 8.8	11.6, 9.2	10.4, 8.7	0.01
Currently taking insulin, %	30.3	39.3	27.4	<.001
Ankle brachial index categories, %				
≤0.9 (low)	17.6	19.7	16.9	0.26
0.91-1.30	67.1	65.2	67.7	
>1.3 (high)	8.1	6.7	8.5	
Non-Compressible arteries	7.2	8.4	6.8	
Peripheral artery disease, %	25.5	29.6	24.1	0.02
Chronic renal dysfunction, %	3.7	3.8	3.7	0.91
Number of hypertension drugs, mean, SD	2.3, 1.0	2.5, 1.0	2.2, 1.0	<.001
Sitting systolic BP average, mean, SD	130.8, 18.7	132.0, 20.1	130.4, 18.3	0.14
Systolic BP > 140, %	25.5	27.6	24.8	0.25
Total cholesterol ≥ 200 mg/dl, %	24.4	26.7	23.6	0.18
Low density lipids mg/dl, mean, SD	98.6, 36.5	101.2, 40.6	97.8, 34.9	0.12
Low density lipids ≥ 100 mg/dl, %	42.1	46.3	40.7	0.04
Albumin creatinine ratio > 30 mg/g, %	33.4	38.2	31.7	0.02
History of MI, %	29.5	32.8	28.5	0.09
History of CHF with treatment, %	8	12.2	6.6	<.001
Proximal LAD ≥ 50% stenosis, %	12.4	10.5	13	0.16
Three vessel disease, %	28.6	27.7	28.9	0.62
Insulin Providing, %	50.1	51.9	49.6	0.39
Prompt Revascularization, %	49.4	48.3	49.8	0.59
CABG, %	24.3	21.4	25.3	0.09

Key: BP - blood pressure, CABG – coronary artery bypass graft, CHF – congestive heart failure, LAD – left anterior descending, MI – myocardial infarction, MNSI – Michigan neuropathy screening instrument, SD – standard deviation, T2DM – Type 2 diabetes mellitus

Table 19. Five year event rates for BARI 2D cardiovascular endpoints stratified by baseline self-efficacy score and by randomized cardiac treatment

Outcome	Cardiac Treatment	Poor (n=449)	Fair-Excellent (n=1,368)	p-value
Death	ALL	12.7%	10.0%	0.12
	MED	12.4%	10.1%	0.27
	REV	13.0%	9.9%	0.27
Death/MI/Stroke	ALL	27.3%	20.9%	0.01
	MED	30.1%	20.8%	0.01
	REV	24.3%	20.9%	0.27
Subsequent Procedure	ALL	42.7%	35.1%	0.003
	MED	52.6%	44.9%	0.02
	REV	32.1%	25.0%	0.08
Subsequent PCI	ALL	33.6%	23.6%	<.001
	MED	40.1%	28.0%	0.002
	REV	26.8%	19.1%	0.06
Subsequent CABG	ALL	12.2%	14.7%	0.58
	MED	16.5%	20.7%	0.54
	REV	7.5%	8.5%	0.86

Key: CABG – Coronary artery bypass graft, MED – medical therapy, MI – myocardial infarction, PCI – percutaneous coronary intervention, REV – prompt revascularization

Table 20. The hazard ratio of cardiovascular outcomes for self efficacy and change in self-efficacy based on Cox proportional hazard regression models

		Set 1: Adjusted for study design variables				*Set 2: Adjusted for study design variables and baseline covariates**			
		Baseline SE		Baseline SE + Change		Baseline SE		Baseline SE + Change	
Outcome	**Predictors**	**HR**	**P-Value**	**HR**	**P-Value**	**HR**	**P-Value**	**HR**	**P-Value**
Death	Poor Self-efficacy	1.26	0.11	1.47	0.01	1.04	0.79	1.24	0.22
	SE Score Decrease ≥1.5			2.13	<.001			2.32	<.001
	SE Score Increase ≥1.5			0.97	0.88			0.91	0.70
	Assigned IP treatment	0.98	0.86	0.97	0.82	1.04	0.78	1.04	0.80
	Assigned REV treatment	1.03	0.82	1.01	0.93	1.02	0.87	0.99	0.95
	Randomization stratum CABG	1.10	0.53	1.14	0.39	0.89	0.49	0.93	0.64
Death/ MI/Stroke	Poor Self-efficacy	1.34	0.01	1.43	0.02	1.22	0.10	1.42	0.01
	SE Score Decrease ≥1.5			1.17	0.30			1.79	<.001
	SE Score Increase ≥1.5			0.94	0.74			0.86	0.39
	Assigned IP treatment	1.07	0.47	1.09	0.51	1.15	0.17	1.15	0.17
	Assigned REV treatment	0.95	0.57	0.76	0.03	0.92	0.43	0.90	0.30
	Randomization stratum CABG	1.16	0.17	1.08	0.60	1.01	0.92	1.05	0.71
Sub. Procedure	Poor Self-efficacy	1.30	0.004	1.23	0.11	1.20	0.06	1.13	0.27
	SE Score Decrease ≥1.5			0.93	0.60			1.16	0.12
	SE Score Increase ≥1.5			1.03	0.84			1.29	0.05
	Assigned IP treatment	1.10	0.22	1.30	0.01	1.11	0.21	1.12	0.20
	Assigned REV treatment	0.49	<.001	0.54	<.001	0.49	<.001	0.49	<.001
	Randomization stratum CABG	0.82	0.04	0.71	0.01	0.81	0.06	0.81	0.05
Sub. PCI	Poor Self-efficacy	1.43	<.001	1.39	<.001	1.32	0.02	1.26	0.07
	SE Score Decrease ≥1.5			1.26	0.03			1.17	0.16
	SE Score Increase ≥1.5			1.21	0.18			1.22	0.18
	Assigned IP treatment	1.14	0.18	1.13	0.19	1.17	0.11	1.18	0.11
	Assigned REV treatment	0.60	<.001	0.60	<.001	0.58	<.001	0.58	<.001
	Randomization stratum CABG	0.29	<.001	0.29	<.001	0.29	<.001	0.29	<.001
Sub. CABG	Poor Self-efficacy	0.95	0.74	0.97	0.85	0.85	0.34	0.84	0.34
	SE Score Decrease ≥1.5			1.11	0.49			1.05	0.78
	SE Score Increase ≥1.5			0.99	0.95			1.06	0.78
	Assigned IP treatment	1.01	0.92	1.01	0.94	1.01	0.94	1.01	0.95
	Assigned REV treatment	0.36	<.001	0.36	<.001	0.39	<.001	0.39	<.001
	Randomization stratum CABG	2.91	<.001	2.93	<.001	2.89	<.001	2.88	<.001

Key: H.R. – hazard ratio, MED – medical therapy, REV – prompt revascularization, SE – self-efficacy, Sub. - subsequent
*Adjusted for baseline values of age, sex, race/ethnicity, insulin use, post high school education, cigarette use, HbA1c, clinical neuropathy, duration of diabetes, peripheral artery disease, micro albuminuria, history of MI, history of congestive heart failure, and proximal LAD with ≥50% stenosis.

Table 21. The odds ratio of angina for baseline self-efficacy and change in self-efficacy from mixed models

	Set 1: Adjusted for Time			*Set 2: Adjusted for Time, Treatment and Baseline Variables**		
Variable	**Estimate**	**OR**	**p-value**	**Estimate**	**OR**	**p-value**
Poor baseline self-efficacy	0.11	1.11	<.001	0.03	1.03	0.83
Follow up years 1 - 5 (per 1 yr)	-0.04	0.96	<.001	-0.10	0.91	<.001
Angina at baseline				0.07	1.07	0.58
Assigned insulin providing treatment				-0.03	0.97	0.76
Assigned prompt revascularization				-0.22	0.80	0.08
CABG				-0.01	0.99	0.97
Variable	**Estimate**	**OR**	**p-value**	**Estimate**	**OR**	**p-value**
Poor baseline self-efficacy	0.13	1.14	<.001	0.17	1.18	0.54
SE Score Decrease ≥1.5	0.07	1.07	0.001	0.001	1.00	1.00
SE Score Increase ≥1.5	-0.02	0.98	0.58	-0.24	0.79	0.33
Follow up years 2 - 5 (per 1 yr)	-0.04	0.96	<.001	-0.14	0.87	<.001
Angina at baseline				-0.21	0.81	0.19
Assigned insulin providing treatment				-0.11	0.90	0.49
Assigned prompt revascularization				-0.15	0.86	0.36
CABG				0.005	1.00	0.98

Key: OR – odds ratio, SE – self-efficacy, yr - year

*Adjusted for baseline values of angina, age, sex, race/ethnicity, insulin use, post high school education, cigarette use, HbA1c, clinical neuropathy, duration of diabetes, peripheral artery disease, micro albuminuria, history of MI, history of congestive heart failure, and proximal LAD with ≥50% stenosis.

No interaction p-values for self-efficacy and cardiac treatment were significant (p's >0.40), therefore association between self-efficacy and angina did not differ by treatment.

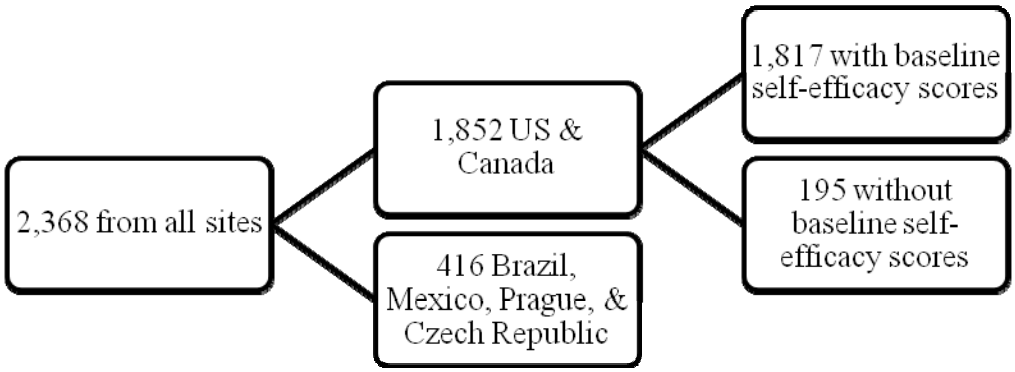


Figure 19. Population flowchart for Aim 3

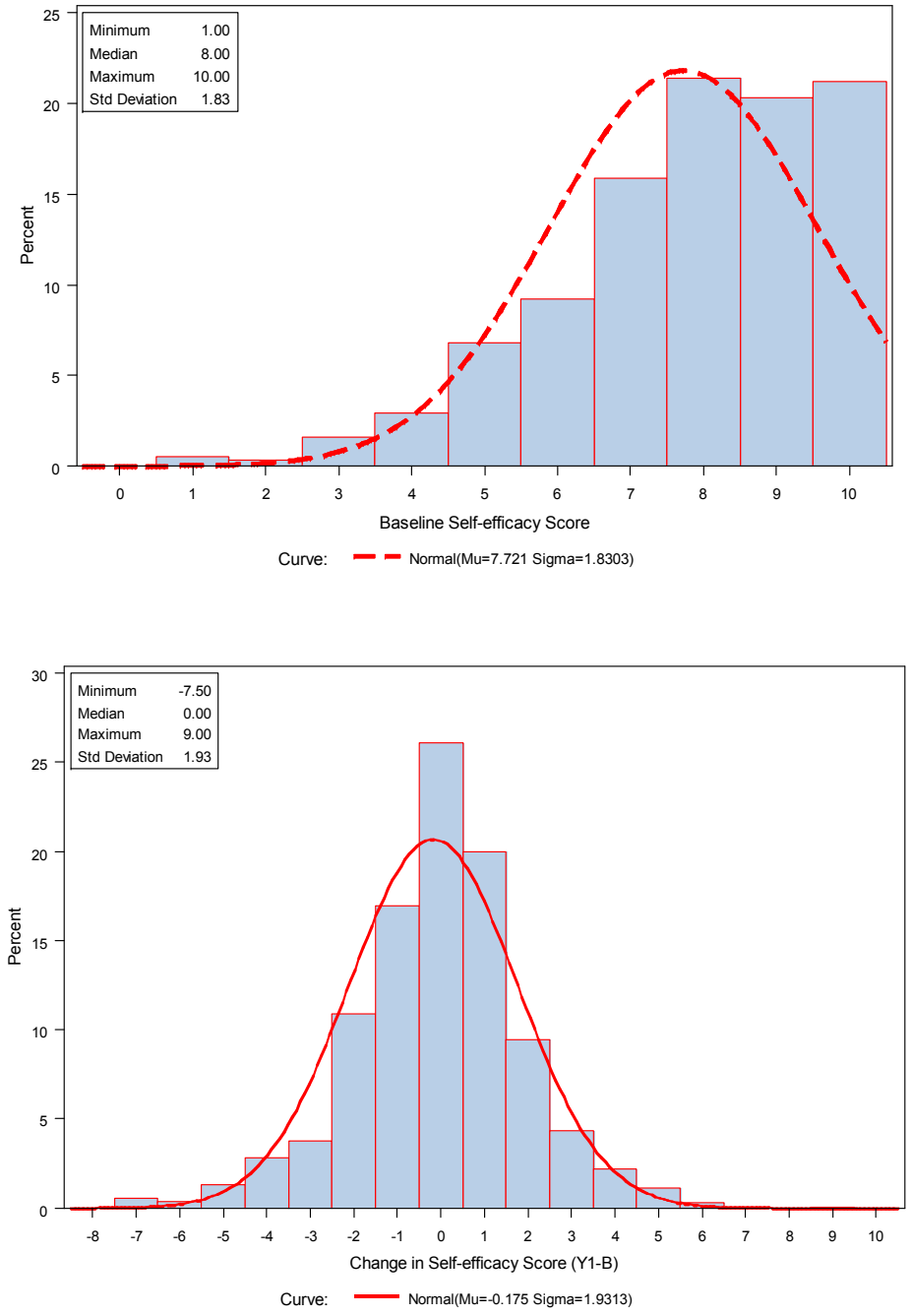
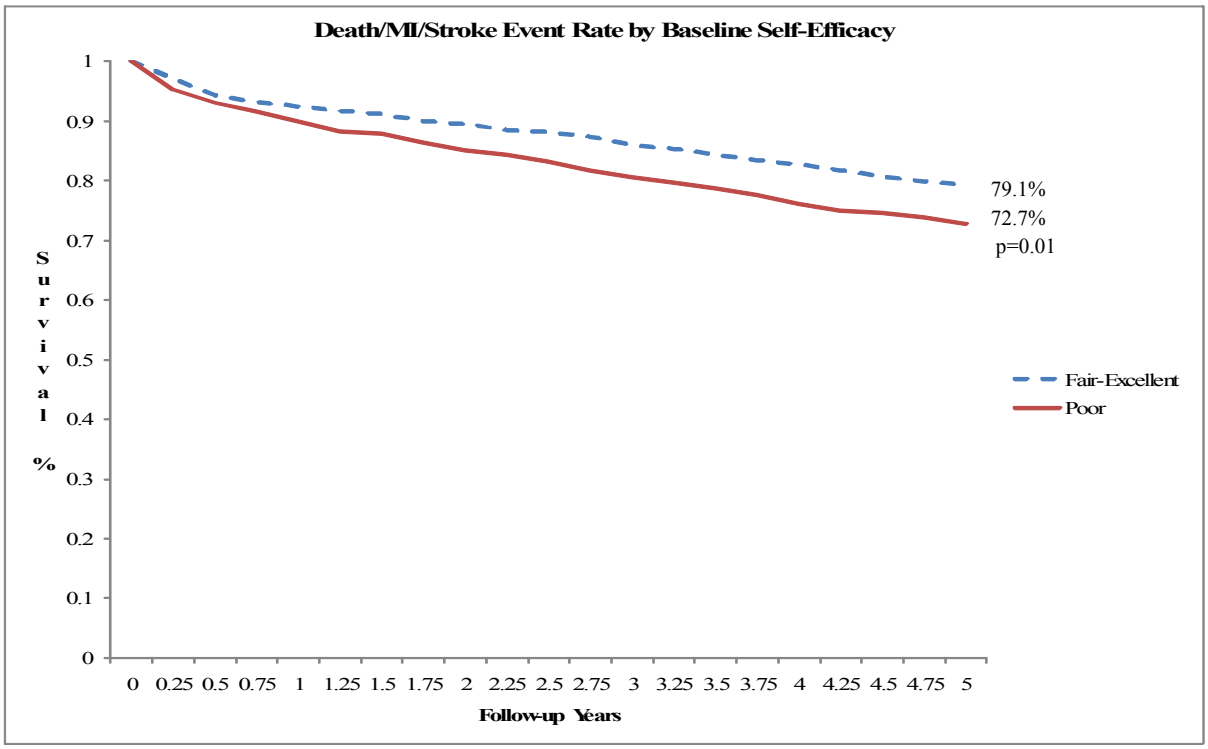
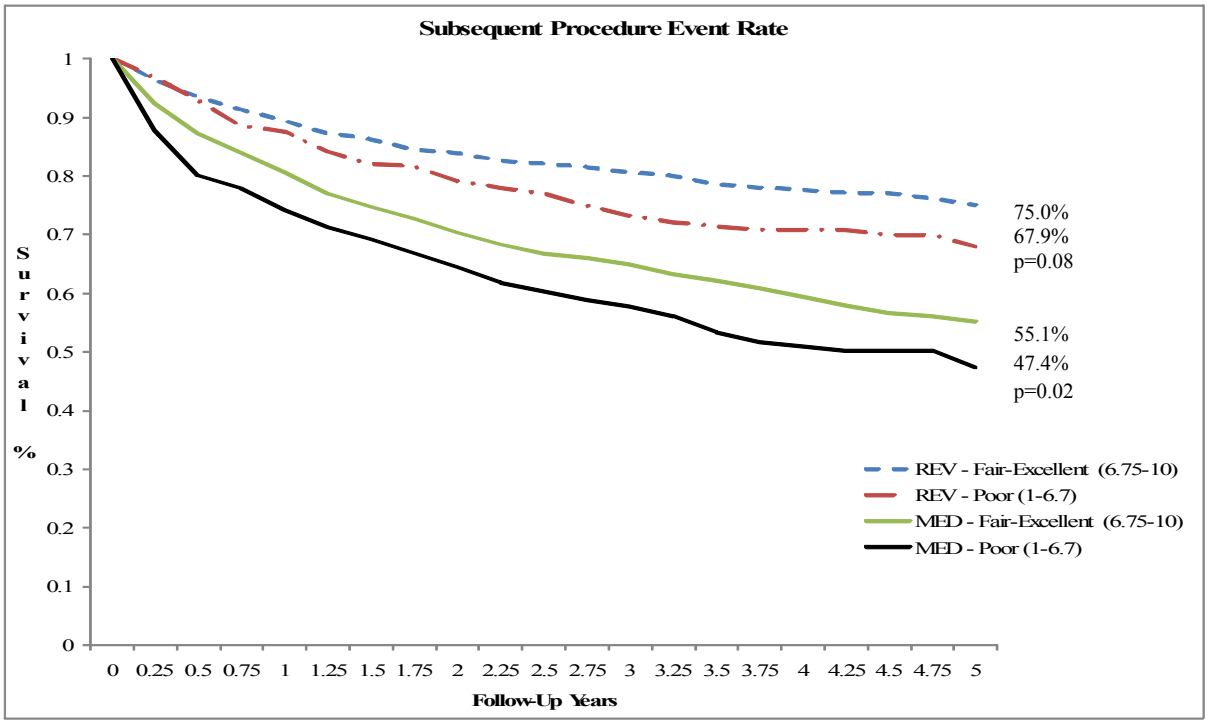


Figure 20. The distribution of the baseline self-efficacy score and change in self-efficacy score from baseline to Year 1





Key: MED – medical therapy, REV – immediate revascularization

Figure 21. Survival and freedom from event distribution by self-efficacy scores and cardiac therapy

6.0 CONCLUSION

The primary goal of these analyses was to determine the relationship between self-efficacy and clinical risk factors, treatment, and outcomes of patients with comorbid CAD and T2DM. The first paper indicated that in patients with self-efficacy scores ≤8, randomized treatment for CAD and T2DM and the type of assigned revascularization procedure did not affect the patients' confidence in managing their conditions throughout the BARI 2D trial. These patients, however, did benefit from their participation in BARI 2D, as reflected by an increase in self-efficacy over time. Senuzun et al. (2006) demonstrated that self-efficacy enhancing programs do in fact increase self-efficacy and improve clinical risk factors in patients. BARI 2D, with its coordinated clinical care, lifestyle risk factor program, and empowering clinical staff, may have simultaneously improved the patients confidence in being able to manage their medical conditions.

In the second paper, the associations between the clinical risk factors of HbA1c, lipids, blood pressure, physical functioning, and BMI and self-efficacy were examined. Over the course of the study, better self-efficacy was related to improved glycemic control and physical functioning. In line with Bandura's theory of self-efficacy, a feedback loop was shown in which risk factors were associated with future self-efficacy, which in turn was associated with future risk factors (A. Bandura, 1977). Compared to the racial/ethnic minorities, the feedback loop was

strongly observed in White nH patients. Black nH patients were more likely than White nH and Hispanic patients to have lower self-efficacy as HbA1c control improved, indicating a form of health pessimism in Black nH patients. The discrepancy in the patterns in the Black nH patients is mirrored in the study by Martin et al. (2004) that showed that high self-efficacy was not associated with weight loss in Black women. Despite high self-efficacy, these participants' mean weight did not increase or decrease. It is not noted in our study, nor in the study by Martin et al. (2004), if self-efficacy was associated with the patients' perceived stage of change (A. Bandura, 1997). Patients with higher self-efficacy may have believed they have the confidence to manage their condition, but may not have been in the stage of change that prompts them to initiate these behaviors. Future research regarding self-efficacy should also measure the patient's stage of change.

The third set of analyses examined the association between self-efficacy and cardiac outcomes. Poor baseline self-efficacy (≤6.7) was associated with an increased risk of death/MI/stroke, subsequent revascularization procedures, and subsequent PCIs, but was not associated with death, subsequent CABGs, and angina. The association between self-efficacy and death/MI/stroke remained significant after adjustment for baseline confounders, while the other two associations became non-significant. A decrease in self-efficacy from baseline to Year 1 was associated with the primary and secondary outcomes of death and death/MI/stroke. This stresses the importance of developing initiatives to boost patients' confidence in their disease management through diabetes and CAD management programs that emphasize positive feedback and social support.

Our analyses demonstrated strong results because our patients were part of a large-scale, prospective, randomized clinical trial. Previous research by Sarkar et al. laid the groundwork for

research in this area through the use of patients enrolled in the Heart and Soul observational study (Sarkar, et al., 2007; Sarkar, et al., 2009; Sarkar, et al., 2006). The research from the Heart and Soul study showed significant associations between self-efficacy in cardiac control, symptoms, and outcomes. However, it was limited by non-randomized cardiac treatment. The BARI 2D study had the advantage of randomizing the treatment received in a large, diverse patient population, and following these patients over a mean period of 5.3 years. Despite differences in the study design, both studies showed the influence of self-efficacy on cardiac risk factors and outcomes. The culmination of results from both studies is generalizable to patients eligible for elective surgery and to those eligible for non-elective surgery.

6.1 PUBLIC HEALTH IMPACT

Despite treatment differences for T2DM and CAD in BARI 2D, self-efficacy was associated with clinical risk factors and cardiac outcomes in patients with CAD and T2DM. These results have multiple public health implications within the financial system, health care system, and on an individual level.

Changes in health care reform have an increased focus on preventative health care and provision of health care, regardless of pre-existing conditions (U.S._Department_of_Health_&_Human_Services, 2010). In 2009, the direct (medical expenses) and indirect (lost productivity, disability) costs of CAD and stroke in the US totaled approximately $475.3 billion (NHLBI, 2009). The total costs for diabetes in 2007 were $174 billion (ADA, 2009). The prevention, progression, and course of T2DM and CAD are partially

modifiable through self-management. The health care system should address the issue of increasing a patient's confidence, which in turn can decrease cardiac morbidity and mortality, and possibly decrease the financial impact of these leading diseases in the US.

From the perspective of health care professionals, our research shows that assessing a person's confidence in managing their conditions not only serves as a strong predictor of clinical risk factors, but is indicative of a person's clinical history. From the patients' perspective, it stresses the importance of improving and maintaining self-confidence in the face of comorbid conditions to improve health and prevent serious complications. The source of confidence maintenance can be internal or sought from external sources such as caregivers, loved ones, and learning from success stories through others with the same conditions. This is especially important for minorities, who are faced with multiple health disparities in diagnoses, treatment, and outcomes, and report lower self-efficacy as compared to Whites. For some patients, T2DM and CAD are seen as conditions they can conquer, and these patients make efforts to do so. For other patients, these diseases are seen in a fatalist manner, in which futile efforts do not alleviate the advancement of death.

In conclusion, future research in this area should focus on the impact of public health initiatives to increase a patient's confidence in managing and conquering their diseases and the financial impact of these initiatives on society. In those with a history of poor clinical control, these initiatives must focus on shifting the patients' sense of learned helplessness into one of empowerment.

APPENDIX A: SELF EFFICACY ASSESSMENT*

SECTION E: QUALITY OF LIFE

4. We would like to know how confident you are in doing certain activities. For each of the following questions, please circle the number that corresponds to your confidence that you can do these things regularly at the present time.

4.1 Having diabetes and heart disease often means doing different tasks and activities to manage your condition. How confident are you that you can do all the things necessary to manage your condition on a regular basis?

Not at all Totally
Confident 1 2 3 4 5 6 7 8 9 10 Confident

How confident are you that you can…

4.2 Do the different tasks and activities needed to manage your diabetes and heart disease so as to reduce your need to see a doctor?

Not at all Totally
Confident 1 2 3 4 5 6 7 8 9 10 Confident

4.3 Reduce the emotional distress caused by your diabetes and heart disease so that it does not affect your everyday life?

Not at all Totally
Confident 1 2 3 4 5 6 7 8 9 10 Confident

4.4 Do things other than just taking medication to reduce how much your diabetes and heart disease affect your everyday life?

Not at all Totally
Confident 1 2 3 4 5 6 7 8 9 10 Confident

** Reprinted from BARI 2D Data Forms Manual (BARI_2D_Coordinating_Center, 2002).*

APPENDIX B: REASONS FOR LOST-TO-FOLLOW UP IN PAPER 1

Type of event ***N*** ***%***	**Follow-up period** **Year 1 (N=889)**	**Year 2 (N=873)**	**Year 3 (N=827)**	**Year 4 (N=711)**
Inactivation: Rescission of consent	4	3	1	2
	40	30	10	20
Inactivation: Complete	3	3	0	1
	42.86	42.86	0	14.29
Inactivation: AFD	8	4	1	0
	61.54	30.77	7.69	0
Reactivation	0	0	0	2
	0	0	0	100
Vital status - alive	15	12	86	667
	1.92	1.54	11.03	85.51
Vital status - unknown	7	3	2	5
	41.18	17.65	11.76	29.41
Close out	4	4	73	606
	0.58	0.58	10.63	88.21
Death	16	15	22	39
	17.39	16.3	23.91	42.39
Total*	57	44	185	1322

*Events are not mutually exclusive.

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