THE DEVELOPMENT AND IMPLEMENTATION OF SECONDARY PREVENTION MEASURES FOR CORONARY ARTERY DISEASE

BY

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## List of Abbreviations

- **ACCF**: American College of Cardiology Foundation
- **ACE**: angiotensin-converting-enzyme
- **ACE-I/ARB**: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers
- **ACORN**: Ambulatory Care Outcomes Research Network
- **ACS**: acute coronary syndromes
- **AHA**: American Heart Association
- **AHEAD**: Action for Health in Diabetes
- **ARI**: acute renal insufficiency
- **BMI**: body mass index
- **CABG**: coronary artery bypass graft
- **CAD**: coronary artery disease
- **CHF**: congestive heart failure
- **CMS**: Centers for Medicare & Medicaid Services
- **COAP**: Clinical Outcomes Assessment Program
- **COPD**: chronic obstructive lung disease
- **CRI**: chronic renal insufficiency
- **CRUSADE**: Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines
- **CVA**: cerebrovascular accident
- **CVD**: cardiovascular disease
- **CAD**: coronary heart disease
- **DASH**: Dietary Approaches to Stop Hypertension
- **HOPE**: Heart Outcomes Prevention Evaluation
- **LDL**: low density lipoprotein
LVEF- left ventricular ejection fraction
MI- myocardial infarction
NIH- National Institutes of Health
PCI- percutaneous coronary intervention
PVD- peripheral vascular disease
RAAS- renin-angiotensin-aldosterone system
RCT- randomized controlled trial
SHEP- Systolic Hypertension in the Elderly Program
STEMI- ST-segment elevation myocardial infarction
STS- Society of Thoracic Surgeons
TNT- Treating to New Targets
Abstract

Heart disease, and in particular coronary artery disease (CAD), has long been one of the leading causes of death in the US. In order to reduce the morbidity and mortality from CAD, secondary prevention practice guidelines have been developed by the major cardiovascular societies in the US and abroad to provide a benchmark for the care of patients with CAD. Previous studies have shown that patients undergoing coronary artery bypass graft (CABG) surgery after an acute myocardial infarction are less likely to receive these secondary prevention measures at hospital discharge relative to similar patients undergoing percutaneous coronary interventions (PCI). Although adherence to guidelines-based therapy has been imperfect for both procedures, secondary prevention adherence rates at discharge have been improving over time, particularly as public reporting of hospital performance has been implemented. This thesis will focus on the development of these guidelines, trends in adherence to these recommendations in Washington State, and the challenges of using these endpoints as markers of the quality of health care delivery.
Chapter 1: The Development of Secondary Prevention Guidelines for Coronary Artery Disease in the United States

I. Current Epidemiologic Trends of Cardiovascular Disease in the United States

Cardiovascular disease (CVD) is a broadly defined classification of pathologic conditions that include: hypertension, coronary artery disease (CAD), myocardial infarction (MI or “heart attack”), angina pectoris, cerebrovascular accident (CVA or “stroke”), congestive heart failure (CHF), peripheral vascular disease (PVD), and sudden cardiac death. An estimated 82,600,000 American adults (> 1:3) have one or more types of cardiovascular disease and, of this group, 40,400,000 are estimated to be ≥60 years of age. The average annual incidence of cardiovascular events rises from 3 per 1,000 men at 35 to 44 years old to 74 per 1,000 men at 85 to 94 years of age. These rates are similar for women, delayed by about 10 years. Thus, before the age of 75, a higher proportion of men will experience one or more forms of cardiovascular disease than women, though this gender gap narrows with advancing age.¹

Every year since 1900 (except for 1918 during the influenza epidemic), CVD has accounted for more deaths than any other disease in the United States. In the most recent national vital statistics report from 2008, CVD was listed as the primary cause for 32.8% (811,940) of all 2,471,984 deaths, close to 1 out of every 3. On average, this translates to >2,200 Americans dying from CVD each day, an average of 1 death every 39 seconds.² According to a recent report from the National Center for Health Services, the chance of CVD being listed as the major cause of a person’s death in the US is 47%; other reported attributable causes of death were 22% for cancer, 3% for accidents, and 2% for DM (not CVD-related). This report also states that if all forms of CVD were
eliminated, life expectancy in the US would rise by almost 7 years while if all major forms of cancer were eliminated, the estimated gain would be ~3 years.³

CAD contributes to more than half of all CVD events in men and women <75 years of age.¹ CAD is generally used to refer to the pathologic process affecting the coronary arteries (usually atherosclerosis) and is sometimes used synonymously with coronary heart disease (CHD). CAD includes the diagnoses of angina pectoris, MI, silent myocardial ischemia, and CAD-related mortality. Data from NHANES from 2005-2008 showed that the total CAD prevalence is 7.0% in US adults ≥20 years of age, 8.3% for men and 6.1% for women.⁴ Data from the Framingham Heart Study reported that the lifetime risk of developing CAD after 40 years of age is 49% for men and 32% for women.⁵ Below 65 years of age, the annual incidence of CAD in men (12 per 1,000) more than equals the rate of all the other CVD diagnoses combined (7 per 1,000); in women, it is roughly equivalent to the rate of other CVD diagnoses (5 per 1,000).⁶ Projections show that by 2030 an additional 8 million people in the US are likely to be diagnosed with CAD, a 16.6% increase in prevalence from 2010.⁷

In 2004, CAD was estimated to be responsible for 1.2 million hospital stays in the US and was the most expensive condition treated in the hospital, resulting in over 44 billion dollars in expenses.⁸ CAD caused approximately 1 out of every 6 deaths in the US in 2008 with a crude death rate of 122.7. In 2008, CAD accounted for 49.9% of all deaths attributable to CVD.¹ However, one study reported that from 1998 to 2008, the annual death rate due to CAD declined 28.7%.¹ Another reported that from 1980 to 2000 in the US, the age-adjusted death rate for CAD fell from 542.9 to 266.8 deaths per 100,000 among men and from 263.3 to 134.4 deaths per 100,000 among women, resulting
in 341,745 fewer deaths from CAD in 2000. This study attributed approximately 47% of the decrease in CAD-related deaths to increased use of evidence-based medical therapies (including CAD secondary preventive therapies, initial treatments for acute MI, treatments for CHF, and revascularization for chronic angina) and 44% to changes in risk factors in the population attributable to lifestyle and environmental changes, with the largest reductions in CAD death credited to the increased use of secondary prevention measures.  

II. The Development of Prevention Measures for Coronary Artery Disease

Prevention activities are divided into four levels: primordial, primary, secondary, and tertiary. The main distinction between the four is the stage of disease at which they are implemented. Primordial prevention consists of actions to minimize future hazards to health and hence inhibit the establishment factors (environmental, economic, social, behavioural, cultural) known to increase the risk of disease. Primary prevention is the maintenance of health through individual or community efforts so that the pathology of disease never starts. These efforts occur before the onset of disease with the goal of reducing the incidence of disease. Secondary prevention focuses on the reduction in the expression and severity of clinical disease. These efforts are aimed at delaying the onset and duration of clinical disease after pathological onset. Secondary prevention efforts do not prevent disease occurrence, but identify asymptomatic individuals with pathologic disease prior to the onset of clinical symptoms. For some diseases, secondary prevention reduces disease prevalence by delaying the onset of clinical disease and disease duration (e.g. AIDS when HIV is diagnosed and managed at an earlier stage, preventing it from progressing to AIDS). For other diseases, secondary prevention efforts will lead to an
increase in the incidence and prevalence as asymptomatic individuals are identified at an earlier stage (e.g. breast cancer). The overarching goal of secondary prevention is to improve survival from the disease. Tertiary prevention is aimed at slowing or blocking the progression of a disease once symptoms have occurred in order to reduce impairments and disabilities, improve quality of life, and improve survival among diseased individuals. The goal of tertiary prevention is to improve survival and reduce disease sequelae in patients whom the disease has already manifested symptoms or syndromes. It is common practice to combine secondary and tertiary prevention efforts into one group called “secondary prevention” measures, which broadly refers to efforts made to reduce morbidity and mortality after disease diagnosis and/or manifestation. An example of this would be efforts to reduce further morbidity and CAD events after a MI- these are commonly known as CAD secondary prevention measures.

Given that CAD is the most common cause of mortality from CVD and the most common cause of death in the US, substantial efforts have been made to offer guidance to clinicians in CAD prevention. The most comprehensive and widely disseminated of these guidelines in the US are published by the American Heart Association (AHA) in joint cooperation with the American College of Cardiology Foundation (ACCF). The AHA/ACCF started releasing guidelines on the secondary prevention of CAD in 1995, along with three updates since then, the most recent released in 2011.

The goals of these guidelines are to improve outcomes in patients with CAD and reduce the economic burden of CAD. The initial set of secondary prevention guidelines released by the AHA/ACCF in 1995 are introduced with the statement that comprehensive risk factor interventions for CAD can: “extend overall survival, improve
quality of life, decrease the need for interventional coronary procedures (PCI and CABG surgery), and reduce the incidence of recurrent MI'. The introduction to these guidelines also notes that, while the studies and trials behind the recommendations provide evidence of significant improvements in clinical outcomes with these interventions, their application was inconsistent across medical care settings and patient groups, which is still the case today. Further, the guidelines now strongly support the concept that these medical therapies should be started in the hospital, prior to discharge. These recommendations are based on compelling data indicating that in-hospital initiation of medical therapy (as opposed to starting them on a follow-up clinic visit post-discharge) can improve patient compliance and outcomes.

As new evidence from clinical trials and other studies emerged, these guidelines are periodically updated to reflect changes in consensus statements about secondary CAD prevention. There has been increasingly compelling evidence that aggressive risk factor management clearly improves survival and reduces morbidity for patients with CAD. The guidelines released in 2011 are the most comprehensive to date and offer recommendations ranging from lifestyle modifications to pharmacologic therapy.

These guidelines offer 4 classifications of recommendations (I, IIa, IIb, and III) based on the size of treatment effect and 3 Levels of estimates of certainty of treatment effect (A, B, and C) based on available scientific evidence (Table I). Class I indicated therapies have a large treatment effect size and are the most highly recommended interventions. Class II recommendations are broken into class IIa and IIb. Benefit definitely outweighs risk for IIa interventions, though additional studies would be needed to show a larger treatment effect in order to change the recommendation to a Class I.
Class IIb treatments probably have benefit that outweighs the risk, but additional studies with much broader scopes regarding these therapies are needed in order to raise their current level of recommendation. Class III therapies have either been shown no benefit or harm to subjects and are not endorsed by the AHA/ACCF.

**Table I**: AHA/ACCF Classifications of Recommendations and Levels of Evidence

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<td><strong>Class I</strong>: Benefit &gt;&gt;&gt; Risk. Intervention should be performed/administered</td>
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<tr>
<td><strong>Class IIa</strong>: Benefit &gt;&gt; Risk. It is reasonable that intervention is performed/administered</td>
</tr>
<tr>
<td><strong>Class IIb</strong>: Benefit probably &gt; Risk. Usefulness/efficacy less well-established by evidence/opinion</td>
</tr>
<tr>
<td><strong>Class III</strong>: No benefit or harm to patients from intervention</td>
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<tr>
<td><strong>Level A</strong>: Sufficient evidence from multiple randomized clinical trials or meta analyses</td>
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<tr>
<td><strong>Level B</strong>: Limited evidence from nonrandomized studies or a single randomized trial</td>
</tr>
<tr>
<td><strong>Level C</strong>: Very limited evidence based on consensus opinion of experts</td>
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Treatments with Level of Evidence A have high estimates of certainty of their treatment effect. Usually this means multiple populations have been evaluated in multiple randomized controlled trials (RCT) and/or meta-analyses have been performed comparing this intervention across groups. The precision of treatment effect is less so with Level B therapies, usually due to the limited populations that have been studied or lack of validation of a single small randomized studies or several observational studies.
Level C therapies have the least evidence for use and usually represent the consensus opinion of experts. However, it is important to note that recommendations with Level of Evidence B or C does not imply that the recommendation is weak or based on poor data since some of the interventions addressed cannot be addressed well by clinical trials.

The classifications of the size of treatment effect and levels of estimates of treatment effect are then combined into specific recommendations for individual therapies. For example, a therapy can have a Class I, Level A recommendation, which means that there is sufficient evidence from multiple trials and/or studies that have proven the intervention to be effective. Another example might be an intervention that has a Class Iib, Level B recommendation, which means that the evidence for the intervention’s efficacy is less well established and that there might be conflicting evidence from a single trial or multiple observational studies.

Given the lack of underlying data or uncertainty of Class II recommendations, many clinicians focus on Class I recommendations in the daily care of patients. The following sections will focus on the most recent Class I (Level of Evidence A, B, and C) recommendations issued by the AHA/ACCF in 2011 for the secondary prevention of coronary and other atherosclerotic vascular disease and the evidence behind these guidelines.  

III. AHA/ACCF Class I Recommended Interventions for Secondary Prevention of Coronary Heart Disease

Smoking

Cigarette smoking and exposure to tobacco smoke are associated with premature death from chronic diseases, economic losses to society, and a substantial burden on the
United States health-care system. During 2000-2004, the CDC estimated that smoking resulted in an estimated annual average of 269,655 deaths among males and 173,940 deaths among females in the United States. The three leading specific causes of smoking-attributable death were lung cancer (128,922), ischemic heart disease (126,005), and chronic obstructive pulmonary disease (COPD). A longitudinal study that looked at morbidity and mortality rates among smokers who quit versus those that kept smoking noted that overall morality was 8.83 per 1000 person-years in sustained quitters versus 10.38 per 1000 person-years in continuing smokers (p 0.03). This included a 2.75 increased likelihood of death due to CVD in continued smokers versus quitters during the mean 14.5 year follow-up period. Several studies have looked at environmental tobacco exposure’s positive relationship with CVD risk as well and were included in a 2006 report from the Surgeon General and report from the Institute of Medicine that called for stricter control on public second-hand tobacco smoke exposure and formed the platform for banning public smoking in several states.

The goal of smoking interventions in patients with CAD is complete cessation of use and exposure to environmental tobacco smoke (Table II). A Cochrane analysis of pooled data from 17 randomized trials that compared brief advice to no advice or usual care showed a significant increase in the odds of smoking cessation (odds ratio [OR]=1.74; 95% confidence interval [CI], 1.48-2.05). While tobacco dependence is a chronic disease that often requires repeated interventions and multiple attempts to quit, many studies offer encouraging data on the efficacy of various cessation methods. A cluster-randomized, controlled trial conducted in the Virginia Ambulatory Care Outcomes Research Network (ACORN) found that including current tobacco use with
routine vital signs (heart rate, blood pressure, etc) increased tobacco counseling at primary care practices. This type of strategy is intended to ensure that tobacco use is systematically assessed and treated at every clinical encounter. These guidelines also recommend pharmacologic smoking cessation strategies (both nicotine- and non-nicotine-based) in detail as the combination of counseling and pharmacologic intervention has been found to be more effective than either alone.22

Table II: AHA/ACCF Class I Recommendations for Smoking in Secondary CAD Prevention

<table>
<thead>
<tr>
<th>• Ask about tobacco use at each clinic visit <em>(Level of Evidence B)</em></th>
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<tr>
<td>• Tobacco users should be advised to quit at every clinic visit <em>(Level of Evidence A)</em></td>
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<tr>
<td>• Tobacco users’ willingness to quit should be assessed at every visit <em>(Level of Evidence C)</em></td>
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<tr>
<td>• Tobacco users should be counseled and have a plan for quitting developed that includes pharmacotherapy and/or referral to a smoking cessation program <em>(Level of Evidence A)</em></td>
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<tr>
<td>• Follow-up should be arranged to assess cessation efforts <em>(Level of Evidence C)</em></td>
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<tr>
<td>• Patients should be advised to avoid all environmental tobacco exposure at every clinic visit <em>(Level of Evidence B)</em></td>
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Blood Pressure Control

The ACCF/AHA guidelines regarding blood pressure control are congruent with the Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).23 JNC 7 defines optimal blood pressure for all patients (regardless of CAD status) as <120/80 mm Hg. Prehypertension is defined as 120-139/80-89 mm Hg. Elevated blood pressure, or hypertension, is therefore defined as
≥ 140/90 mm Hg. For patients with CAD, the ACC/AHA guidelines have the same goal blood pressure of < 140/90 mm Hg as in JNC 7 (Table III). While the JNC 7 guidelines place a lower goal of ≤130/80 for patients with diabetes and chronic kidney disease, the ACC/AHA guidelines do not address these patient groups specifically.

Table III: AHA/ACCF Class I Recommendations for Blood Pressure Control

- All patients with CAD should be counseled on lifestyle modifications, including: weight control, exercise, dietary sodium restriction, alcohol moderation, and dietary fresh fruit, vegetables, and low-fat dairy products (Level of Evidence B)
- Patients with Blood pressure ≥ 140/90 mm Hg should be treated with pharmacotherapy, initially with β-blockers and/or ACE inhibitors, in addition to other agents as needed to achieve goal blood pressure (Level of Evidence A)

Regardless of whether a CAD patient has been diagnosed with hypertension, all patients with CAD should be counseled on lifestyle modifications that will favorably affect blood pressure control, which include: weight control, exercise, dietary sodium restriction, moderation of alcohol intake, and an increase in dietary fruits, vegetables, and low-fat dairy products. Many of the dietary recommendations came from studies from the Dietary Approaches to Stop Hypertension (DASH) research group. These studies showed that a diet rich in fruits, vegetables, and low-fat dairy foods and with reduced saturated and total fat can substantially lowered blood pressure and offered an additional approach to preventing and treating hypertension outside of a strictly pharmacologic approach. In the general population, this diet was found to reduce systolic blood pressure by an additional 5.5 mm Hg and diastolic blood pressure by 3.0 mm Hg compared to a
In subjects with hypertension, there were more substantial decreases of 11.4 and 5.5 mm Hg, respectively, compared to the control diet (p<0.01). This same group also showed that this diet, combined with a low sodium (< 50 mmol/day) intake, led to a mean decrease in systolic blood pressure of 7.1 mm Hg in participants without hypertension, and a decrease of 11.5 mm Hg in participants with hypertension. A meta-analysis of studies that evaluated the effect of aerobic exercise on blood pressure found that, while the regimens analyzed varied widely, the overall effect was a significant reduction in both mean systolic (3.84 mm Hg, 95% CI, 2.72 to 4.97 mm Hg) and diastolic blood pressures (2.58 mm Hg 95% CI 1.81 to 3.35 mm Hg).

For patients with CAD and hypertension, the initial pharmacologic agents recommended for treatment include β-blockers and angiotensin-converting-enzyme inhibitor (ACE inhibitors). The Systolic Hypertension in the Elderly Program (SHEP) found a relative risk (RR) of 0.67 (95% CI 0.56-0.80) for the secondary combined endpoint of CVA, non-fatal MI, and CAD-related death in patients on antihypertensive treatment over a mean 4.5 year follow-up period compared to untreated patients with hypertension. The Heart Outcomes Prevention Evaluation (HOPE) study investigators published a RCT comparing ramipril (an ACE inhibitor) and placebo in patients with CAD or CAD risk-equivalents (cerebrovascular disease, peripheral artery disease, DM or 20-year Framingham risk of ≥20%). During a mean follow-up of 5 years, the Ramipril group had a RR of 0.78 (95% CI 0.70-0.86) for the combined primary endpoint of acute MI, CVA, or CVD-related death. Additional evidence for the use of ACE inhibitors as the preferred first line agents for blood pressure control in patients with CAD came from
the LIFE study, which showed significant reductions in morbidity and mortality in the treatment of hypertensive patients with CVD with Losartan compared to placebo.²⁹

Most of the data for the use of β-blockers as first line agents to treat hypertension in patients with known CAD is extrapolated from trials evaluating their efficacy in reducing morbidity and mortality post-MI.³⁰-³² However, few studies have specifically compared the use of different anti-hypertensive agents in this subgroup. The REACH study was a prospective international database comparing outcomes in patients with known CAD and prior MI, known CAD without prior MI, and those with CAD risk factors. While they did not target subjects with hypertension, the majority (>70% in all groups studied) had a history of hypertension. They specifically compared the use of β-blockers in these three groups and found no significant difference in long-term outcomes between the groups taking and not taking a β-blocker with a trend towards worse outcomes after 3 years of therapy in those with only CAD risk factors.³³ Therefore, while β-blockers appear to have a beneficial effect in the short-term treatment of patients post-MI, it is unclear what their role is long-term in the treatment of hypertension in patients with CAD, despite their inclusion in the secondary prevention guidelines.

Lipid Management

The ACCF/AHA class I guideline recommendations for lipid management (Table IV) defer for the most part to the parameters released by the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). The overall goal of cholesterol treatment in patients with known CAD is to reduce their levels of low density lipoprotein (LDL) cholesterol levels by initiating dietary changes and therapy with a statin, a medication that inhibits the
enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Patients with known CAD should all be started on an agent from this class of medications, regardless of initial LDL cholesterol level, with a goal LDL level of <100 mg/dL. A secondary goal in patients with triglyceride levels of $\geq 200$ mg/dL should be a non-HDL cholesterol (non-HDL cholesterol = LDL cholesterol + [triglyceride level/5]) goal of <130 mg/dL for secondary CVD prevention.

The DELTA study looked at the effects of reducing dietary saturated fatty acids on plasma lipids and lipoproteins and found that stepwise reductions in saturated fatty acid intake resulted in parallel reductions in plasma total and LDL cholesterol levels and risk for CAD.\textsuperscript{34} Studies on diets recommended by the National Cholesterol Education Program (NCEP), which are low in total calories, fatty acids, and total cholesterol, found that these diets could result in significant decreases in fasting LDL cholesterol levels as well.\textsuperscript{35, 36}

Most of the trials that evaluated statin use in patients with either acute coronary syndromes (ACS, usually related to CAD) or with known CAD utilized higher doses of the more potent statins (e.g. atorvastatin 80mg daily). However, the positive outcomes seen from these studies are thought to be a class effect, with the goal of increasing statin therapy to the most potent regimen that results in LDL and non-HDL levels as close to goal as possible without causing untoward side effects (most often myalgias). The PROVE IT-TIMI 22 trial illustrated that maintaining low levels of LDL cholesterol is central to preventing additional atherosclerotic development and subsequent cardiovascular events in patients with ACS at 30-day follow-up.\textsuperscript{37}
**Table IV**: AHA/ACCF Class I Recommendations for Lipid Management

- A lipid panel should be obtained for all patients *(Level of Evidence B)*
- Lifestyle modifications, as previously mentioned, are recommended *(Level of Evidence B)*
- Intake of saturated fats should be reduced to <7% of total calories, *trans* fatty acids to <1% of all calories, and cholesterol to <200 mg/day *(Level of Evidence B)*
- Statin therapy should be prescribed for all patients with CVD in the absence of contraindications or adverse side effects *(Level of Evidence A)*
- The dose of statin should be titrated to achieve LDL cholesterol level <100 mg/dL and at least a 30% lowering of baseline LDL level *(Level of Evidence C)*
- Patients with triglyceride levels ≥ 200 mg/dL should be treated with statins to lower non-HDL cholesterol to <130 mg/dL *(Level of Evidence B)*
- Patients with triglycerides >500 mg/dL should be started on fibrate therapy in addition to a statin to prevent pancreatitis *(Level of Evidence C)*

The Treating to New Targets (TNT) group showed that high dose statin therapy (atorvastatin 80mg daily) resulted in lower LDL cholesterol levels and significant decreases in major adverse cardiovascular events (defined as death from CAD, nonfatal non-procedure-related MI, resuscitation after cardiac arrest, or fatal or nonfatal CVA) in patients with stable CAD over a 5 year period. The IDEAL trial evaluated the use of high dose atorvastatin (80mg daily) versus low dose simvastatin (20mg daily) among
patients with prior MI over a 5 year period and did not find a significant reduction in the primary outcome of cardiovascular or all-cause mortality, but did reduce the risk of nonfatal acute MI in the high-dose atorvastatin group.\textsuperscript{39} A study released by the Heart Protection Study Collaborative Group reported that adding simvastatin to existing optimal treatment regimens safely produced a 22.3\% relative risk reduction compared to placebo in the rates of rates of MI, CVA, and revascularization for patients with CAD, regardless of initial cholesterol concentrations.\textsuperscript{40} A meta-analysis published in 2010 by Baigent, et al. evaluated data from 26 RCTs evaluating statin therapy and found that reductions in LDL cholesterol produced significant reductions in the incidence of MI, coronary revascularization, and ischemic stroke, with no evidence of a threshold effect within the cholesterol range studied, arguing for increasingly intensive lowering of LDL for CVD prevention.\textsuperscript{41} This meta-analysis, along with data from the PROVE IT trial, have altered practice patterns to aim for target LDL cholesterol levels of ≤70 mg/dL for patients with CAD and CAD-equivalents, which was reflected as an optional goal in an update to the ATP III guidelines released in 2004 and is likely to be reflected as a major treatment goal in the upcoming Adult Treatment Panel IV guidelines.\textsuperscript{37}

**Physical Activity**

The ideal physical activity regimen consists of at least 30 minutes of moderate-intensity activity, such as brisk walking, 7 days per week, with a minimum of 5 days per week. These sessions should be supplemented by a concurrent increase in the activities of daily living, such as walking breaks at work and household work, to improve cardiorespiratory fitness (**Table V**). These references are in line with the 2007 guideline recommendations from the AHA’s Exercise, Cardiac Rehabilitation, and Prevention
committee regarding the core components of CAD secondary prevention exercise programs. Exercise capacity, often measured utilizing the duration of exercise in minutes during certain treadmill protocols and/or peak oxygen consumption (VO₂ peak), has been used as a prognostic indicator in patients being evaluated for and with known CAD. Vanhees, et al. evaluated a cohort of patients after acute MI or CABG surgery utilizing a graded uninterrupted exercise test performed to exhaustion and found that adjusted all-cause and cardiovascular mortality decreased with increasing peak oxygen uptake. They concluded that exercise capacity was an independent predictor for all-cause and cardiovascular mortality in CAD patients. Kavanagh, et al. reported similar results in separate large cohorts of men and women after acute MI, CABG surgery, or with known ischemic heart disease. They reported VO₂ peak values of <15, 15 to 22, and >22 mL/kg/min yielded respective multivariate adjusted hazard ratios (HR) of 1.00, 0.62, and 0.39 for CVD-related and 1.00, 0.66, and 0.45 respectively for all-cause mortality in the male cohort during the median 7.9 years of follow-up. In the female cohort, they reported that patients with VO₂ peak values ≥13 ml/kg/min has a HR of 0.71 (95% CI 0.53-0.95) for all-cause mortality compared to the group with values <13 ml/kg/min. Considered as a continuous variable, a 1 ml/kg/min increase in VO₂ peak was associated with a 10% lower cardiac mortality during the median 4.5 years of follow-up. These data argue that improving VO₂ max with regimented exercise will decrease a subject’s risk for major adverse cardiovascular events.
Table V: AHA/ACCF Class I Recommendations for Physical Activity

- For all patients, 30-60 minutes of moderate-intensity aerobic activity at least 5, and preferable 7, days per week along with an increase in daily lifestyle activities to improve cardiorespiratory fitness (Level of Evidence B)
- All patients should receive risk assessment with a physical activity history and/or exercise test to guide prescription of physical activity levels (Level of Evidence B)
- Patients should be counseled to report symptoms related to exercise for evaluation (Level of Evidence C)

Cardiac Rehabilitation

The guidelines put a large focus on referring all patients with recently diagnosed CAD to cardiac rehabilitation as a means of reinforcing structured exercise, nutritional counseling, and other lifestyle modifications (Table VI). Taylor et al. published a meta-analysis on randomized controlled trials evaluating the effectiveness of exercise-based cardiac rehabilitation in patients with CAD, including 48 trials with a total of 8,940 patients. Compared with usual care, cardiac rehabilitation was associated with reduced all-cause (OR = 0.80, 95% CI 0.68 to 0.93) and cardiac mortality (OR = 0.74, 95% CI 0.61 to 0.96), along with significant reductions in total cholesterol levels, triglyceride levels, and systolic blood pressure. Clark, et al. published a similar meta-analysis looking at the effectiveness of cardiac rehabilitation programs with and without exercise components. They found similar reductions in CAD-related endpoints in programs with and without exercise components and concluded that a relatively wide variety of
secondary prevention programs can be implemented to improve health outcomes in patients with CAD.\textsuperscript{49}

**Table VI: AHA/ACCF Class I Recommendations for Cardiac Rehabilitation**

- All patients with ACS or immediately post cardiac revascularization (CABG surgery or PCI) should be referred to a comprehensive outpatient cardiac rehabilitation program either prior to discharge or at the first office follow-up visit (*Level of Evidence A*)

- All patients with the diagnosis of ACS, chronic angina, peripheral vascular disease, or with coronary revascularization (CABG surgery or PCI) should be referred to a comprehensive cardiac rehabilitation program (*Level of Evidence A except for chronic angina, which is Level B*)

- A home-based cardiac rehabilitation program can be supervised for a center-based program in low-risk patients with CAD (*Level of Evidence C*)

Taylor, et al. also published a meta-analysis of the effectiveness of unsupervised, home-based cardiac rehabilitation programs compared with supervised, facility-based cardiac rehabilitation. Twelve RCTs with a total of 1,938 participants were included, though the majority of studies recruited a lower risk patient (without concurrent CHF) following an acute MI and/or revascularization. They reported no difference in outcomes of overall mortality, cardiac events, exercise capacity, blood pressure control, or cholesterol levels between the two settings of rehabilitation and concluded that both home-based and formal cardiac rehabilitation appear to be equally effective in improving outcomes in patients with CAD.\textsuperscript{50} Clark, et al. published a follow-up meta-analysis of
cost-effectiveness between these two rehab settings and concluded that home-based secondary prevention programs for patients with CAD are an effective and relatively low-cost complement to hospital-based cardiac rehabilitation and should be considered for lower risk patients without access to hospital-based services.\textsuperscript{51}

**Weight Management**

Obesity plays a major role in adversely affecting major CAD risk factors, including hypertension, dyslipidemia, and diabetes, along with being a major component of the metabolic syndrome, another major risk factor for CAD.\textsuperscript{52} The AHA/ACCF objectives for weight management focus on goals for body mass index (BMI) and waist circumference, along with goals for initial weight loss strategies (Table VII). Ideal BMIs between 18.5-24.9 kg/m\textsuperscript{2} in both men and women and should be assessed at every clinic visit. Similarly, waist circumference should be assessed at every clinic visit (either with BMI or in place of BMI), with a goal of <35 inches (<89 cm) for women and <40 inches (<102 cm) for men. If CAD patients are above these goals, weight reduction should be encouraged via a balanced combination of increased physical activity and exercise and a reduction in caloric intake. The initial goal of weight loss therapy should be to reduce body weight by 5-10\% from baseline.

**Table VII: AHA/ACCF Class I Recommendations for Weight Management**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI and/or waist circumference should be assessed at every clinic visit, with a goal BMI between 18.5-24.9 kg/m\textsuperscript{2}</td>
<td>B</td>
</tr>
<tr>
<td>Waist circumference should be &lt;35 inches (&lt;89 cm) for women and &lt;40 inches (102 cm) for men</td>
<td>B</td>
</tr>
<tr>
<td>If weight loss is indicated, the initial goal should be 5-10% from baseline</td>
<td>C</td>
</tr>
</tbody>
</table>
Much of the evidence underlying these recommendations was coalesced in the Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults released by the National Institutes of Health (NIH) in 1998, reiterated by a statement from the AHA’s Council on the Clinical Implications of Obesity.\textsuperscript{53, 54} A prospective cohort study by Calle, et al. reported that a higher BMI (>24.9 kg/m\textsuperscript{2}) was significantly predictive of death from CVD, especially in men (RR 2.90, 95\% CI 2.37 to 3.56).\textsuperscript{55} Several studies have shown that BMI > 24.9 kg/m\textsuperscript{2} is associated with an increased risk for ACS, both in the setting of the metabolic syndrome, and as an independent risk factor.\textsuperscript{56, 57} Jacobs, et al. examined the association between waist circumference and mortality among a large cohort of men and women \geq 50 years old in the Cancer Prevention Study II Nutrition cohort. They found that, after adjustment for BMI and other risk factors, there was a significant increase in cardiovascular death in men with waist circumferences \geq 100 cm and in women \geq 75 cm.\textsuperscript{58}

Interestingly, several studies have also reported an obesity paradox in CAD, including patients after coronary revascularization.\textsuperscript{52, 59, 60} In a systematic review of 40 cohort studies, Romero-Corral et al. reported that overweight and obese (BMI \geq 25 kg/m\textsuperscript{2}) CAD patients have a lower risk for total and CV mortality compared with underweight and normal-weight CAD patients. However, in patients with a BMI \geq 35 kg/m\textsuperscript{2}, there was an excess risk for CV mortality without any increase in total mortality. These investigators hypothesized that the paradox in outcomes for overweight and mildly obese CAD groups was due to the lack of discriminatory power of BMI to differentiate between adipose and lean body mass.\textsuperscript{60} However, a study by Lavie, et al. compared patients with high and low percent body fat and found similar results.\textsuperscript{61} The obesity paradox has also
been demonstrated in patients after MI and revascularization, with significantly higher overall mortality rates for patients with normal BMI patients (BMI <24.9 kg/m$^2$) compared with overweight or obese patients, though rates of myocardial infarction and revascularization do not appear to significantly differ.$^{60,62}$ These studies suggest that despite the fact that obesity increases the risk for developing CAD, only moderate-to-severe obesity (BMI $\geq$ 35 kg/m$^2$) may adversely affect prognosis in patients with established CAD.

**Type 2 Diabetes Mellitus Management**

CVD is the major cause of morbidity and mortality for individuals with diabetes mellitus (DM) and the largest contributor to the direct and indirect costs of diabetes.$^{63}$ Other risk factors for CVD, such as hypertension and dyslipidemia, commonly coexisting with type 2 DM, though type 2 DM itself also confers independent risk for CVD. Numerous studies have shown the efficacy of controlling individual cardiovascular risk factors in preventing or slowing CVD in people with diabetes and significant reductions in morbidity and mortality have been shown when multiple risk factors are addressed together with intensive pharmacotherapy.$^{64}$ The AHA/ACCF CAD secondary prevention guidelines regarding the management of type II DM are aimed at the prevention of cardiovascular complications from the disease and not necessarily towards primary management of the disease itself. They state that care for the patient with both comorbidities should be coordinated with another provider, such as an endocrinologist or primary care physician, whose focus is aimed primarily at primary management of DM. The only other class I recommendation made includes a focus on lifestyle modifications, similar to those mentioned in the section on blood pressure management (Table VIII).
These recommendations are consistent with the standards of medical care in diabetes released by the American Diabetes Association in 2011.\textsuperscript{63}

\textbf{Table VIII:} AHA/ACCF Class I Recommendations for Type 2 Diabetes Mellitus Management

- Care should be coordinated with the patient’s primary care provider and/or endocrinologist (\textit{Level of Evidence} \textit{C})

- Encourage lifestyle modifications such as increasing daily physical activity and exercise, weight modification, blood pressure control, and lipid management (\textit{Level of Evidence} \textit{B})

For individuals with type 2 DM, several studies have demonstrated that moderate weight loss (5\% of body weight) is associated with decreased insulin resistance, improved measures of glycemia and lipemia, and reduced blood pressure, all risk factors for CAD.\textsuperscript{54} The Look AHEAD (Action for Health in Diabetes) trial reported that intensive lifestyle interventions (diet and exercise regimens designed to produce 7\% weight loss/year) produced significant increases in weight loss, improvements in treadmill fitness, improvements in blood pressure control, and increased HDL cholesterol compared to diabetic education alone, with benefits sustained at 4 year follow-up.\textsuperscript{65} Exercise is also an important part of the diabetes management plan as regular exercise has been shown to improve blood glucose control, reduce CVD risk factors, contribute to weight loss, and improve overall well-being.\textsuperscript{63}
Influenza Vaccination

The guideline recommendation regarding influenza vaccination in patients with known CAD is relatively simple- CAD patients without contraindication should have an annual influenza vaccination (Table IX). This is consistent with scientific statements released by the Center for Disease Control (CDC) and AHA/ACCF specifically on influenza vaccination in patients with known CAD.66, 67 This recommendation is similar to that for groups with other significant chronic comorbidities that have worse outcomes with influenza infection compared to patients without these comorbidities.66

Table IX: AHA/ACCF Class I Recommendations for Influenza Vaccination

- Patients with CAD should have an annual influenza vaccination (Level of Evidence B)

Ciszewski, et al. conducted the FLUCAD trial, one of the only randomized trials investigating the effects of influenza vaccination in patients with known CAD. Interestingly, they did not find clinically significant differences in the end points of cardiovascular death or major adverse cardiovascular events, though there was question as to whether the trial was underpowered.68 Gurfinkel, et al. published the FLUVACS study to look at the effect of influenza vaccination in patients with ACS and in CAD patients with planned percutaneous coronary intervention (PCI). They found that the incidence of the primary endpoint of cardiovascular death was significantly reduced at one year follow-up in those that received the vaccine (RR 0.34, 95% CI 0.17 to 0.71).69
Antiplatelet Agents and Anticoagulants

Most of the class I recommendations for antiplatelet agents from the AHA/ACCF guidelines for secondary CAD prevention revolve around the administration of antiplatelets, specifically aspirin and clopidogrel (a P2Y12 receptor antagonist) (Table X). Aspirin is a long-standing mainstay in secondary prevention therapy for CAD.\(^{15,70}\) The Antithrombotic Trialists’ Collaboration published a meta-analysis of 16 secondary prevention trials comparing long-term aspirin therapy versus placebo and reported a significant annual absolute risk reductions in vascular events (MI, CVA, or vascular death) of 1.5%, of 0.46% in CVA alone, and of 1.0% in CAD events, with a non-significant increase in hemorrhagic stroke.\(^{71}\) This same group released a similar meta-analysis evaluating 287 studies involving 135,000 patients comparing antiplatelet therapy versus control in patients with CAD or CAD risk-equivalents. Overall, among these high risk patients, the reported that antiplatelet therapy (most studies evaluated Aspirin 75-150mg daily though some looked at Clopidogrel and Ticagrelor as well) significantly reduced the combined outcome of any serious vascular event by about one quarter; non-fatal myocardial infarction by one third, non-fatal stroke by one quarter, and vascular mortality by one sixth.\(^{72}\) Chesebro et al. performed a RCT evaluating the use of dipyridamole (a platelet adenosine antagonist with antiplatelet effects) + aspirin compared to placebo in preventing saphenous vein closure in patients s/p CABG surgery and found that the antiplatelet combination led to significantly lower rates of graft closure on vein-graft angiography performed at a median 12 months after surgery.\(^{73}\) Similar results were found in a smaller RCT by Lorenz, et al.\(^{74}\) These studies were followed by a prospective cohort study by Mangano, et al. that reported significant reductions in MI,
stroke, renal failure, and bowel ischemia in CABG patients who received aspirin post-op compared to those that did not.\textsuperscript{75}

**Table X**: AHA/ACCF Class I Recommendations for Antiplatelet Agents and Anticoagulation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin 75-162mg daily is recommended for all patients with CAD unless contraindicated</td>
<td>A</td>
</tr>
<tr>
<td>In CAD patients with an allergy to Aspirin, Clopidogrel 75mg daily is recommended as an alternative</td>
<td>B</td>
</tr>
<tr>
<td>A P2Y12 receptor antagonist is recommended in combination with Aspirin in all patients after ACS or PCI with stent placement</td>
<td>A</td>
</tr>
<tr>
<td>For PCI patients that receive a bare-metal stent or drug-eluting stent, Clopidogrel 75mg daily, Prasugrel 10mg daily, or Ticagrelor 90mg twice daily should be given for at least 12 months in combination with Aspirin</td>
<td>A</td>
</tr>
<tr>
<td>Aspirin 100mg to 325mg daily should be started within 6 hours of CABG surgery to reduce the incidence of saphenous vein closure</td>
<td>A</td>
</tr>
<tr>
<td>Antiplatelet therapy is recommended over anticoagulation with a vitamin K antagonist to treat patients with atherosclerosis</td>
<td>A</td>
</tr>
<tr>
<td>Use of Warfarin in conjunction with Aspirin and/or Clopidogrel is associated with an increased risk of bleeding and should be monitored closely</td>
<td>A</td>
</tr>
</tbody>
</table>

The CAPRIE study was designed to assess the relative efficacy of clopidogrel (75 mg once daily) versus aspirin (325 mg once daily) in reducing the risk of a composite
outcome cluster of ischemic CVA, MI, or vascular death in patients with CAD or CAD risk-equivalents. For the primary outcome, the relative risk reduction was 8.7% (95% CI 0.3-16.5) in favor of Clopidogrel, with a significantly increased number of patients with hemorrhagic death and intracranial hemorrhage in the Aspirin group. However, given the small relative risk reduction and markedly increased price of Clopidogrel compared to Aspirin, many interpret the CAPRIE trial as evidence that clopidogrel is an adequate (and safe) substitute for aspirin in patients who are intolerant of aspirin.

Yusef, et al. published a RCT in 2001 evaluating the addition of clopidogrel to aspirin versus aspirin alone in ACS patients (the CURE trial) with non-ST-segment elevation and found that the clopidogrel + aspirin group had a relative risk for the primary outcome (composite of death from cardiovascular causes, nonfatal myocardial infarction, and stroke) of 0.80 (95% CI 0.72-0.90) compared to the aspirin group alone. The dual antiplatelet group also had a significant increase in major bleeding episodes but a nonsignificant difference in life-threatening bleeding and hemorrhagic strokes compared to the aspirin alone group. Mehta, et al. then released a substudy of the CURE trial evaluating patients who received PCI and found a relative risk for the primary endpoint of 0.70 (0.50-0.97) in the long-term dual antiplatelet group compared to the aspirin alone group, with no significant difference in major bleeding between the groups. The CREDO investigators followed these trials with a RCT investigating the benefit of long-term (12-month) treatment with clopidogrel after PCI and to determine the benefit of initiating clopidogrel with a preprocedure loading dose (300mg) in addition to aspirin therapy. They found that long-term clopidogrel therapy was associated with a significant 26.9% relative reduction (95% CI 3.9-44.4%) in the combined endpoint of
death, MI, or stroke, without a significant long-term risk of major bleeding. The TRITON-TIMI 38 trial compared prasugrel (a P2Y12 receptor antagonist similar to clopidogrel) + aspirin to clopidogrel + aspirin in patients with ST-segment elevation myocardial infarction (STEMI). At 15 month follow-up, the prasugrel group had a hazard ratio (HR) of 0.79 (95% CI 0.65-0.97) for the combined primary endpoint of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke compared to the clopidogrel group without a significant difference in major bleeding between the groups outside of patients that went emergently for CABG surgery. This lead to the adoption of prasugrel as an alternative treatment for ACS patients receiving PCI with stenting (bare or drug-eluting). The most recent P2Y12 receptor antagonist evaluated in the treatment of CAD is ticagrelor, which has a more rapid onset and more pronounced platelet inhibition than clopidogrel. The PLATO group released a RCT in 2009 that showed a HR 0.84 (0.77 to 0.92) for the primary endpoint of death from vascular causes, myocardial infarction, or stroke at mean 12 month follow-up in ACS patients receiving ticagrelor versus clopidogrel, which lead to ticagrelor’s inclusion in the most recent update of the AHA/ACCF CAD secondary prevention guidelines. Notably, patients receiving ticagrelor were shown to have a significantly higher incidence of major bleeding compared to the clopidogrel group (4.5% vs. 3.8%, p 0.03).

A RCT by Hurlen, et al. evaluated aspirin alone versus warfarin alone versus aspirin + warfarin after acute MI and found that, while the addition of warfarin to aspirin led to decreased primary outcome events (composite of death, nonfatal MI, and ischemic stroke), there was a significant increase in major non-fatal bleeding episodes in the aspirin + warfarin group over the mean four year follow-up. A systematic review by
Anand, et al. found that while antiplatelet therapy plus warfarin at higher INRs (increased systemic anticoagulation) lowered primary events after acute MI, this was balanced with significantly higher bleeding risk. Warfarin therapy at lower INRs, while minimizing bleeding risks, did not reduce cardiovascular end points.\textsuperscript{85} Mohr, et al. published a RCT randomizing patients with peripheral vascular disease (PVD, a CAD equivalent) to antiplatelet alone versus antiplatelet + warfarin and found no difference in the outcomes of myocardial infarction, stroke, or death from cardiovascular causes over the mean follow-up of 35 months. They did, however, show a significant increase in life-threatening bleeding in the antiplatelet + warfarin group compared to the antiplatelet alone group (RR 3.41, 1.84 to 6.35).\textsuperscript{86} The CHAMP study found similar results of no added clinical benefit of warfarin therapy combined with low-dose aspirin beyond that achievable with aspirin monotherapy but again showed an increased incidence of major bleeding episodes over the aspirin monotherapy group.\textsuperscript{87}

**Renin-Angiotensin-Aldosterone System Blockers**

The major focus of the AHA/ACCF guidelines in regards to renin-angiotensin-aldosterone system (RAAS) blockers is in patients with CAD and certain comorbidities, mainly CHF, DM, and chronic renal insufficiency (CRI) (\textbf{Table XI}). Garg, et al. published a meta-analysis in 1995 coalescing data from randomized, placebo-controlled trials of angiotensin- converting-enzyme (ACE) inhibitors. They found that the administration of ACE inhibitors in patients with ischemic CHF (LVEF \(\leq\) 40\%) lead to a reduced OR of 0.77 (95\% CI 0.65-0.91) for mortality when compared to placebo in the included trials. The reduction in mortality appeared to be primarily due to fewer deaths from progressive heart failure.\textsuperscript{88} The HOPE study investigators performed a RCT
evaluating ramipril (an ACE inhibitor) versus placebo in patients with CAD or CAD-equivalents without known left ventricular dysfunction but without evidence of clinical CHF. They found that treatment with ramipril significantly reduced the rates of death from cardiovascular causes (RR 0.74, p<0.01), MI (RR 0.80, p<0.01), stroke (RR 0.68, p<0.01), death from any cause (RR 0.84, p 0.01), coronary revascularization (RR 0.85, p<0.01), and subsequent CHF (RR 0.77, p<0.01).\(^{28}\)

**Table XI**: AHA/ACCF Class I Recommendations for Renin-Angioensin-Aldosterone System Blockers

- ACE inhibitors should be started and continued indefinitely in all patients with CAD who’s left ventricular ejection fraction is \(\leq 40\%\) and/or have diabetes, hypertension, or chronic renal insufficiency, unless contraindicated (*Level of Evidence A*)

- The use of angiotensin II receptor antagonists are recommended in CAD patients who meet criteria for ACE inhibitor therapy but are ACE inhibitor intolerant (*Level of Evidence A*)

- Patients post-myocardial infarction without significant renal dysfunction (eGFR <30 ml/min) or hyperkalemia (serum K >5.0 mEq/L) who have a left ventricular ejection fraction \(\leq 40\%\) and either DM or symptomatic heart failure who are already receiving therapeutic doses of an ACE inhibitor and \(\beta\)-blocker should be started on an aldosterone inhibitor (*Level of Evidence A*)

The CHARM-Overall RCT compared candesartan (an angiotensin II receptor antagonist or ARB) to placebo in patients with CHF (left ventricular ejection fraction
[LVEF] ≤ 40%), the majority of which had CAD or CAD risk-equivalents. Over a median 37.7 month follow-up, they found that candesartan significantly reduced the combined endpoint of cardiovascular death and hospital admission for CHF (adjusted HR 0.82, 95% CI 0.75-0.88), though the effect on all-cause death was statistically insignificant. The Losartan Heart Failure Survival Study ELITE II investigators compared captopril (an ACE inhibitor) to losartan (an ARB) in a RCT recruiting a similar patient group and found no significant difference in all-cause mortality between the two groups. Pfeffer, et al. published a RCT comparing groups administered valsartan (an ARB), captopril, or both in patients after an acute MI. They found that valsartan was as effective as captopril in preventing all-cause mortality during the median 24.7 month follow-up and that the combination group significantly increased the rate of adverse events without improving overall survival. These trials underscored that recommendation of using ARBs in CAD patients that meet criteria for ACE inhibitor administration but are ACE inhibitor intolerant.

Pitt, et al. reported a RCT evaluating the use of eplerenone (an aldosterone inhibitor) in addition to optimal medical therapy in patients with acute MI complicated by left ventricular dysfunction (LVEF ≤40%) and CHF. During the mean follow-up of 16 months, significant reductions were reported in the primary endpoints of overall mortality (RR 0.85, 95% CI 0.75-0.96) and cardiovascular death (RR 0.83, 95% CI 0.72 to 0.94) in the eplerenone group compared to placebo. Zannad, et al. published a RCT comparing the use of eplerenone in patients with chronic systolic heart failure (LVEF ≤35%) and mild symptoms (NYHA class II symptoms) after a MI already on optimal medical therapy. The trial was stopped prematurely after a median follow-up period of 21 months
as there was a significant reduction in the composite primary endpoint of death from cardiovascular causes or hospitalization due to heart failure (HR 0.63, 95% CI 0.54 to 0.74). These studies proved the efficacy of adding aldosterone blockade to optimal medical therapy in CAD patients with certain comorbidities.

**β-Blockers**

β-blockers have been a mainstay of long-term therapy in patients with CAD. Current AHA/ACCF guidelines recommend their use in all patients after an ACS or MI, including those with LVEF ≤ 40% after MI ([Table XII](#)). Freemantle, et al. published a systematic review of RCTs evaluating the short-term (≤ 6 weeks after MI) and long-term effects (6-48 months after MI) of β-blockers after an acute MI. They reported an insignificant reduction in mortality in patients put on β-blockers compared to placebo in the short-term studies, thought the long-term studies showed a significant reduction in overall mortality, with an OR of 0.77 (95% CI 0.69-0.85) in the β-blocker groups compared to placebo. Of note, most of the studies included in this analysis were performed before thrombolytic treatment for acute MI had become mainstream. In a meta-analysis by Peuter, et al. evaluating trials comparing β-blockers to placebo after an ACS, it was reported that non-specific β-blockers significantly reduced total mortality in patients with ACS (RR 0.73, 95% CI 0.64-0.82) compared to placebo. In 2012, Bangalore, et al. released a longitudinal study from the Reduction of Atherothrombosis for Continued Health (REACH) registry looking at the association of β-blocker use with cardiovascular events in stable patients from 3 different groups: those with a prior history of MI, those with CAD but no history of MI, and those with only risk factors for CAD (including CAD risk-equivalents). Over a median follow-up time of 44 months, event
rates were not significantly different in patients using β-blockers compared with those without β-blocker use for any of the outcomes tested (cardiovascular death, nonfatal MI, or nonfatal stroke) in any of the 3 cohorts. Some view this as a challenge to the notion that β-blockers should be prescribed indefinitely in CAD patients, especially given that longitudinal data in multiple other studies seems to show a reduced favorable effect on mortality that starts around 3 years after an acute MI.33

Table XII: AHA/ACCF Class I Recommendations for β-Blockers

- β-blockers should be started and continued for 3 years in all patients with normal left ventricular function who have had a MI or ACS (Level of Evidence A)

- β-blockers should be prescribed in all patients with left ventricular systolic dysfunction (LVEF ≤ 40%) with CHF or after a MI, unless contraindicated (Level of Evidence B)

IV. Trends in Coronary Heart Disease Secondary Prevention Guideline Adherence in the United States

As guidelines for CAD secondary prevention were released and began to be incorporated into clinical practice, they began to be viewed as standards of care for patients with CAD. However, multiple studies have shown imperfect compliance with these recommendations, particularly after coronary revascularization procedures post-MI. While compliance with these guidelines has been imperfect after both major types of coronary revascularization (CABG surgery and PCI), noncompliance rates with these measures has been significantly higher in patients after CABG surgery compared to PCI. Foody, et al. performed a retrospective dataset analysis from the Centers for Medicare &
Medicaid Services (CMS) National Heart Care Program comparing the prescription of several CAD secondary prevention therapies (aspirin, β-blockers, ACE inhibitors, and lipid lowering therapy) at discharge for eligible patients that underwent CABG surgery after an acute MI versus those treated non-surgically. Among ideal candidates for treatment, CABG patients were less likely to receive β-blocker (61.5% versus 72.1%, \( p < 0.01 \)), ACE inhibitors (55.5% versus 72.1%, \( p < 0.01 \)), and lipid lowering therapies (34.7% versus 55.7%, \( p < 0.01 \)) at time of discharge. Hiratzka, et al. reported a retrospective analysis of the AHA’s Get With the Guidelines-Coronary Artery Disease database to determine whether compliance with secondary prevention performance measures for CABG patients was different from that for nonsurgical patients (PCI versus non-invasive medical management). They reported that CABG patients were less likely to receive aspirin (OR 0.22, 95% CI 0.16-0.29), lipid lowering agents (OR 0.45, 95% CI 0.37-0.55), ACE inhibitors (OR 0.46, 95% CI 0.40-0.52), and smoking cessation counseling (OR 0.87, 95% CI 0.77-0.97) at discharge in eligible patients compared to patients undergoing PCI, with a non-significant difference in β-blocker prescription (OR 0.82, 95% CI 0.67-1.00) between these groups.

Peterson, et al. reported a retrospective database analysis of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) registry in 2006 examining how hospital compliance with AHA/ACCF CAD secondary prevention guideline adherence varied among 350 academic and non-academic medical centers across the US between January 1, 2001, and September 30, 2003 in patients admitted with ACS. They reported that the degree of composite guideline adherence was significantly associated with in-
hospital mortality, with observed mortality rates decreasing from 6.31% for the lowest adherence quartile to 4.15% for the highest adherence quartile (p<0.01). After adjustment, every 10% increase in composite adherence at a hospital was associated with an analogous 10% decrease in its patients' likelihood of in-hospital mortality (adjusted OR 0.90, 95% CI 0.84-0.97). This study was one of the first studies that showed that guidelines-based performance metrics could be used to improve in-hospital outcomes for ACS. Given the multiple studies showing improved clinical outcomes in patients that received eligible guideline-recommended therapies, Bauer, et al. conducted a prospective, multicenter observational study in the Acute Coronary Syndromes registry of 11,823 patients admitted with acute MI with the objective of determining factors associated with provider nonadherence to secondary prevention measures. They found that certain clinical comorbidities were associated with noncompliance, such as renal insufficiency, PVD, chronic anticoagulation therapy, older age, and chronic obstructive lung disease (COPD), which are all more common in patients undergoing CABG surgery versus PCI.

These studies illustrated that there were significant differences in compliance at hospital discharge with secondary prevention performance measures for CAD patients undergoing CABG surgery compared to PCI. There was some evidence that process of care differences could explain some of these differences. In many hospitals, CABG patients are cared for in different nursing units, by different nursing personnel, and using different clinical pathways than those patients having PCI. Patients undergoing CABG also tend to be older, have an increased number of baseline comorbidities, and can be more prone to in-hospital complications, which could affect providers’ inclination to
prescribe secondary prevention measures at discharge. This so-called “treatment-risk paradox” has been proposed to be playing a major role in the lack of adherence to guideline-based therapy. Since CABG patients represented a group for whom secondary prevention had proven benefits, they were a group with potentially large benefits from further quality improvement interventions.

Publication of these studies has led to widespread efforts to educate practitioners, improve hospital processes, and implement public reporting of hospital quality measures. A RCT published by Williams, et al. randomized 458 hospitals participating in the Society of Thoracic Surgeons (STS) National Cardiac Database to low-intensity continuous quality improvement interventions (educational information designed to influence the prescription of recommended medications at hospital discharge, site-specific feedback, periodic newsletters, etc) versus placebo. They reported that these low-intensity educational efforts led to significant improvements in the prescription of β-blockers and lipid lowering agents to eligible patients after CABG surgery both at discharge and on long-term (median 24 month) follow-up. They concluded that low-intensity continuous quality improvement efforts could improve the adoption of secondary prevention measures into clinical practice.100 In 2006, the Society of Thoracic Surgeons launched the Quality Measurement Task Force to measure and improve adherence to quality metrics among surgical programs. The SYNTAX trial was on-going during this time, compared PCI and CABG for treating patients with previously untreated three-vessel or left main coronary artery disease. Results from sub-studies from this trial showed that the prescription of CAD secondary prevention therapies improved in CABG surgery patients during this period, thought to be due to efforts by the STS, though they
still lagged behind those for patients undergoing PCI. It remains to be seen if further efforts by the STS have led to continued improvements in CAD secondary prevention guidelines compliance for patients undergoing CABG surgery compared to PCI.

V. Why Guideline Implementation Has Been Imperfect

The publication of guidelines does not mean that the recommendations they endorse will automatically be translated into daily practice, as demonstrated by the low adherence rates to CAD secondary prevention guidelines. Many reasons have been cited for this lack of adherence, such as poor dissemination of the guidelines, lack of knowledge of the science behind the guidelines, information overload of busy practitioners, poor documentation of compliance, concern about instituting therapies in the acute setting, among many others. Pearson, et al. published an example of this looking at the number of patients with goal LDL cholesterol levels in the Lipid Treatment Assessment Project. They found that although 95% of physicians involved in the project were aware of specific guidelines for cholesterol goals, only 18% of the same physicians’ patients met the recommended LDL cholesterol goals.

Many different strategies are available to change physician practice and implement guidelines. Most of the strategies employ different educational interventions. Although education alone can be performed with minimal expense, most studies demonstrate that traditional educational strategies often fail to produce sustained changes in clinical practice, including continuing medical education. Retrospective feedback has also been shown to have limited impact on patient care. Concurrent feedback, in contrast, has been shown to be more effective and result in consistent changes in care and computerized clinical decision support can be a cost-effective method of providing
concurrent feedback. Economic incentives also influence physician behavior. However, few trials have been performed to evaluate the effects of economic incentives on improve performance, likely because of the difficulty of randomization of incentives and the controversy and ethical problems surrounding providing incentives. A RCT by Kouides, et al. showed that incentives improved influenza immunization among the elderly, though a RCT published by Hillman, et al. reported that incentives plus feedback failed to improve breast cancer screening in women > 50 years old.

Many of the factors previously mentioned are primarily within the control of the prescribing physician. However, there are a host of other patient- and system-level factors that that likely play a role in the observed differences in adherence rates, including but not limited to: socioeconomic factors, insurance status, local reimbursement policies and rates, hospital size, and geographic location. Physicians generally have a relatively low awareness of how these issues affect their patients’ care and educational efforts aimed at ameliorating this knowledge gap could result in potential improvements in this patient group’s overall post-revascularization care.

Conclusion

Clinical practice guidelines have shown significant promise in improving patient outcomes. However, significant hurdles exist in implementing these recommendations. Both provider and systems level interventions have shown promise in changing clinical practice patterns, though these efforts in isolation have produced suboptimal results. Continued investigations into methods that improve guideline adherence are warranted, especially as we move into an era where physician and group practice patterns will fall under increasing scrutiny.
Chapter 2: Trends in Adherence to Secondary Prevention Guidelines for Patients Undergoing Coronary Revascularization in Washington State: An Analysis of the COAP Registry

**Background:** Previous studies indicate that patients undergoing CABG surgery are less likely to receive guidelines-based CAD secondary prevention therapy at discharge compared to those undergoing PCI following an acute ST-segment elevation myocardial infarction (STEMI). We aimed to evaluate whether these differences have persisted following the recent implementation of public reporting of hospital metrics in Washington State.

**Methods and Results:** The Clinical Outcomes Assessment Program (COAP) database was retrospectively analyzed to evaluate adherence to secondary prevention guidelines at discharge in patients who underwent coronary revascularization after an acute STEMI in Washington State. From 2004-2007, 9,260 patients received PCI while 692 underwent CABG for this indication. Measures evaluated included prescription of aspirin, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACE-I/ARB), and lipid lowering medications.

Overall, adherence rates for both the individual medications and composite adherence scores for both groups significantly improved over the four year period investigated ($p \leq 0.03$ for trend for all four medications studied). While there was not a significant difference in the adjusted odds of receiving aspirin, β-blockers, or lipid lowering medications between the two procedures at the end of the study period, there continued to be a significant difference in the odds of receiving ACE-I/ARBs between
the two groups (adjusted OR 2.27 [95% CI 1.49, 3.48] for the PCI compared to CABG group in 2007).

**Conclusions:** Rates of guidelines-based secondary prevention medication adherence in STEMI patients that underwent CABG surgery have been steadily increasing in Washington State, temporally associated with the implementation of public reporting of quality measures.
Introduction

Previous studies have shown that patients undergoing CABG surgery after an acute MI are less likely to receive secondary prevention measures at discharge relative to similar patients undergoing PCI.\textsuperscript{96, 97} Although adherence to guidelines-based therapy has been imperfect for both procedures, secondary prevention adherence rates at discharge have been improving over time, particularly as public reporting of hospital performance has been implemented.\textsuperscript{96, 98, 99, 102} COAP is a quality improvement initiative developed for hospitals that perform coronary revascularization in Washington State.\textsuperscript{111} Our aim was to utilize data from COAP to evaluate whether there was a temporal association between prescription of guidelines-based secondary prevention therapy at discharge and the institution of public reporting among patients with acute STEMI undergoing CABG surgery compared to PCI in Washington State.

Methods

Study Design and Population

We performed an observational analysis using data from COAP, which is a quality improvement initiative of the Foundation for Health Care Quality. The registry prospectively collects demographic, procedural, and in-hospital outcomes data on all patients that undergo coronary revascularization in all 35 hospitals that perform these procedures in Washington State. This process has been in place since 1999 and public reporting began in 2005. Abstractors at these hospitals, using the medical record, enter key variables on standardized data collection forms. Demographics, CAD risk factors, procedural, and outcome information are recorded. Confidential comparative quarterly and annual reports are distributed to the hospitals by COAP. Hospitals have access to
their own results but are blinded to the identity of other hospitals. Data is also provided to develop annual risk-adjusted comparative reports for each institution. A more extensive detailed report on the data collection process has been previously reported.\textsuperscript{111, 112}

We retrospectively identified all patients with documented STEMI that underwent coronary revascularization (PCI or CABG surgery) during their index hospitalization from January, 2004, through December, 2007. 9,952 patients met these criteria, 9,260 (93.0\%) of which received PCI and 692 (7.0\%) of which underwent CABG surgery. Baseline characteristics, presentation variables, clinical management, and procedural complications were determined for each group. The clinical management interventions investigated were whether these patients were discharged with 4 of the class I recommendations from the 2006 ACC/AHA secondary prevention guidelines, including: prescription of aspirin, \(\beta\) blockers, lipid lowering therapy, and angiotensin converting enzyme inhibitors (ACE-I)/angiotensin II receptor blockers (ARB).\textsuperscript{113} Notably, the recommendations from the 2006 guidelines regarding these interventions do not significantly differ from the most current 2011 AHA/ACCF secondary prevention guidelines.\textsuperscript{114} Unless a contraindication was documented, all patients were assumed to be candidates for aspirin, \(\beta\) blockers, and lipid lowering therapy at the time of discharge. Patients were considered to be candidates for ACE-I/ARBs if their left ventricular ejection fraction (LVEF) was documented to be \(\leq 40\%\) and/or if they had a history of DM, hypertension, or CRI, which included 662 CABG patients and 7,293 patients that underwent PCI during the study period. The percent adherence for each discharge medication was determined by dividing all patients who were given the intervention by
all those eligible for the intervention, excluding those with documented contraindications. A composite medication adherence score was calculated for each patient by dividing the number of prescribed medications (aspirin, β blockers, lipid lowering therapy, and ACE-I/ARBs) by the number for which they were eligible. For temporal analyses, date of admission was used to categorize patients into quarters from the first quarter of 2004 through the fourth quarter of 2007.

**Statistical Analysis**

Dichotomous variables were compared using the Pearson $\chi^2$ test and continuous variables were compared using the two-sided Student’s t-test. Temporal trends were evaluated using the Pearson’s $\chi^2$ test of trend. Unadjusted and adjusted odds ratios of non-adherence for each intervention were calculated for patients undergoing PCI compared to CABG surgery. Interactions between covariates and type of revascularization method on the outcomes investigated were evaluated by the Wald test and a likelihood ratio test when including an interaction term in the multivariable analysis. Covariates tested for significant interactions included: gender, race, procedure priority, and year of procedure, none of which proved to be statistically significant.

Using backwards selection, the covariates in the data set found to be statistically significantly associated with the odds of being discharged with the medications investigated in the unadjusted analyses were: age, history of PVD, hypertension, DM, CHF, or prior MI, procedure priority, year procedure was performed, LVEF, and shock. Acute renal insufficiency (ARI) was defined as an increase in hospital creatinine by 50% above admission creatinine level for analytic purposes. These patients were not excluded from candidacy for ACE-I/ARB since ARI is not by itself a contraindication for ACE-
I/ARB. Tests for trend in the adjusted models compared outcomes for subjects with procedures performed in 2007 compared to those performed in 2004 to evaluate adjusted temporal associations.

As seen with most large dataset analyses, missing data were present. All variables used in the adjusted risk models had rates <1.0%. For the interventions investigated, rates of missing data were as follows: 1.7% for aspirin, β blockers, and lipid lowering therapy, and 1.8% for ACE-I/ARB therapy during the period studied. Given that the frequency of missing data was relatively low, when missing data was present for each of the four therapies investigated, it was assumed that the subject did not receive the medication on discharge.

All analyses were performed using JMP Pro, Version 10 (SAS Institute Inc., Cary, NC). Since this analysis utilized de-identified data, it met criteria for exemption from the University of Washington IRB review, where the dataset is stored, and was approved by the Wake Forest University IRB, where the analysis was performed.

**Results**

Patients that underwent CABG surgery were older, more likely to be male, and generally had more comorbidities and cardiovascular risk factors compared to patients undergoing PCI, aside from smoking status and history of prior MI (Table XIII). Patients that underwent CABG surgery were also more likely to have a LVEF \( \leq 40\% \), present in cardiogenic shock and/or need an intra-aortic balloon pump during hospitalization, have acute renal injury, and require post-procedure dialysis compared to patients undergoing PCI.
Patients undergoing PCI had statistically significantly higher unadjusted adherence rates of discharge with prescriptions for aspirin, ACE-I/ARB, and lipid lowering therapy compared to those undergoing CABG during the four year time period studied (Table XIV). The composite measure of discharge medication adherence was also higher for PCI during the study period (73.4% vs. 42.8%, p <0.01). However, there was a significant increase in adherence rates for all 4 therapies over the time period studied for both PCI and CABG (p-value for trend ≤0.03 within each treatment group during the study period for all 4 measures). Composite adherence rates for both groups showed a strong improvement over time (Figure 1).
Table XIII. Baseline characteristics and presentation variables for patients with STEMI undergoing coronary revascularization in Washington State from 2004-2007

<table>
<thead>
<tr>
<th>Variable</th>
<th>CABG (N= 692)</th>
<th>PCI (N= 9,260)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years</td>
<td>64.5 (11.0)</td>
<td>61.4 (12.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male gender</td>
<td>542 (78.4%)</td>
<td>6,826 (73.8%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Caucasian race</td>
<td>617 (89.2%)</td>
<td>8,291 (89.5%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Asian race</td>
<td>19 (2.7%)</td>
<td>207 (2.2%)</td>
<td>0.88</td>
</tr>
<tr>
<td>African American race</td>
<td>5 (0.7%)</td>
<td>174 (1.9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hispanic race</td>
<td>27 (3.9%)</td>
<td>248 (2.7%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Race other</td>
<td>24 (3.5%)</td>
<td>340 (3.7%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Smoker</td>
<td>417 (60.4%)</td>
<td>5,707 (61.7%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Diabetes</td>
<td>202 (29.2%)</td>
<td>1,783 (19.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>121 (17.6%)</td>
<td>518 (5.6%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>140 (20.2%)</td>
<td>963 (10.4%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>87 (12.6%)</td>
<td>488 (5.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>485 (70.1%)</td>
<td>5,288 (57.1%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prior coronary revascularization</td>
<td>218 (31.5%)</td>
<td>1,899 (20.5%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dialysis</td>
<td>13 (1.9%)</td>
<td>70 (0.8%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>372 (53.9%)</td>
<td>5,264 (57.0%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Three-vessel coronary disease</td>
<td>157 (22.7%)</td>
<td>838 (11.1%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean LVEF</td>
<td>46.6% (14.7)</td>
<td>49.7% (13.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Condition</td>
<td>PCI (N=720)</td>
<td>CABG (N=6,000)</td>
<td>P-value</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------------</td>
<td>----------------</td>
<td>---------</td>
</tr>
<tr>
<td>Emergent</td>
<td>117 (25.6%)</td>
<td>7,727 (83.5%)</td>
<td></td>
</tr>
<tr>
<td>Salvage</td>
<td>5 (0.7%)</td>
<td>66 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>Cardiogenic shock on presentation</td>
<td>101 (14.6%)</td>
<td>679 (7.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IABP† employed during hospitalization</td>
<td>171 (24.7%)</td>
<td>175 (1.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intra- or post-procedure myocardial infarction</td>
<td>5 (1.3%)</td>
<td>36 (0.9%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Post-procedure cerebrovascular accident</td>
<td>7 (1.0%)</td>
<td>53 (0.6%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Acute renal injury</td>
<td>112 (16.4%)</td>
<td>702 (8.1%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Post-procedure dialysis required</td>
<td>10 (1.4%)</td>
<td>30 (0.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean length of stay in days</td>
<td>9.2 (6.2)</td>
<td>4.2 (27.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVEF ≤ 40%</td>
<td>247 (35.7%)</td>
<td>1,857 (20.1%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean pre-procedure creatinine</td>
<td>1.16 (0.82)</td>
<td>1.07 (2.87)</td>
<td>0.02</td>
</tr>
<tr>
<td>Procedure priority</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Elective</td>
<td>102 (14.7%)</td>
<td>315 (3.4%)</td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>408 (59.0%)</td>
<td>1,147 (12.4%)</td>
<td></td>
</tr>
</tbody>
</table>

†Reported as number (%) unless noted to be mean value (SD); †IABP, intra-aortic balloon pump.

While the unadjusted odds of discharge with guidelines-based medical therapy were significantly higher for patients that underwent PCI compared to CABG for each of the medications investigated, after adjustment for baseline comorbidities, presentation variables, and temporal trends, the odds of discharge on aspirin $\beta$-blockers, and lipid lowering medications were similar between the two groups by the end of the study period in 2007 (Table XV). After adjustments, PCI patients still had significantly higher odds of being discharged with ACE-I/ARB (adjusted OR 2.27 [95% CI 1.49, 3.48]). However, in the adjusted model, there were also significant trends towards increased adherence in both the PCI and CABG groups for most of the four medications evaluated. For aspirin prescription in the CABG group, the OR for 2007 compared to 2004 was 3.96 (95% CI
1.46, 11.34). For the PCI group, the OR for 2007 compared to 2004 was 1.39 (95% CI 0.87, 2.22). For β-blocker at discharge for the CABG group, the OR for prescription at discharge for 2007 compared to 2004 was 2.04 (95% CI 0.89, 4.84) while for the PCI group it was 1.80 (1.30, 2.50). For lipid lowering medications, the OR for prescription at discharge for 2004 compared to 2007 for CABG subjects was 6.36 (95% CI 2.95, 14.47) and for PCI it was 1.27 (95% CI 0.92, 1.73). For ACE-I/ARBs the OR for prescription at discharge for CABG patients for 2007 compared to 2004 was 2.41 (95% CI 1.36, 4.32) and for PCI was 1.80 (95% CI 1.41, 2.31).

**Table XIV.** Adherence rates to guidelines-based secondary prevention measures at hospital discharge following STEMI stratified by revascularization method and year.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Procedure</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2004-2007</th>
<th>p-value for trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>CABG (N)‡</td>
<td>183</td>
<td>206</td>
<td>152</td>
<td>151</td>
<td>692</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCI (N)</td>
<td>2,307</td>
<td>2,230</td>
<td>2,357</td>
<td>2,365</td>
<td>9,260</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CABG</td>
<td>87.4%</td>
<td>93.7%</td>
<td>95.4%</td>
<td>93.4%</td>
<td>92.3%</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>95.2%</td>
<td>95.9%</td>
<td>92.1%</td>
<td>97.3%</td>
<td>95.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>p-value‡</td>
<td>&lt;0.01</td>
<td>0.15</td>
<td>0.16</td>
<td>0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>B blocker</td>
<td>CABG</td>
<td>82.0%</td>
<td>89.8%</td>
<td>93.4%</td>
<td>89.4%</td>
<td>88.4%</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>88.3%</td>
<td>91.4%</td>
<td>88.3%</td>
<td>94.7%</td>
<td>90.7%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>----------</td>
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<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>p-value</td>
<td>0.01</td>
<td>0.44</td>
<td>0.05</td>
<td>&lt;0.01</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE-I/ARB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG (N)</td>
<td>151</td>
<td>180</td>
<td>131</td>
<td>128</td>
<td>590</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI (N)</td>
<td>1,531</td>
<td>1,586</td>
<td>1,616</td>
<td>1,666</td>
<td>6,399</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>31.5%</td>
<td>38.8%</td>
<td>51.4%</td>
<td>55.2%</td>
<td>43.1%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>60.6%</td>
<td>68.2%</td>
<td>69.3%</td>
<td>75.0%</td>
<td>68.3%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid lowering therapy</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>70.5%</td>
<td>83.5%</td>
<td>92.8%</td>
<td>90.1%</td>
<td>83.5%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>90.5%</td>
<td>91.7%</td>
<td>88.3%</td>
<td>92.6%</td>
<td>90.8%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.09</td>
<td>0.24</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite Adherence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>30.1%</td>
<td>34.0%</td>
<td>55.3%</td>
<td>57.6%</td>
<td>42.8%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>67.0%</td>
<td>71.8%</td>
<td>75.1%</td>
<td>79.3%</td>
<td>73.4%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
p-values for trend compare year-to-year trends for a specific procedure group during the study period; these p-values compare annual percentages between procedure groups; the N for aspirin, β-blockers, and lipid lowering therapy are all the same for the PCI and CABG groups for each year evaluated; the N are different for ACE-I/ARB as specified in the Table.

**Figure 1.** Composite guidelines-based secondary prevention medication prescription adherence at discharge for STEMI patients undergoing coronary revascularization by quarter. Error bars represent standard error.
Discussion

In an observational analysis of a state-wide registry of patients undergoing coronary revascularization after STEMI, we found that patients that underwent CABG had a lower rate of guidelines-based therapies prescribed at discharged compared to patients undergoing PCI over the 4-year period studied. We demonstrated that these differences diminished over time and were partly explained by patient-level differences.

Previous Studies on Secondary Prevention Guidelines Adherence

Foody et al. evaluated 37,376 patients included in the CMS’ National Heart Care Program from April, 1998 to March, 1999. Among CABG patients in that one-year sample, aspirin, β blockers, ACE-I, and lipid lowering therapy were 10% to 20% less frequently prescribed than in similar patients that underwent PCI.96 Similar results were published by Fox et al. in a retrospective analysis in 2002 from the Manchester Heart Centre PCI and CABG registries.115 Hiratzka et al. evaluated hospitals participating in the Get with the Guidelines program from 2000-2005 and reported an increase in the discharge medication performance measures following CABG during that period, though the rates were still significantly lower than PCI.97 Publication of these and similar studies lead to widespread efforts to educate practitioners, improve hospital processes, and implement public reporting of hospital quality measures. A study conducted from 2002-2005 of the STS’ National Cardiac Database showed that low-intensity educational efforts, including both provider and patient instruction, along with site-specific feedback, led to improved adoption of secondary
Table XV. Unadjusted and adjusted* odds ratios for adherence to prescription of guidelines-based secondary prevention therapies at discharge for patients undergoing PCI compared to CABG surgery

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>2.82</td>
<td>2.58 (1.40, 4.63)</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>1.58</td>
<td>1.07 (0.51, 2.13)</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>1.79</td>
<td>1.61 (0.68, 4.49)</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>2.55</td>
<td>2.00 (0.75, 4.83)</td>
<td></td>
</tr>
<tr>
<td>2004-2007</td>
<td>1.61</td>
<td>1.39 (0.96, 1.98)</td>
<td></td>
</tr>
<tr>
<td><strong>β-blocker</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>1.66</td>
<td>1.43 (0.89, 2.27)</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>1.20</td>
<td>1.02 (0.57, 1.77)</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>1.89</td>
<td>1.89 (0.92, 4.33)</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>2.11</td>
<td>1.96 (0.92, 3.96)</td>
<td></td>
</tr>
<tr>
<td>2004-2007</td>
<td>1.27</td>
<td>1.09 (0.81, 1.45)</td>
<td></td>
</tr>
<tr>
<td><strong>Lipid Lowering</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>3.99</td>
<td>3.14 (2.07, 4.74)</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>2.19</td>
<td>1.56 (0.96, 2.50)</td>
<td></td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>1.70</td>
<td>1.46 (0.70, 3.36)</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>1.38</td>
<td>1.09 (0.51, 2.16)</td>
<td></td>
</tr>
<tr>
<td>2004-2007</td>
<td>1.94</td>
<td>1.61 (1.24, 2.07)</td>
<td></td>
</tr>
<tr>
<td><strong>ACE Inhibitor/ARB</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>3.35</td>
<td>3.18 (2.20, 4.64)</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>3.39</td>
<td>3.41 (2.39, 4.91)</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>2.86</td>
<td>2.65 (2.02, 3.33)</td>
<td></td>
</tr>
</tbody>
</table>
2007 & 2.13 (1.51, 1.77) & 2.27 (1.49, 3.48) \\
2004-2007 & 2.43 (1.72, 3.43) & 2.26 (1.47, 3.51) \\
\hline
Composite & 
2004 & 4.73 (3.43, 6.60) & 3.37 (2.34, 4.89) \\
2005 & 4.95 (3.67, 6.72) & 3.45 (2.25, 4.91) \\
Adherence & 2006 & 2.44 (1.75, 3.40) & 1.91 (1.26, 2.88) \\
2007 & 2.81 (2.00, 3.94) & 2.28 (1.50, 3.46) \\
2004-2007 & 3.68 (3.15, 4.31) & 2.71 (2.25, 3.26) \\
\hline

\*Adjusted for: age, diabetes, PVD, hypertension, prior MI, CHF, procedure priority, year procedure performed, LVEF, and shock. ACE-I/ARB refers only to patients who were considered eligible and was adjusted for ARI during hospitalization in addition to the variables above.

prevention measures in post-CABG patients. In 2005, the Society of Thoracic Surgeons launched the Quality Measurement Task Force to measure and improve adherence to quality metrics among surgical programs, which was implemented by hospitals in Washington State between 2005-2006. Our data show a significant improvement in the investigated measures during the time period in late 2005 to early 2006 in which CMS began requesting public reporting and COAP began publishing hospital level quality data, with substantial improvement in discharge prescriptions among patients who underwent CABG during their hospitalization. Our results are very similar to those presented in the SYNTAX trial, which was conducted over a similar same period. This is only a temporal association though and the etiology of the changes in prescribing practices noted in our study is likely multifactoral, including the
Exploring Differences in Secondary Prevention Adherence

Given the data supporting the use of the medications evaluated in this study in reducing peri-MI morbidity and mortality, it is encouraging to see that the use of these medications post-CABG has been trending towards rates closer to those for post-PCI patients. The fact that patient comorbidities appear to explain at least some of the variation in these performance measures between these two groups implies that adherence to quality measures is not simply a problem with differences in hospital processes for CABG versus PCI patients. Patients undergoing CABG tend to be older, have an increased number of baseline comorbidities, and are more prone to post-procedure anemia, hypotension, and/or ARI, which may impact providers’ inclination to prescribe secondary prevention measures at discharge. This so-called “treatment-risk paradox” may be playing a major role in the lack of adherence to guidelines-based therapy and interventions aimed at increasing adherence should be targeted at improving documentation of contraindications and educating practitioners about evidence-based therapies in patients with severe, comorbid illnesses, regardless of the procedure received. One of the largest discrepancies observed in this study between CABG and PCI patients was seen in the prescription of ACE-I/ARBs at discharge, even after adjustment for ARI, which potentially reflects issues related to hypotension and impairment of renal function in the post-operative period. The COAP database did not capture whether patients had a history of CRI prior to admission, so we may have underrepresented the number of patients eligible for ACE-I/ARBs at discharge, which
would affect adherence estimates. Although it may not be necessary to start an ACE-I/ARB immediately at discharge in such patients, this data underscores the importance early interaction with a combined multidisciplinary team to ensure that providers caring for post-surgical patients prioritize the implementation of secondary prevention measures as soon as patients’ conditions permit in the follow-up period.

**Limitations**

As this is a registry-based study, we could not differentiate between failure to document a contraindication or oversight by the discharging provider in prescribing the indicated therapy at discharge. Similarly, metrics in COAP are limited to in-hospital measures, so patients in which surgeons and cardiologists chose to start therapy in the first or second week post-discharge to ensure that post-operative renal insufficiency and/or anemia had stabilized would not be reflected by this data. We also restricted our analysis to patients with STEMI due to potential inconsistencies and limited specificity of the diagnoses of non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina. Finally, we are presenting an association between public reporting and improved guidelines adherence, but the retrospective nature of this analysis restricts our ability to speculate further than the temporal association between these trends.

**Conclusions**

Trends in guidelines-based secondary prevention adherence from 2004-2007 for CABG patients post-STEMI in Washington State showed improvement, concurrent with the institution of public reporting by COAP. The reduction in hospital mortality and major adverse cardiac events in long-term follow-up associated with secondary
prevention at discharge underscores the importance of continuing towards improving adherence to these guidelines-based measures.
Chapter 3: Additional Secondary Prevention Metric Analyses in the COAP Registry

I. Cardiac Rehabilitation

The COAP Registry was designed to capture multiple aspects of the acute care of subjects undergoing coronary revascularization in Washington State. As described in Chapter 2, a major aspect of the care of this patient group is the medication regimen prescribed at discharge. However, medical therapy is only part of the comprehensive set of recommendations by the AHA and ACCF in regards to CAD secondary prevention. As described in Chapter 1, referral to cardiac rehabilitation is also a class I recommendation as exercise in a structured environment has been proven to decrease both morbidity and mortality in this patient group.\textsuperscript{15} Structured rehabilitation became a class I recommendation in 2006.\textsuperscript{113,119} Therefore, the COAP registry was modified in at the end of 2005 to start keeping track of referral to cardiac rehabilitation for this subject group starting in 2006.

Analysis of Cardiac Rehabilitation Adherence

There was very good documentation of whether subjects were referred for rehabilitation at discharge in the COAP registry in 2006-2007, with 0.2\% (N=4/2509) of subjects with missing data in 2006 and 0.8\% (N=20/2516) in 2007. Given the low rate of missing data, it was assumed that if there was a missing value for this variable in the database that they were not referred. All subjects in our study were assumed to be candidates for cardiac rehabilitation referral at the time of discharge unless noted to be ineligible. 303 CABG subjects from 2006-2007 and 4,722 PCI subjects from 2006-2007 were deemed eligible for this analysis.
Table XVI shows that there are significant differences in the unadjusted rates of cardiac rehabilitation referral at discharge from 2006-2007 between the two groups. Notably, rates of compliance with this measure are much higher for the CABG group, in stark contrast to the four medications investigated in Chapter 2. The rates of compliance with cardiac rehabilitation prescription at discharge were significant below those for three of the four medications (aspirin, β blockers, and cholesterol lowering medications) investigated for both procedures. This reduced compliance with the rehabilitation metric resulted in significantly reduced composite adherence rates for both groups when compared to the rates excluding cardiac rehab referral compliance (Figure 2, compared to Figure 1 in Chapter 2). Therefore, while the compliance with rehab referral was significantly better in the CABG group compared to those undergoing PCI, if this metric is included in the reported in the composite adherence scores, both subject groups appear to have much worse composite adherence scores compared to their scores excluding this metric. Interestingly, including this metric resulted in no statistical difference in adjusted overall compliance with these 5 metrics at discharge between the two procedures for 2006 and 2007 (Tables XVI and XVII).
Table XVI. Adherence rates to cardiac rehabilitation referral at hospital discharge following STEMI stratified by revascularization method and year.

| Intervention                  | Procedure | 2006   | 2007   | 2004-2007 | p-value for trend*
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Rehabilitation</td>
<td>CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Referral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=303)</td>
<td></td>
<td>70.4%</td>
<td>72.2%</td>
<td>71.3%</td>
<td>0.33</td>
</tr>
<tr>
<td>PCI</td>
<td></td>
<td>45.4%</td>
<td>51.1%</td>
<td>48.2%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Composite Adherence</td>
<td>CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=692)</td>
<td></td>
<td>34.7%</td>
<td>42.4%</td>
<td>38.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PCI (N=9,260)</td>
<td></td>
<td>33.7%</td>
<td>41.9%</td>
<td>37.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.77</td>
<td>0.91</td>
<td>0.78</td>
<td></td>
</tr>
</tbody>
</table>

p-values for trend compare year-to-year trends for a specific procedure group during the study period; these p-values compare annual percentages between procedure groups
**Figure 2.** Composite guidelines-based secondary prevention medication prescription adherence at discharge, including cardiac rehabilitation referral, for STEMI subjects undergoing coronary revascularization by quarter. Error bars represent standard error.
Table XVII. Unadjusted and adjusted* odds ratios for adherence to prescription of guidelines-based secondary prevention therapies, including cardiac rehabilitation referral, at discharge for subjects undergoing PCI compared to CABG surgery

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>2006</td>
<td>0.35 (0.24, 0.50)</td>
<td>0.35 (0.21, 0.49)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>2007</td>
<td>0.40 (0.28, 0.58)</td>
<td>0.26 (0.17, 0.40)</td>
</tr>
<tr>
<td>Referral</td>
<td>2006-2007</td>
<td>0.38 (0.29, 0.48)</td>
<td>0.29 (0.21, 0.41)</td>
</tr>
<tr>
<td></td>
<td>2004</td>
<td>4.73 (3.43, 6.60)</td>
<td>3.37 (2.34, 4.89)</td>
</tr>
<tr>
<td>Composite</td>
<td>2005</td>
<td>4.95 (3.67, 6.72)</td>
<td>3.45 (2.25, 4.91)</td>
</tr>
<tr>
<td>Adherence</td>
<td>2006</td>
<td>0.95 (0.68, 1.35)</td>
<td>0.77 (0.50, 1.17)</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>0.98 (0.70, 1.37)</td>
<td>0.65 (0.43, 1.01)</td>
</tr>
</tbody>
</table>

*Adjusted for: age, diabetes, peripheral vascular disease, hypertension, prior myocardial infarction, congestive heart failure, procedure priority, year procedure performed, left ventricular ejection fraction, and shock

One of the explanations for the difference in compliance rates between subject groups could be the condition of subjects after their respective procedures. As shown in Chapter 2, CABG subjects are more likely to be older and have more comorbidities prior to their procedure and have more post-procedure complications, leading to a length of stay almost twice as long as those for subjects undergoing PCI (9.2 vs 4.2 days, p<0.01). Post-CABG subjects are likely to need rehabilitation for reasons in addition to solely cardiac reasons, including the performance of activities of daily living, etc. due to the more extensive nature of the procedure, which would lead to a higher rate of prescribing post-procedure rehabilitation. This brings up the possibility of differential
misclassification as well, as subjects post-CABG could have been labeled as receiving a referral to cardiac rehabilitation on discharge if they went to a skilled nursing facility for reasons other than being post-MI, which would skew the results towards higher compliance in post-CABG subjects. Unfortunately the COAP database does not capture the ultimate disposition of subjects after discharge, so this postulate was unable to be validated in this data set.

It is also unclear why referrals for post-procedure rehabilitation were lower for both groups in general, similar to the prescription of ACE-I/ARBs. There is always the possibility that providers were unaware of the class I recommendation for this metric as this transition did not occur until 2006 and it has been well documented that it takes several years for recommendations to be disseminated and embraced by the general medical community.\textsuperscript{120} Another possibility for the poor compliance with this metric could be the relative lack of supervised rehabilitation centers in Washington State. While the COAP registry includes 35 hospitals that perform coronary revascularization spread across the state, there are only 10 certified rehabilitation sites in the state, mostly located in larger cities (Seattle, Spokane, Olympia, and Yakima), which could limit many subjects cared for at hospital sites without an associated rehabilitation facility from participating in therapy. This could represent a large barrier in compliance with this metric for subjects care for at facilities far away from these centralized rehabilitation facilities, especially since home-based physical activity regimens are only recommended for low risk subjects (i.e. non-ACS subjects).\textsuperscript{15}
I. Tobacco Cessation Counseling

Smoking cessation counseling has long been a part of the treatment of subjects after an acute MI to prevent progression and recurrence of atherosclerotic CAD. This intervention received official mention in the CAD secondary prevention guidelines as a class I recommendation back in 2001 and is supported by literature dating prior to the early 1990’s. Given the importance of tracking this measure in this patient group, the COAP database tracks whether subjects identified as regular smokers in the past 12 months preceding their acute MI received tobacco cessation counseling prior to discharge.

The COAP registry was initially set up to look at readily trackable and reproducible measures, such as interventions performed and medications prescribed during the acute hospitalization of this patient population. However, as the registry grew and became increasingly utilized, more measures were added to increase the breadth of the scope of care these subjects received during their hospitalization. As with cardiac rehabilitation measures, smoking cessation counseling metrics were not well-captured until later in the database’s implementation, with good reporting not occurring until 2006, leaving 2 years (2006, 2007) during our study period to investigate compliance with this metric, similar to the time frame for cardiac rehabilitation referral. Unfortunately, while cardiac rehabilitation had low rates of missing data (<1.0% for both years investigated), the rate of missing data for smoking cessation counseling was high for both procedures in both years: 19.9% (N= 469/2357) for PCI in 2006, 22.6% (N= 535/2365) in PCI for 2007, 28.9% (N=44/152) for CABG in 2006, and 23.2% (N=35/151) for CABG in 2007.
An analysis comparing those with recorded data regarding whether they received appropriate smoking cessation counseling versus those with missing data for this metric showed that the distribution of missing variables for whether subjects receiving smoking cessation counseling was not random. When looking at the entire group (PCI and CABG subjects), it was found that if you were identified as a smoker prior to coronary revascularization (p <0.01) or you were an emergent procedure (as opposed to an elective procedure, p 0.02), you were significantly more likely to have missing data with regards as to whether you received appropriate smoking cessation counseling at discharge. When this was broken into groups based on revascularization method (PCI vs CABG), post-PCI current smokers (p <0.01) were more likely to have missing data while post-CABG current smokers (p <0.01), females (p <0.01), and those with emergent procedures (p <0.02) were more likely to have missing data for this metric. Therefore, it appears that there was a significant amount of bias in whether subjects’ were recorded as having received smoking cessation counseling. Given the higher percentage of males and lower percentage of emergent procedures in the CABG group, if subjects with missing data are imputed as not having received the metric, this may falsely elevate the compliance of the CABG compared to the PCI group. If, however, subjects with missing data are excluded from the analysis of this metric, it is less clear how this misclassification will affect the results, though bias is likely to result.

The lack of 4 year followup and high missing data rate for this metric lead to its exclusion in the main analyses in Chapter 2, but given its relative importance in the care of post-MI subjects, some analyses of adherence to this metric will be presented in this Chapter. For these analyses, we only evaluated subjects reported as smokers in the past
12 months as candidates for smoking cessation counseling. While there are several ways
to handle missing data in a database like COAP, given the high frequency of missing
data, we will present that data in 2 formats, one of which excludes subjects with missing
data and one which imputes nonadherence to those subjects with missing data, since all
of the subjects with missing data were identified as smokers prior to their admission. The
reason for imputing nonadherence for these subjects instead of using more sophisticated
modeling (normal-model multiple imputation, maximum likelihood methods, etc.) is that
all of the missing values are linked to subjects known to be current smokers, likely
illustrating a selection bias in the data set. Further imputations would likely provide little
to no additional information due to the high frequency of missing data.

**Smoking Cessation Counseling Adherence, Excluding Those with Missing Data**

Excluding subjects with missing data, 106 CABG and 1,881 PCI subjects were
identified as current smokers and thus eligible for smoking cessation intervention during
2006-2007. Compliance was quite good for both groups, with improvements in
compliance with the metric from 2006-2007 ([Table XVIII](#)). While anything less than
100% compliance with smoking cessation counseling would decrease these the composite
compliance frequencies for these subjects compared to leaving the smoking cessation
metric out (see compliance rates in Table 2 of Chapter 2), adding it to the 4 medications
investigated in Chapter 2 did not change the composite compliance rates in a clinically
meaningful way except for the CABG group in 2006. [Figure 3](#) and [Table XIX](#) re-
illustrate that adding smoking cessation into the unadjusted composite scores continues to
show PCI subjects as having almost twice the composite adherence rates at discharge
compared to CABG subjects during 2006-2007, without any clinically significant
difference in composite adherence when compared to adherence without adding in the smoking cessation metric. Given the instability of the estimates for smoking cessation, this was not unexpected. When these metrics were adjusted for subject-level differences though, there was still a difference between the two procedures in the odds of receiving all of the metrics they were eligible for, favoring PCI subjects. However, this is a simplistic method of accounting for missing data and the conclusions without using more sophisticated methods are likely biased.

Table XVIII. Adherence rates to guidelines-based secondary prevention measures, including smoking cessation counseling, at hospital discharge following STEMI stratified by revascularization method and year.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Procedure</th>
<th>2006</th>
<th>2007</th>
<th>2006-2007</th>
<th>p-value for trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking Cessation</td>
<td>CABG</td>
<td>55</td>
<td>51</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>916</td>
<td>965</td>
<td>1,881</td>
<td></td>
</tr>
<tr>
<td>Counseling</td>
<td>CABG</td>
<td>87.2%</td>
<td>96.1%</td>
<td>91.5%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>88.3%</td>
<td>92.1%</td>
<td>90.3%</td>
<td>0.04</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.82</td>
<td>0.26</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>Composite Adherence</td>
<td>CABG (N=692)</td>
<td>41.2%</td>
<td>49.6%</td>
<td>47.7%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>PCI (N=9,260)</td>
<td>65.2%</td>
<td>68.3%</td>
<td>67.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

p-values for trend compare year-to-year trends for a specific procedure group during the study period; *these p-values compare annual percentages between procedure groups
Figure 3. Composite guidelines-based secondary prevention medication prescription adherence at discharge, including smoking cessation counseling, for STEMI subjects undergoing coronary revascularization by quarter. Error bars represent standard error.
Table XIX. Unadjusted and adjusted* odds ratios for adherence to prescription of guidelines-based secondary prevention therapies, including smoking cessation counseling, at discharge for subjects undergoing PCI compared to CABG surgery

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>2006</td>
<td>1.10 (0.45, 2.35)</td>
<td>0.59 (0.18, 1.67)</td>
</tr>
<tr>
<td>Cessation</td>
<td>2007</td>
<td>0.48 (0.08, 1.58)</td>
<td>0.48 (0.03, 2.65)</td>
</tr>
<tr>
<td>Counseling</td>
<td>2006-2007</td>
<td>1.16 (0.61, 2.51)</td>
<td>0.64 (0.23, 1.53)</td>
</tr>
<tr>
<td>Composite</td>
<td>2004</td>
<td>4.73 (3.43, 6.60)</td>
<td>3.37 (2.34, 4.89)</td>
</tr>
<tr>
<td>Adherence</td>
<td>2005</td>
<td>4.95 (3.67, 6.72)</td>
<td>3.45 (2.25, 4.91)</td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>2.53 (1.71, 3.69)</td>
<td>1.68 (1.07, 2.81)</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>2.37 (1.50, 4.12)</td>
<td>2.31 (1.22, 3.11)</td>
</tr>
</tbody>
</table>

*Adjusted for: age, diabetes, peripheral vascular disease, hypertension, prior myocardial infarction, congestive heart failure, procedure priority, year procedure performed, left ventricular ejection fraction, and shock

Smoking Data Imputing Values for Those with Missing Data

Using the same 2 years of data (2006-2007), subjects identified as current smokers and with missing values for whether they received smoking cessation counseling at discharge were then assumed to not have receive counseling. As previously mentioned, the reason for this assumption for these subjects instead of using more sophisticated modeling was that all of the missing values are linked to subjects known to be current smokers, likely illustrating a selection bias in the data set. Using this method, there were 184 CABG subjects and 2,878 PCI subjects identified as current smokers and thus eligible for smoking cessation intervention during this 2 year period. Given the high
rate of missing data for this metric during that period, this resulted in significant
decreases in adherence with this metric for both procedure groups and subsequent
decreases in the odds of composite adherence for both groups as well (Tables XX and
XXI). Interestingly, using this imputation method results in no difference in the adjusted
odds of composite adherence between the two groups in 2006 or 2007. However, the
odds ratios for composite adherence adding in either cardiac rehabilitation or smoking
cessation counseling (excluding subjects with missing values or using imputed values)
are significantly ameliorated compared to the odds ratios using just the 4 medications
investigated in Chapter 2, again illustrating the possible differences in outcomes that
could be reported for these subject groups using the same data set, which could have
large ramifications for public reporting and performance-based reimbursement,
depending on which metrics are used in these calculations.
Table XX. Adherence rates to guidelines-based secondary prevention measures, including smoking cessation counseling with imputed variables, at hospital discharge following STEMI stratified by revascularization method and year.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Procedure</th>
<th>2006</th>
<th>2007</th>
<th>2004-2007</th>
<th>p-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CABG (N)</td>
<td>98</td>
<td>86</td>
<td>184</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCI (N)</td>
<td>1,384</td>
<td>1,494</td>
<td>2,878</td>
<td></td>
</tr>
<tr>
<td>Smoking Cessation Counseling</td>
<td>CABG</td>
<td>49.0%</td>
<td>57.0%</td>
<td>52.7%</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>58.5%</td>
<td>59.5%</td>
<td>59.0%</td>
<td>0.57</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.07</td>
<td>0.64</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Composite Adherence</td>
<td>CABG</td>
<td>22.1%</td>
<td>31.3%</td>
<td>28.6%</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>PCI</td>
<td>46.4%</td>
<td>47.6%</td>
<td>46.9%</td>
<td>0.36</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

p-values for trend compare year-to-year trends for a specific procedure group during the study period
† these p-values compare annual percentages between procedure groups
Table XXI. Unadjusted and adjusted\(^*\) odds ratios for adherence to prescription of guidelines-based secondary prevention therapies, including smoking cessation counseling with imputed variables, at discharge for subjects undergoing PCI compared to CABG surgery.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>2006</td>
<td>1.47 (0.97, 2.21)</td>
<td>1.18 (0.68, 2.02)</td>
</tr>
<tr>
<td>Cessation</td>
<td>2007</td>
<td>1.11 (0.71, 1.72)</td>
<td>1.35 (0.76, 2.39)</td>
</tr>
<tr>
<td>Counseling</td>
<td>2006-2007</td>
<td>1.29 (0.96, 1.74)</td>
<td>1.23 (0.83, 1.82)</td>
</tr>
<tr>
<td></td>
<td>2004</td>
<td>4.73 (3.43, 6.60)</td>
<td>3.37 (2.34, 4.89)</td>
</tr>
<tr>
<td>Composite</td>
<td>2005</td>
<td>4.95 (3.67, 6.72)</td>
<td>3.45 (2.25, 4.91)</td>
</tr>
<tr>
<td>Adherence</td>
<td>2006</td>
<td>2.18 (1.32, 2.87)</td>
<td>1.35 (0.91, 1.98)</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>1.65 (1.17, 2.85)</td>
<td>1.60 (1.05, 2.31)</td>
</tr>
</tbody>
</table>

\(^*\)Adjusted for: age, diabetes, peripheral vascular disease, hypertension, prior myocardial infarction, congestive heart failure, procedure priority, year procedure performed, left ventricular ejection fraction, and shock.

II. Measuring Performance

The second and third Chapters of this thesis focused on several metrics by which providers and hospitals can be evaluated as an approximate of the quality of health care they deliver. Health care quality has been classically assessed utilizing three different measurements: structural measures, process measures, and outcome measures. This three-element model was developed by Avedis Donabedian in 1966 and is still widely used.\(^{121}\) Structural measures are the characteristics associated with a health care setting,
such as such as specifications for a building, management systems, board certification, etc. Process measures are the activities performed in the health care setting. They can measure whether, for example, evidence-based care guidelines were followed, but do not indicate whether a patient’s health actually improved since they focus on the care process itself and not the outcome of these actions. These measures are used based on the assumption that better outcomes should result from the implementation of evidence-based care process measures. Outcome measures are the results achieved for a patient after a given set of interventions are implemented. They seek to determine whether the desired outcome(s) resulted from a given intervention. Outcome measures can be either a direct measure of an outcome of interest or a surrogate measure of an outcome, assumed to be a proxy for a particular outcome. An example of a direct measure of the recurrence of CAD would be measuring whether a patient had a MI during a period of time while a surrogate measure for CAD might be whether a subject undergoes PCI during that period, since it is usually assumed that a subject undergoes PCI to treat CAD.

In general, the data needed for determining performance with these 3 general types of measures are obtained through three sources: administrative data, medical records, and patient surveys. Administrative data are derived mostly from insurance claims and enrollment files. Such data are relatively easy and inexpensive to collect but lack clinical detail. Medical records provide substantially more detailed information regarding the patients’ medical conditions and treatment(s) rendered but are substantially less standardized, resulting in significant variations in the quality of this type of data. Survey data are typically collected to measuring patient experience with care. In the US, the Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey is a well-
known example of this type of survey. The survey was developed by the AHRQ, has been endorsed by the National Quality Forum, and is publicly reported by many health insurance plans.\textsuperscript{122}

**Use of Performance Measure Data**

Performance measure data is often used for three main purposes: quality improvement efforts, pay-for-performance incentive programs, and public reporting of outcomes. Public reporting serves several important purposes, including informed decision-making for consumers (patients) and providing some accountability for taxpayers and other purchasers of health care. For example, CMS utilizes its large administrative datasets to make performance measurement data available to aid its subscribers in selecting providers and care facilities. Their website provides comparative performance information for hospitals, nursing homes, and providers they have the choice of using for health-related services. However, the impact of these measures on patient choices is unclear. It has been reported that these public reports seem to have insignificant impacts on the selection of providers and facilities by patients, thought to be because patients are unaware that this type of information is available.\textsuperscript{123}

CMS also uses performance measurements as part of a payment scheme in several of its pay-for-performance projects, which provide financial rewards or penalties to providers and facilities based on their performance on certain quality measures. This structure is centered on rewarding optimal care at the lowest feasible cost. A recent example of this type of program is Medicare’s ESRD Quality Incentive Program, which began in 2010 and began affecting payment to providers in 2012. The program is essentially a bundled-payment and quality incentive program for dialysis facilities. The
program measures included outcomes, process of care, safety measures, and patient-experience reporting. Both achievement of certain benchmarks and improvement over time are rewarded.\textsuperscript{124}

**Obstacles in Measuring Health Care Quality**

There has been heavy reliance on process, structural, and outcome measures to assess the quality of health care. However, each of these gauges has significant limitations that can skew the view of actual care being provided by providers and/or institutions. For example, a common structural measure is the volume of a certain type of procedure performed by a certain provider or institution. This measure is commonly used as there is evidence that for many procedures, higher volumes translate to improved outcomes.\textsuperscript{125} However, the relationship between volume and outcomes is variable by both procedure and provider and may not always be an accurate reflection of the care being provided.\textsuperscript{126}

Process measures are the most commonly used type of quality measure currently as they usually reflect professional standards of care. The provider is generally thought to have more control as to whether these measures are met as opposed to more nebulous concepts such as organizational culture or available technology, which can also affect patient care and are more difficult to measure.\textsuperscript{127} The metrics used in our study (Chapters 2 and 3) would be included in this group.

Despite the prevalence of process measures in many quantifications of the value of health care delivery, there are significant challenges posed by utilizing these metrics which can present a misleading picture of the care being delivered. First, there are few true process measures available with which to evaluate the complex milieu of health care
delivery. We have metrics to evaluate diagnosis errors and the appropriateness of intervention (or lack thereof), but what about measures regarding efficiency, care coordination, resource utilization, and healthcare team dynamics? These variables can have significant impacts on patient satisfaction and outcomes but we have few, if any, metrics by which to measure them. There is also evidence that many of the long-standing process measures utilized in process of care evaluations are not always predictive of outcomes, nor do they always direct consumer decisions. In fact, several CMS process measures for MI, CHF, and pneumonia have been shown to not be predictive of overall short-term mortality. There is also a concern that facilities could shift resources towards meeting certain performance measures to receive a “good score” while diverting from areas that do not have adequate measures of quality. Finally, there are practical difficulties to process measurements, such as a reliance on measures that are easily obtainable from the medical record, such as lab tests, procedures, or prescriptions as they can be more readily be put into a database format for analysis.

Given the limitations in structural and process metrics in assessing quality, there is an increasing interest in measuring outcome metrics. Outcome metrics encompass some intangible variables that can be lacking in process measures and are a more tangible measure of value to consumers. However, there are significant impediments to accurately measuring outcomes metrics as well. One problem is surveillance bias, a nonrandom type of information bias. Surveillance bias revolves around the idea that “the more you look, the more you find”. Closer monitoring for something can lead to higher rates of detecting the item of interest. There is also the problem of sample size. Poor outcomes are usually relatively rare, so large sample sizes are needed to have acceptable
power to detect differences in these infrequent outcomes between providers, facilities, etc. One method to deal with this is coalescing data either of longer periods of time or clustering smaller groups into larger entities, though this decreases the specificity in the comparison of the outcomes given that individual members or certain temporal periods may drive the overall results of the outcome comparison.

Another challenge associated with outcome metrics is the validity of outcome measure of interest. In other words, is the metric being used truly measuring the outcome of interest? Outcome measures used to assess health care quality have shown a lack of validity for multiple reasons, including the use of multiple heterogenous and/or inconsistent data sources, excluding pertinent subjects from calculations (exclusion bias), and use of outcomes that do not accurately reflect the concept of quality it was intended to measure.\textsuperscript{134} Another difficulty with outcome measures lies in the risk adjustments often needed for accurate comparisons. An individual patient’s outcome is not simply the result of the effectiveness of medical care, but is also impacted by a patient-level factors (socioeconomic status, comorbidities, etc), facility level factors (size of facility, geographic location, nurse: patient ratios, etc), and treatment/procedural-level factors that can vary widely from patient-to-patient experience. One of the advantages of outcome measures is that some of these factors are accounted for when looking at an individual outcome (as opposed to a process measure, as previously noted); however, this is not the case when outcomes between individuals, practitioners, or facilities are compared head-to-head.\textsuperscript{135} While there are numerous risk adjustment methods to take into account these differences in patients, providers, and facilities, there is no one standard method widely
used and different risk adjustment approaches that utilize dissimilar operational decisions have different consequences on outcomes, making cross-comparisons difficult.\textsuperscript{136}

While measuring the quality of health care can provide data to guide quality improvement, consumer information, and incentivization, it is technically difficult and prone to error. There have been multiple reports illustrating the widespread variation in the process and outcome metrics commonly used to assess quality.\textsuperscript{137} However, efforts are being made to standardize some of the variables underlying these inconsistencies. The AHA and ACCF have developed specific guidelines for the collection of data and how to specifically address some of the challenges of measuring health care quality in several scientific statements.\textsuperscript{138, 139} The Institute of Medicine also released \textit{Crossing the Quality Chasm} in 2001, which encouraged the need for increased accountability and transparency behind the variations in care affecting health outcomes.\textsuperscript{140}

The measures used in our study (Chapters 2 and 3) are process measures and, as such, are imperfect measures of patient outcomes. They were readily available from an existing database but are limited by temporal restraints and limitations from retrospective database extraction. However, they were chosen for the study as they are the measures cited by agencies reporting to the public on health care quality and used as metrics by institutions providing reimbursement for the care of the subjects studied. Therefore, while they are imperfect measures, they reflect metrics both providers and hospitals are gearing care towards in order to attract business and obtain payment for services. Given the imperfections and wide variation in these metrics, there is a significant need for improved collection of process and outcome metrics along with the myriad of variables that can affect them. There is also a question of whether these process measures should
be bundled as a composite measure of care. The analyses in Chapter 3 showed how widely these composite measurements can vary depending on how you measure the various metrics and what is included in the bundles. These are just a few of the numerous issues that need to be tackled moving forward in order to more accurately measure and compare the value of care STEMI patients are receiving across Washington State.

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- **Wake Forest University Health Science**, Winston-Salem, NC. July 2011-June 2013. NIH T32 CVD Epidemiology Training Program (T32 HL076132), Dr. David Herrington, Program Director


- **University of Virginia School of Medicine**, Charlottesville, VA. August 2004 – May 2008. M.D.
- Furman University, Greenville, SC. August 2000- June 2004. B.S., Chemistry with minor in Biochemistry, magna cum laude.

Honors and Awards

Postgraduate
- First place, Fellow Research Gold Award, Department of Internal Medicine Sixth Annual Resident and Fellow Research Day, Wake Forest University School of Medicine, 2012
- Honorable Mention, 2010 Johns Hopkins General Internal Medicine Housestaff Research Awards Competition, 2010

Research Experience

Fellowship
- **Topic:** The HEART Pathway trial. A RCT investigating use of the HEART score in triaging patients with chest pain in the Emergency Department. **Role:** co-investigator. **Where:** Wake Forest Baptist Medical Center. **When:** September 2012 to present.

- **Topic:** The association between self-assessed medication compliance scores and blood pressure control: A sub-study of the SPRINT trial. **Mentor:** David Goff, Jr, MD, PhD. **Role:** principal investigator. **Where:** Wake Forest Baptist Medical Center. **When:** May 2012 to present.

- **Topic:** Systolic Blood Pressure Intervention Trial (SPRINT). SPRINT is a RCT examining the effect of a high blood pressure treatment strategy aimed at reducing systolic blood pressure to a lower goal than is currently recommended. **Role:** Site Co-Investigator in charge of recruitment. **Where:** Wake Forest Baptist Medical Center. **When:** February 2012 to present.

- **Topic:** The interaction between thoracic aortic stiffness and left ventricular function: A study of the MESA cohort. **Mentor:** Greg Hundley, MD. **Role:** co-investigator. **Where:** Wake Forest Baptist Medical Center. **When:** May 2012 to present.

- **Topic:** Guidelines-based treatment of anemic patients with acute ST-elevation myocardial infarctions: a report from the NCDR ACTION-GWTG registry. **Mentor:** David Herrington, M.D. **Role:** principal investigator. **Where:** Wake Forest Baptist Medical Center. **When:** May 2011 to November 2012.

- **Topic:** Diagnostic Time Course, Treatment Patterns, and Outcomes for STEMI Patients with Non-Diagnostic Initial ECG: A Report from the AHA Mission:
Lifeline Program. Mentor: David Herrington, M.D. Role: principal investigator.
Where: Wake Forest Baptist Medical Center. When: April 2011 to December 2012.

Residency

Medical School
Publications


**Abstract Presentations**


**Publications In Review**


**Research Support**

**Current Research Support**

- Initiative for Healthcare Delivery Innovation Intramural Grant Riley (PI) May 2013-current

“Are serial electrocardiograms Additive to Serial high-sensitivity troponins in Predicting acute Coronary Syndromes in Patients with undifferentiated chest pain (ASAP CATH) Study: An Observational Pilot Study”

The study is a prospective observational study to evaluate the utility of serial ECGs in the evaluation of undifferentiated chest pain in the era of novel troponin assays. The Initiative for Healthcare Delivery Innovation that funded the project is a multidisciplinary group tasked to improve the healthcare delivery processes at Wake Forest Baptist Medical Center.

Role: Principle Investigator

- American Heart Association (AHA) Riley (PI) Winter 2013 Clinical Research Grant, July 1st, 2013-current
“Are serial electrocardiograms Additive to Serial high-sensitivity troponins in Predicting acute Coronary Syndromes in Patients with undifferentiated chest pain (ASAP CATH) Study: An Observational Pilot Study”

A prospective observational study to evaluate the utility of serial ECGs in the evaluation of undifferentiated chest pain in the era of novel troponin assays.

Role: Principle Investigator

Other Experience, Professional Memberships

- Reviewer, Circulation: Cardiovascular Quality and Outcomes, 2012-present
- Reviewer, Journal of the American Heart Association, 2012-current
- Reviewer, BMC Health Services Research, 2013-current
- American Board of Internal Medicine, board-certified diplomat, 2011-current
- Physician Champion, NCDR ACTION Registry cardiovascular data information service group, Wake Forest University Baptist Health, 2011-current
- Attendee, American Heart Association 37th Ten-Day Seminar on the Epidemiology and Prevention of Cardiovascular Disease, 2011