THE EFFECT OF A DISEASE MANAGEMENT ALGORITHM AND DEDICATED POSTACUTE CORONARY SYNDROME CLINIC ON ACHIEVEMENT OF GUIDELINE COMPLIANCE: RESULTS FROM THE PARKLAND ACUTE CORONARY EVENT TREATMENT STUDY

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ABSTRACT

THE EFFECT OF A DISEASE MANAGEMENT ALGORITHM AND DEDICATED POSTACUTE CORONARY SYNDROME CLINIC ON ACHIEVEMENT OF GUIDELINE COMPLIANCE: RESULTS FROM THE PARKLAND ACUTE CORONARY EVENT TREATMENT STUDY

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Background: The application of disease management algorithms by physician extenders has been shown to improve therapeutic adherence in selected populations. It is unknown whether this strategy would improve adherence to secondary prevention goals after acute coronary syndromes (ACSs) in a largely indigent county hospital setting.

Methods: Patients admitted for ACS were randomized at the time of discharge to usual follow-up care versus the same care with additional visits with physician extenders in a dedicated post-ACS clinic. Physician extender visits were conducted according to a treatment algorithm based on contemporary practice guidelines. Groups were compared using the primary end point of achievement of low-density lipoprotein treatment goals at 3 months after discharge with key secondary endpoints including the achievement of additional evidence-based practice goals with up to 1 year of follow up assessment.

Results: One hundred forty consecutive patients were randomized. Rates of use of all evidence-based therapies assessed were high at the time of hospital discharge, and similar between the study groups. A similar proportion of patients returned for study follow-up in both groups at 3 months (54 [79%]/68 in the usual care group vs. 57 [79%]/72 in the intervention group; P = 0.97). Among those completing the 3-month visit, a low-density lipoprotein cholesterol level less than 100 mg/dL was achieved in 37 (69%) of the usual care patients compared with 35 (57%) of those in the intervention group (P = 0.43). There was no statistical difference in implementation of therapeutic lifestyle changes (smoking cessation, cardiac rehabilitation, or exercise) between groups. Prescription rates of evidence-based therapeutics at 3 months were similar in both groups.

Conclusion: The implementation of a post-ACS clinic run by physician extenders applying a disease management algorithm did not measurably improve adherence to evidence-based secondary prevention treatment goals. Despite initially high rates of evidence-based treatment at discharge, adherence with follow-up appointments and sustained implementation of evidence-based therapies remains a significant challenge in this high-risk cohort.

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PRIOR PUBLICATIONS & PRESENTATIONS

Publications:

Yorio JT, Viswanathan S, See R, Uchal L, McWhorter JA, Spencer N, Murphy S, Khera A, de Lemos JA, McGuire DK. The Effect of a Disease Management Algorithm and Dedicated Post-Acute Coronary Syndrome Clinic on Achievement of Guideline Compliance: Results from the Parkland Acute Coronary Event Treatment (PACE-Rx) Study. J Investig Med. 2008 Jan;56(1):15-25.

Presentations:

Yorio, J., Viswanathan, S., See, R., Uchal, L., McWhorter, J., Khera, A., DeLemos, J., McGuire, D. (2006). The Effect of a Disease Management Algorithm and Dedicated Post-ACS Clinic on Achievement of Guideline Compliance: Results from the Parkland Acute Coronary Event Treatment Study. Sixth Annual Cardiovascular Symposium at UT Southwestern, Dallas, TX. Abstract and Poster.

Viswanathan, S., Yorio, J., Uchal, L., McWhorter, J., Khera, A., De Lemos, J., McGuire, D. (2006). Increasing Use of Evidence-Based Therapies Across Ethnic Groups After Acute Coronary Events: Observations from the Parkland Acute Coronary Event Treatment Study. 44th Medical Student Research Forum, Dallas, TX. Abstract and Poster.

Viswanathan, S., Yorio, J., Uchal, L., McWhorter, J., Khera, A., De Lemos, J., McGuire, D. (2005). Increasing Use of Evidence-Based Therapies Across Ethnic Groups After Acute Coronary Events: Observations from the Parkland Acute Coronary Event Treatment Study. Fifth Annual Cardiovascular Symposium at UT Southwestern, Dallas, TX. Abstract and Poster.

Viswanathan, S., Yorio, J., McGuire, D. (2005). Study to Determine Adequacy of Lipid-Lowering and Antihypertensive Therapy in Patients with Acute Coronary Syndrome. 43rd Medical Student Research Forum, Dallas, TX. Abstract and Poster.

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LIST OF DEFINITIONS

ACE-I: Ace-Inhibitor

ACS: Acute coronary syndrome

ASA: Aspirin

BMI: body mass index

BP: blood pressure

CAD: coronary artery disease

CHF: congestive heart failure

CRUSADE: Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA guidelines initiative

EUROASPIRE: European Action on Secondary Prevention through Intervention to Reduce Events survey

GRACE: Global Registry of Acute Coronary Events

LDL: low-density lipoprotein

NSTEMI: non-ST elevated myocardial infarction

PHHS: Parkland Health and Hospital Systems

SBP: Systolic Blood Pressure

SPLINT: Specialist Nurse-Led Intervention to Treat and Control Hypertension and Hyperlipidemia in Diabetes Trial

STEMI: ST elevated myocardial infarction

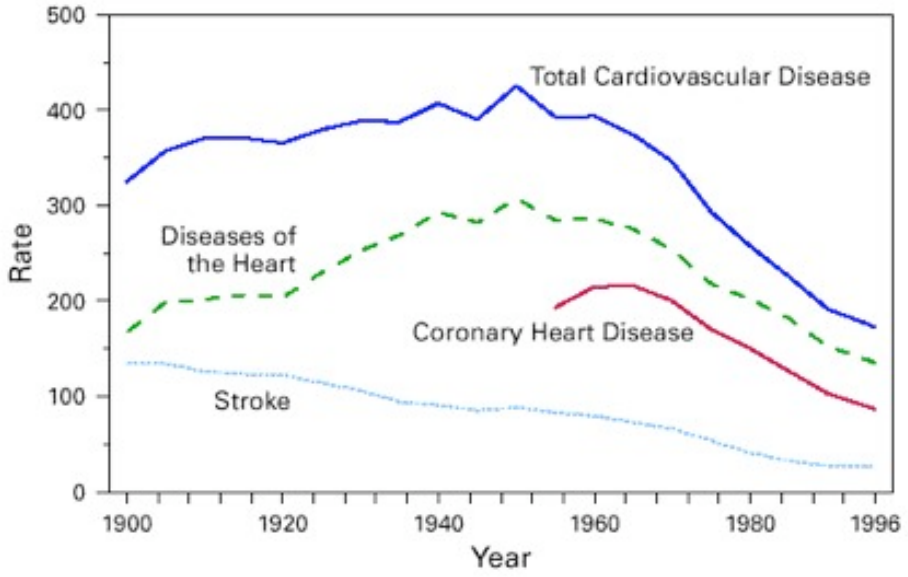
USA: Unstable Angina

CHAPTER ONE
Introduction

Coronary artery disease remains the leading cause of morbidity and mortality in the United States, estimated to cost over 156 billion dollars in 2008[1]. According to the American Heart Association (AHA), coronary artery disease is the number one killer in America responsible for roughly 25% of deaths. The prevalence of CAD in 2005 was 16 million people[1].

One manifestation of coronary artery disease is acute coronary syndrome (ACS). ACS is an umbrella term covering clinical symptoms consistent with myocardial infarction. It includes unstable angina (USA), non-ST-elevation myocardial infarction (NSTEMI), and ST- elevation myocardial infarction (STEMI). All three conditions are caused by the same process, a ruptured atherosclerotic plaque (substrate), platelet aggregation, and thrombus formation. The specific condition, which subsequently evolves, is dependent on the magnitude of platelet aggregation, thrombus formation, and thrombus sustenance. Unstable angina is defined as new onset or recurrence of angina that is progressive, occurs at rest, or does not improve with nitroglycerin. By definition it is a clinical diagnosis with no elevation of cardiac enzymes. Non-ST-elevation myocardial infarction is an acute process of myocardial ischemia resulting in myocardial necrosis (sub-endocardial) with positive cardiac biomarkers but no ST elevations seen on EKG. ST-elevation myocardial infarction implies transmural (full thickness) infarction of myocardial tissue with ST elevations present on EKG and positive cardiac enzymes[2].

Considerable evidence demonstrates that interventions such as risk factor modification through therapeutic lifestyle modification and pharmacologic therapies decrease the risk of future coronary events and patient mortality following an ACS event. These interventions include dietary and smoking cessation counseling, cardiac rehabilitation and physical activity, and treatment with aspirin (ASA)[3, 4], beta-blockers[4, 5], ACE inhibitors[4, 6, 7], and HMG-CoA reductase inhibitors (statins)[8-10]. All of these strategies have been shown to be effective, safe, and cost-effective and have been incorporated into the American College of Cardiology (ACC)/American Heart Association (AHA) treatment guidelines for management of patients following ACS[2, 11]. Indeed, with proven efficacy and broader application of medical (both invasive and non-invasive) therapies, the advent of the Cardiovascular Care Unit (CCU), and increased public awareness, the mortality of CAD has been on the decline since the 1960s (Figure 1)[12].



*Per 100,000 population, standardized to the 1940 U.S. population.
†Diseases are classified according to *International Classification of Diseases* (ICD) codes in use when the deaths were reported. ICD classification revisions occurred in 1910, 1921, 1930, 1939, 1949, 1958, 1968, and 1979. Death rates before 1933 do not include all states. Comparability ratios were applied to rates for 1970 and 1975.

Figure 1. Age-adjusted death rates* for total cardiovascular disease, diseases of the heart, coronary heart disease, and stroke, by year – United States, 1900-1996.[12]

The AHA classifies all of these secondary prevention guidelines as having a Class I indication, meaning their benefit in patients with ACS far outweighs their risk and they should be considered for all ACS patients[13, 14]. The present study examines the compliance with these guidelines, assessing the following evidence-based components: lipid management with statins, antiplatelet agents/anticoagulants, beta-blockers, renin-angiotensin-aldosterone blockers, diet and weight management, smoking cessation and physical activity.

The antiplatelet agent, aspirin, is perhaps one of the most studied drugs in heart disease. Indeed, more than 200,000 patients have been studied in more than 150 randomized clinical trials evaluating aspirin efficacy and safety across a range of doses. The Second International Study of Infarct Survival (ISIS-2) is one of the most widely cited studies demonstrating the benefit of aspirin in secondary prevention of ACS. It was a randomized trial of over 17,000 patients with ACS randomized to streptokinase, one-month therapy with ASA, both, or neither. Patients on ASA had a 25% reduction in 5-week vascular mortality and a 50% reduction in non-fatal re-infarction. These results are not surprising given the pathophysiology of myocardial infarction and the antiplatelet effect of aspirin[15].

Beta-adrenergic receptor blocking agents have multiple actions on the heart, including slowing of the heart rate, reduction in myocardial contractility, increased diastolic filling times, and lowering of systemic blood pressure. These effects are beneficial in the setting of myocardial infarction as they reduce myocardial oxygen demand. They have been proven beneficial in both the early stages of ACS and in secondary prevention. The Beta Blocker Heart Attack Trial (BHAT) was a multicenter, randomized, double blind, placebo controlled trial with roughly 4,000 post-ACS patients conducted in 1982. The study randomized patients to either propranolol or placebo, one week after myocardial infarction. Those in the propranolol cohort

had a decreased all cause mortality and a decrease in mortality from cardiovascular death and sudden cardiac death[16].

Angiotensin-converting enzyme inhibitors block the renin-angiotensin-aldosterone system, which increases vasodilator bradykinin concentrations, reduces the vasocontrictor angiotensin II, and reduces plasma aldosterone concentrations. These effects have been proven beneficial for cardiac oxygen supply and demand. The full effects of this system are still unknown. Supplemental pharmacologic effects may include anti-atherosclerotic effects, improved endothelial function, stabilization of plaques, and fibrinolysis. Numerous studies have shown a benefit of ACE-I in patients with ACS with and without heart failure. In 2000, the Heart Outcome Prevention Evaluation Study (HOPE), a randomized, placebo controlled prospective trial, followed 9,000 patients with CAD without evidence of heart failure for five years. Patients received either placebo or ramipril. The study demonstrated reduced cardiovascular mortality, reduced re-infarction rate, and reduced all cause mortality in the ramipril arm[17].

Numerous studies have also shown the secondary prevention benefit of 3-hydroxy-3-methylglutaryl–coenzyme A (HMG-CoA) reductase inhibitors in patients with ACS. It is well known that there is a direct association between plasma cholesterol levels and coronary artery disease, as it has been well studied in both animal and human subjects. The LIPID Study found that patients on a statin had a 24% reduction in mortality over seven years and had a reduction in the number of myocardial infarctions, strokes and revascularization events[18].

Lifestyle modifications such as diet, exercise, cardiac rehabilitation and smoking cessation have also shown benefit in patients following ACS, and the AHA considers them Class I indications. Dietary restrictions can lead to improvement in cholesterol, blood pressure, and

weight management and also leads to improved diabetes management, a significant risk factor for CAD. The Lyon study randomized patients with ACS to a regular Western Diet or a diet high in fiber, fruits, vegetables, and low in saturated fats. The patients were followed for 48 months and those patients following the experimental diet had significant reductions in composite endpoints that included combinations of cardiac death, nonfatal myocardial infarction, unstable angina, stroke and heart failure[19].

Smoking remains the clear number one preventable risk factor for CAD. Overall, smoking rates in the U.S. are down from previous decades due to improved education about its negative health effects. The Nurses Health Study looked at 120,000 female nurses with known CAD over a period of six years and found an association between smoking and both fatal and non-fatal myocardial infarctions[20]. The AHA now recommends that all physicians ask about tobacco use at every visit, educate the patient about quitting, assess the willingness to quit, and assist with a plan to quit and counseling[13, 14].

Physical activity has been shown to have a beneficial effect on mortality in patients with ACS. While the exact mechanism is unknown, exercise is thought to improve circulation, lead to improved cardiac output, and possibly slow the effects of atherosclerosis. The AHA now recommends 30 minutes of moderate activity at least five days a week and strength training two days a week. This recommendation stems from studies demonstrating a link between poor physical fitness and increased mortality from ACS[21].

Despite the breadth of accumulated evidence, these secondary prevention strategies are underused in patients with established coronary artery disease[22-27]. To bridge this "treatment gap," strategies incorporating disease management programs and treatment algorithms have been used to improve adherence rates in the inpatient setting[28]. Similarly, the implementation of

treatment algorithms by physician extenders in the outpatient setting has been effective in improving patient care and adherence to treatment guidelines for other chronic conditions[29-31]. However, this strategy has been less rigorously evaluated in the post-ACS setting, especially in underserved populations such as those treated in a county hospital system.

The present study was designed to evaluate the effectiveness of a systematic disease-management algorithm applied by physician extenders in a dedicated post-ACS follow-up clinic in a large county hospital system.

CHAPTER TWO
Methods

Patient Population

Patients were recruited from Parkland Memorial Hospital, a tax-supported county hospital in Dallas, Texas, serving a socio-economically underprivileged and racially diverse patient population. Consecutive patients discharged with a primary diagnosis of ACS (unstable angina, non-ST elevation myocardial infarction, ST-elevation myocardial infarction) and qualifying for follow-up care in Parkland Hospital and Health Systems (PHHS) were eligible for the study. Exclusion criteria included pregnancy, age <18, incarceration, and patients referred for coronary artery bypass graft surgery. The University of Texas Southwestern Medical Center at Dallas Institutional Review Board approved the study protocol and each participant prospectively provided informed consent.

Intervention and Data Collection

Using a randomly generated number sequence kept in numbered, sealed envelopes, participants were randomized in a 1:1 strategy to receive either usual post-discharge care (appointments with a cardiologist and a primary care physician within 3 months) or the same care with an additional appointment within 2 weeks of discharge in a dedicated post-ACS clinic with one of two physician extenders (a registered nurse practitioner or a clinical pharmacist).

Patients in both arms of the study were given appointments to see a fellow in the cardiology clinic and a primary care physician within 2-3 months after discharge. The physicians at these encounters were not aware that the patients were participating in the study and were not given any specific guidelines to follow. All subsequent interventions and visits

were left up to the individual physician, but it is typical that post-ACS patients are seen every 3-6 months.

Patients assigned to the physician extender arm were also seen for a 30-minute appointment in the post-ACS clinic approximately two weeks after discharge. Management in the post-ACS clinic was conducted according to an algorithm (Appendix A) based on contemporary practice guidelines, executed by the physician extenders under the supervision of the clinic director (DKM). The purpose of this encounter was to ensure that patients had a full understanding of the severity of their condition and were taking the appropriate steps following discharge. During this appointment, patient questions and concerns were addressed, diet, exercise and smoking cessation counseling with referral were provided, medication was titrated according to Appendix A, and the patients were re-educated on their condition and subsequent medical follow-up.

Patients were asked if they were following the American Heart Association diet that they were educated about before discharge from the hospital. If they were not adherent, the physician extender would further educate them about the diet and refer them to a dietician if necessary. Patients were counseled about smoking cessation and referral to a smoking cessation clinic was made if the patient showed interest. Patients were also encouraged to exercise at least 3 times per week for 30 minutes, and referral to cardiac rehabilitation was confirmed.

Additionally, prescriptions for anti-platelet agents, ACE inhibitors, beta-blockers, and statins were reviewed. These medications were added or titrated per the algorithm as indicated: unless contraindicated, aspirin, beta-blocker and ACE inhibitor therapy were recommended for all patients, while a statin was recommended for all patients whose LDL cholesterol was greater than 100 mg/dl in accordance with contemporary guidelines during the study period.[2] Rationale

for omission of any of the above interventions was recorded. Medications were titrated per protocol towards goal systolic blood pressure of <140 mmHg and LDL-cholesterol of <100mg/dl. If statins were titrated, a follow-up appointment with the physician extender was scheduled in 6 weeks to check lipid levels. If anti-hypertensive medications were titrated, a follow-up appointment with the physician extender was scheduled in 2-3 weeks for a repeat blood pressure check. Titration was then made at each subsequent appointment as needed per patient. Upon reaching goal levels of LDL-cholesterol and systolic blood pressure, the patients would then continue regular follow-up with a fellow in the cardiology clinic.

All follow-up visits in both arms of the study were made according to the usual practices at Parkland except that patients in the physician extender arm were also given advanced telephone reminders from the physician extender to all appointments during the designated study period to ensure they were aware of upcoming visits and had suitable transportation. This was not provided to the usual care group.

Data for all patients were prospectively recorded at the time of hospital discharge and at each visit to the post-ACS clinic. Data for the three month follow-up visit was recorded for any patient who was seen in the appropriate clinic in between 6 weeks and 4 months, and data for the one year follow-up visit was recorded for any patient who was seen in between 6 months and 14 months. For patients assigned to usual care alone, data were abstracted from the Parkland Health System paper and electronic medical record, including data from primary care and cardiology specialty clinic visits. Patients who were lost to follow-up were also contacted at the end of the study in an effort to understand why they did not show up.

Endpoints

The primary endpoint of the study was achievement of LDL target levels (<100 mg/dL) at three months following discharge. Secondary endpoints included achievement of systolic blood pressure < 140 mmHg; prescription of evidence-based medication (aspirin, ACE inhibitors, beta-blockers and statins); number of patients who were compliant with a diet and exercise program as described above; and number of patients who received a referral to smoking cessation clinic and cardiac rehabilitation. All secondary endpoints were evaluated at 3 months and 1 year following discharge.

Statistical Methods

Descriptive statistics (medians/means for continuous variables and percentages for discrete variables) were generated for baseline demographic and clinical characteristics.

Comparisons of the primary and all secondary endpoints were performed using chi-square analysis. All statistical testing was 2-tailed, and a p-value <0.05 was considered significant. A sample size of 140 patients was determined to provide 80% power to detect a difference of 20% in the rate of lipid-lowering therapy use at a significance level of 0.05, assuming a control rate of use of 50% based on historical benchmark data assessed over the 2 years preceding the randomized study.

CHAPTER THREE
Results

Between March 2003 and July 2004, 140 consecutive patients who met the eligibility criteria and agreed to participate in the study were randomized to either the usual care group (n=68) or the physician extender group (n=72). Baseline characteristics are summarized by treatment assignment in Table 1. The two groups were statistically similar except more patients in the usual care group had a prior history of coronary artery disease. Rates of prescription of ASA, ACEI, and beta-blockers at the time of study entry were similar in both groups (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics

	Usual Care	Physician Extender
n	*68*	*72*
Age, yrs	56.2 ± 10.8	55.9 ± 11.3
Women	29 (42.7)	24 (33.3)
Race		
Black	29 (42.7)	26 (36.1)
White	24 (35.3)	23 (31.9)
Hispanic	14 (20.6)	20 (27.8)
Smoking		
Current	24 (35.3)	24 (33.3)
Past	15 (22.1)	15 (20.8)
Never	29 (42.7)	33 (45.8)
Diagnosis		
NSTEMI	32 (47.1)	36 (50.0)
STEMI	20 (29.4)	17 (23.6)
USA	16 (23.5)	19 (26.4)
Prior CAD	43 (63.2)	33 (45.8)
Hypertension	51 (75.0)	49 (68.1)
Hyperlipidemia	34 (50.0)	32 (44.4)
Diabetes	34 (50.0)	40 (55.6)
CHF	15 (22.1)	12 (16.7)
LDL at Goal (<100 mg/	26 (38.2)	28 (38.9)
Systolic BP at Goal (<140 mm HG)	55 (80.9)	57 (79.2)
BMI (kg/m^2)	30.5 ± 6.3	30.6 ± 8.6
Medications at Discharge		
Aspirin	66 (97.1)	70 (97.2)
Beta-Blockers	63 (92.7)	67 (93.1)
ACE-Inhibitors	62 (91.2)	68 (94.4)
Statins	54 (79.4)	65 (90.3)

Values are expressed as no. (%) or mean ± SD.

There was a non-significant difference in the number of patients using statins with 90% in the physician extender group and 79% in the usual care group.

Of the 72 patients assigned to the physician extender group, 49 (68%) attended the post-ACS clinic visit within two weeks of discharge. Fifty-four patients from the usual care group and 57 patients from the physician extender group were seen for the 3-month follow-up visit (79% in each group; p=0.97). Forty-five patients from the usual care group and 47 patients from the physician extender group were seen for the 1-year follow-up visit (1-year follow up rates of 66% and 65%, respectively; p=0.91) (Figure 2).

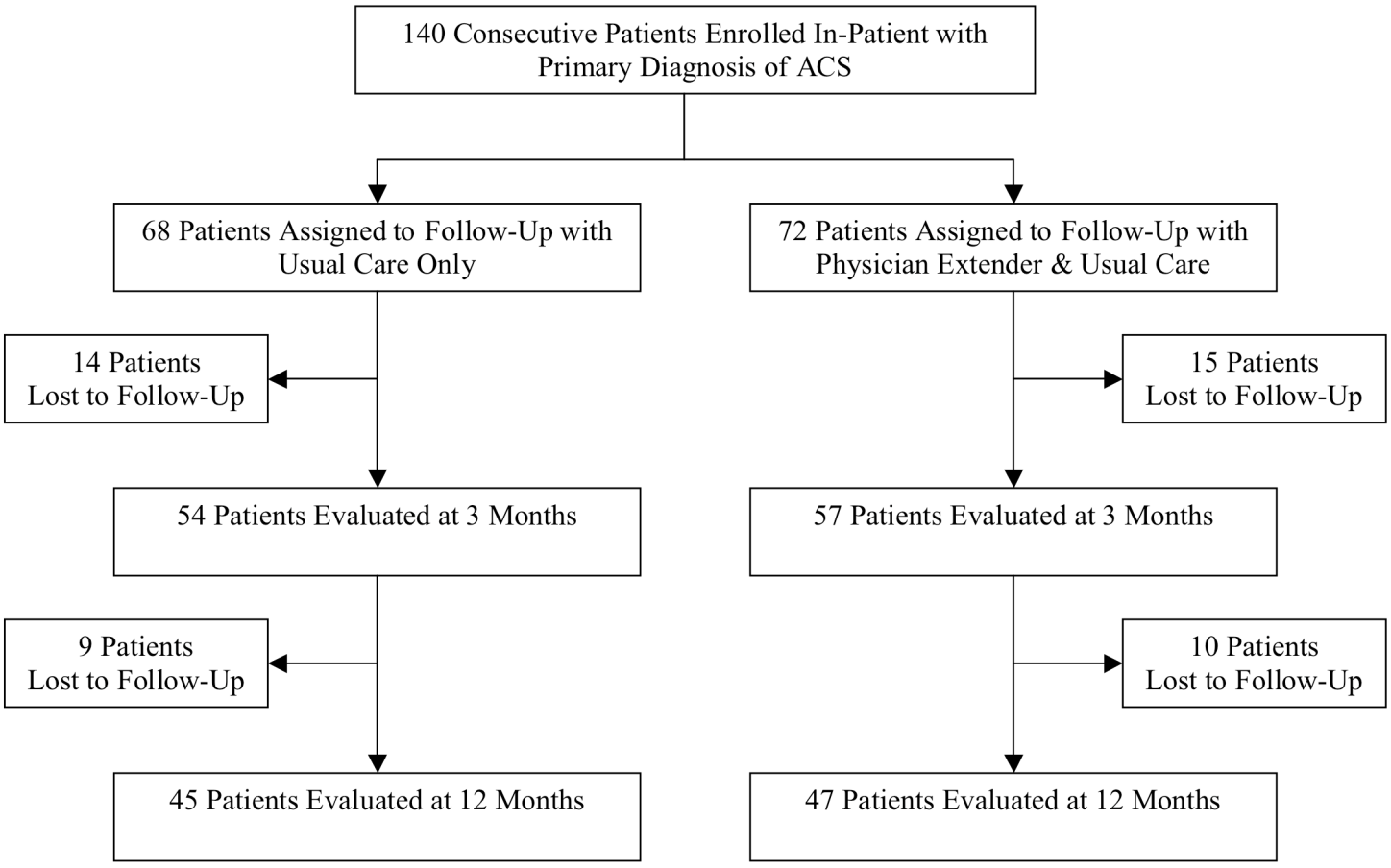


Figure 2. Flow of Patients Through the Study.

At 3 months post-discharge, no significant difference was observed between the usual care and physician extender groups for the primary endpoint of achieving an LDL level <100 mg/dl (n=37; 69% vs. n=35; 61%, respectively; p=0.43; Figure 3). At one-year follow-up, 67% (n=30) of the usual care group and 66% (n=31) of the physician extender group were at LDL treatment goal (p= 0.94; Figure 3).

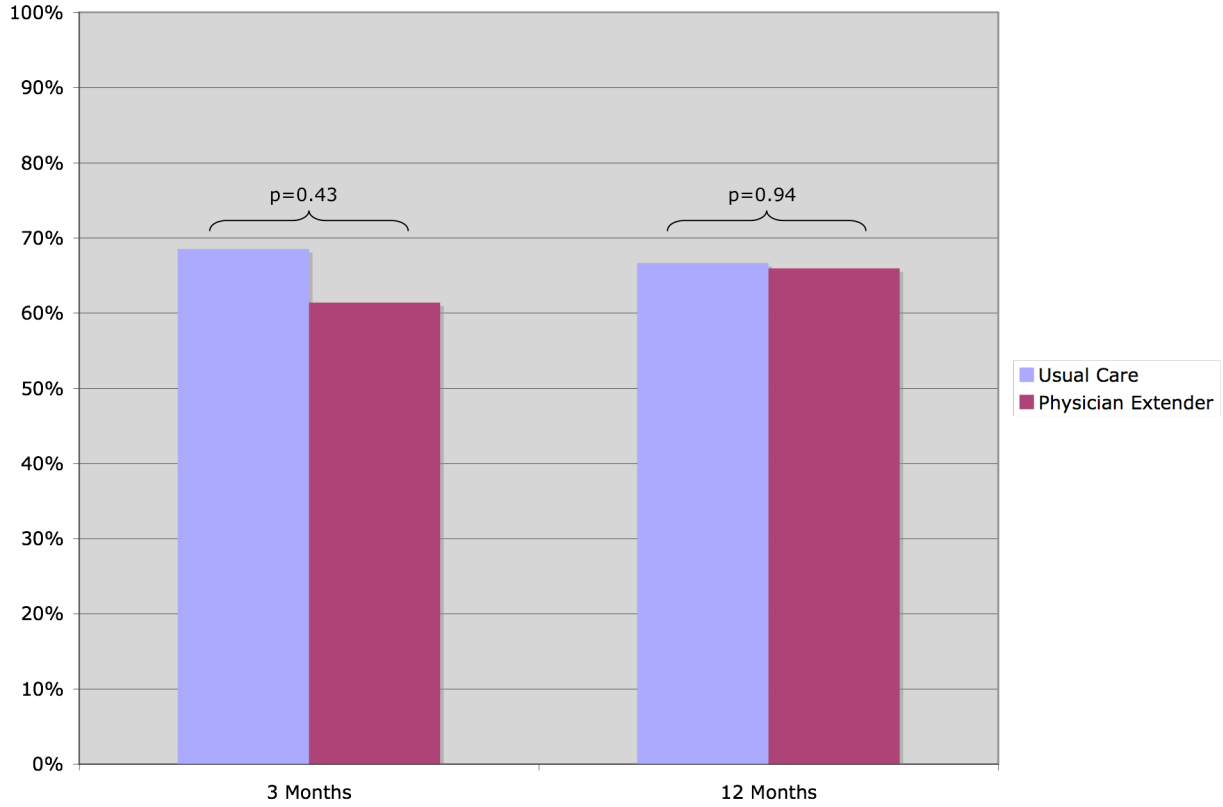


Figure 3. Percentage of patients achieving LDL-c goal <100 mg/dL at 3 months and 12 months.

Analysis of the secondary endpoint of achievement of systolic blood pressure ≤140 mmHg also showed no significant difference between the two groups at 3 months, with 78% (n=42) of patients meeting goal in the usual care group vs. 82% (n=47) of patients in the physician extender group (p=0.54) (Figure 4). At 1 year, a non-significant trend towards higher rates of achievement of blood pressure goal was evident in the physician extender group: 83% (n=39) vs. 67% (n=30) in the usual care arm. (p=0.07; Figure 4).

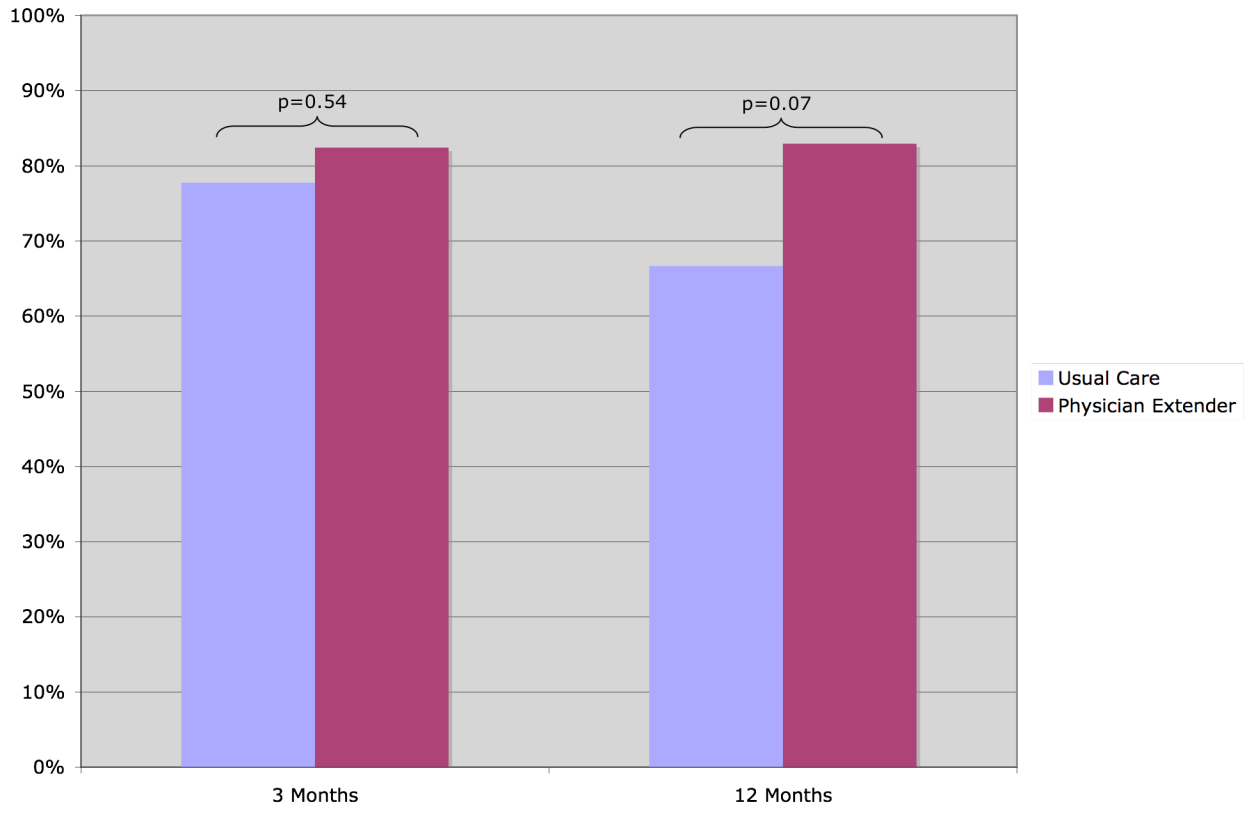


Figure 4. Percentage of patients achieving systolic blood pressure <140 mmHg at 3 months and 12 months.

As presented in Table 2, the prescription rates of aspirin, beta-blockers, ACE-inhibitors and statins at the 3 month and 1 year follow-up visits were not statistically different between the two groups. Documented lifestyle modification, such as the rates of diet and exercise adherence, smoking cessation, and cardiac rehabilitation referral at 3 months and at 1 year are also presented in Table 2. Compared with the usual care group, a significantly higher percentage of patients had documented dietary adherence in the physician extender group at 3 months (17 (29.8%) vs. 4 (7.4%); p=0.01) and at 1 year (14 (29.8%) vs. 3 (6.7%); p=0.01). Similar trends favoring the physician extender group that did not achieve statistical significance were observed for referral to cardiac rehabilitation and adherence with an exercise regiment, with numerically similar rates of referral to a smoking cessation clinic documented for both groups.

Table 2. Treatment and Lifestyle Modifications at 3 month and 12 month visit.

	Usual Care	Physician Extender	P Value
3 months	*n=54*	*n=57*	
Aspirin	49 (90.7)	51 (89.4)	0.83
Beta-Blockers	47 (87.0)	52 (91.2)	0.48
ACE-Inhibitors	45 (83.3)	51 (89.5)	0.34
Statins	48 (88.9)	49 (86.0)	0.64
Diet	4 (7.4)	17 (29.8)	0.01
Exercise	9 (16.7)	15 (26.3)	0.22
Smoking Counseling	15 (27.7)	15 (26.3)	0.86
Cardiac Rehab	22 (40.7)	32 (56.1)	0.1
12 Months	*n=45*	*n=47*	
Aspirin	40 (88.9)	42 (89.4)	0.94
Beta-Blockers	44 (97.8)	43 (91.5)	0.18
ACE-Inhibitors	39 (86.7)	41 (87.2)	0.94
Statins	38 (84.4)	41 (87.2)	0.7
Diet	3 (6.7)	14 (29.8)	0.01
Exercise	4 (8.9)	9 (19.2)	0.09
Smoking Counseling	7 (15.6)	10 (21.3)	0.74
Cardiac Rehab	20 (44.4)	30 (63.8)	0.06

Values are expressed as no. (%) or mean ± SD.

Patients were contacted after the study ended to find out why they did not comply with follow-up visits. In the usual care arm, 23 patients were non-compliant with one-year follow-up compared with 25 patients in the physician extender arm. Common reasons for non-adherence were similar in both groups and included incarceration, lack of transportation, unwillingness to participate, and no longer living in the area. Of note, there were 6 patient deaths in each arm. Five patients in the physician extender group declined to follow-up due to financial reasons compared with one patient in the usual care group.

CHAPTER FOUR
Discussion and Conclusion

In this prospective, randomized trial, the addition of a physician extender to usual care in the management of post-ACS patients in a large county hospital system did not increase the proportion of patients achieving an LDL below the treatment goal of 100 mg/dL at either 3-month or 1-year follow-up visits. Additionally, there was no significant difference between the two groups in prescription rates of evidence-based medications, achievement of goal systolic blood pressure at three months, or in referral to smoking cessation clinic. Trends favoring the physician extender group were evident at 3 months and at 1 year in the rates of referral to cardiac rehabilitation and adherence with exercise, with statistically significant increases in dietary adherence at both time-points. In addition, achievement of blood pressure goals at the later time point of one year trended higher in the physician extender arm, although these differences were not statistically significant.

Our results differ from prior studies, which report additional benefit in adding disease management algorithms with physician extenders in the care of other chronic conditions. One of these studies was the Specialist Nurse-Led Intervention to Treat and Control Hypertension and Hyperlipidemia in Diabetes (SPLINT) trial. This was a randomized controlled implementation trial at Hope Hospital in Salford, United Kingdom, which enrolled 1,407 patients with diabetes presenting with elevated blood pressure greater than 140/80 mmHg and/or total cholesterol above 5.0 mmol/L (~193 mg/dL). Patients were randomized either to usual care or to usual care with specialist nurse-led clinics. Patients in the nurse-led clinic group would attend the clinic every 4-6 weeks until targets were achieved. As noted in Table 3, the addition of algorithm-guided specialty nurse-led clinics showed a significant improvement in reaching target levels of

total cholesterol and blood pressure when compared with usual care. Additionally, a significant improvement in one-year mortality was also seen. However, when looking at the two interventions separately, only the hyperlipidemia nurse-led clinic showed a significant difference, while the difference in the hypertension arm was not significant.[29]

Table 3. Achievement of blood pressure and cholesterol goals in the SPLINT Trial.

	Nurse-Led Clinic	Usual Care	P Value
Combined			
Enrolled	851	846	
Attended Follow-Up	723 (85.0)	739 (87.4)	
Achieved Target	315 (37.2)	261 (30.7)	0.003
Hypertension			
Enrolled	506	508	
Attended Follow-Up	406 (80.2)	429 (84.5)	
Achieved Target	135 (26.6)	122 (24.1)	0.27
Hyperlipidemia			
Enrolled	345	338	
Attended Follow-Up	317 (91.9)	310 (91.7)	
Achieved Target	180 (53.3)	139 (40.3)	0.0007
Overall			
Enrolled	778	629	
Mortality	25 (3.2)	36 (5.7)	0.02

Adapted from New, JP et al. *Diabetes Care* 2003; 26(8):2250-5.

Denver *et al.* published a study performed at Whittington Hospital, an inner-city community of 154,000 adults in North Islington, London of patients with type 2 diabetes and a blood pressure of greater than 140/80 mmHg. One-hundred and twenty patients were enrolled in the study from June 2000 to June 2001. These patients were randomly assigned to conventional primary care or to a nurse-led hypertension group. Patients assigned to the nurse-led clinic group were seen monthly for 3 months and then every 6 weeks for 3 months. The blood pressure of all

patients was then reevaluated at a 6-month visit. Achievement of goal blood pressure was less than 140/80 mmHg for patients without renal complications and less than 120/70 mmHg for patients with renal complications. Target systolic blood pressure at 6 months was achieved in 38% of patients in the nurse-led clinic versus only 12% of patients in the control group (p=0.003). However, a significant difference in diastolic blood pressure was not seen between the two groups.[30]

Another study published by Allen *et al.* examined nurse case management of high cholesterol in patients with coronary heart disease after coronary revascularization. Two hundred and twenty-eight patients were randomized to either seeing a nurse practitioner for 1 year after discharge in addition to usual care versus usual care alone. An LDL cholesterol of less than 100 mm/dL was achieved after one year by 65% of patients in the nurse-led group versus only 35% of patients in the usual care alone group (p=0.0001).[31]

Finally, a trial out of Scotland studied 1173 patients with coronary heart disease from a random sample of 19 general practices. Patients were randomized to control versus additional nurse-led clinics. These nurse-led clinics ran for one year, with the first visit within the first 3 months and any follow-up based on clinical circumstances. Several endpoints were examined, including aspirin management, achievement of goal blood pressure of less than 160/90 mmHg, achievement of goal total cholesterol of less than 5.2 mmol/L (~201 mg/dL), exercise, diet and smoking status. In the end, a significant improvement was seen in aspirin management, blood pressure management, lipid management, moderate physical activity and low fat diet in the nurse-led group when compared to the control group. No difference was found between the two groups with regards to smoking cessation.[32] While this Scotland study is probably the closest in design to our study, to the best of our knowledge, no study to date has evaluated the overall

effect of an algorithm-based management strategy applied by physician extenders following ACS events.

There are several possible reasons for the differences between the present findings and those in prior studies. First, the overall prescription rates of evidence-based therapies among ACS patients at Parkland Memorial Hospital are high. In fact, when compared with previously published reports of national/international registries assessing evidence-based post-ACS treatment at the time of discharge, the discharge prescription rates of aspirin, beta-blockers, ACE-inhibitors, and lipid lowering medications from this study were generally higher (Figure 5). Registries used for comparison were the Global Registry of Acute Coronary Events (GRACE) Registry, the CRUSADE Registry, the Canadian ACS Registry and EUROASPIRE II[27, 33-35].

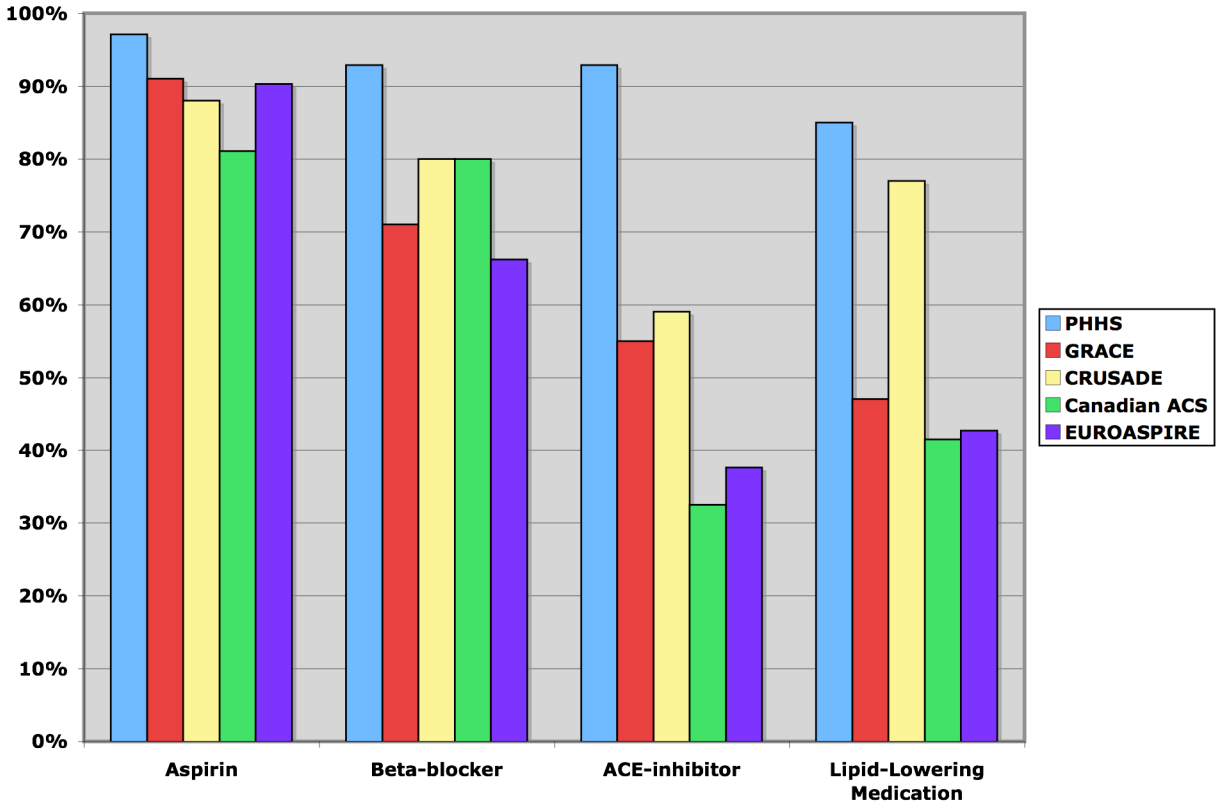


Figure 5. Rates of evidence-based medications at discharge at PHHS and Multinational ACS Registries.

GRACE was a prospective and retrospective study of over 6,000 hospitalized patients diagnosed primarily with unstable angina, non-ST-elevation myocardial infarction and ST-elevation myocardial infarction. It took place across 14 different countries in Europe, North and South America, Australia and New Zealand in 1999-2000[33]. The CRUSADE (Can Rapid Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines) Registry is based on 19,000 ACS patients treated at 300 U.S. hospitals during 2002[34]. The Canadian ACS study examined over 5,500 patients with a discharge diagnosis of ACS in 1997-1999[35]. Finally, EUROSPIRE II (European Action on Secondary Prevention through Intervention to Reduce Events) was a study conducted in 15 European countries in 1999 to 2000 of over 8,0000 patients admitted with a myocardial infarction[34].

Furthermore, when compared to more recent data from the CRUSADE Registry of 138,719 patients from 521 U.S. hospitals during July 2001 to March 2005, the discharge prescription rates of these four medications from this study were still higher. In fact, prescription rates for all four medications, especially ACE-inhibitors, from this study were higher than the top 25 centers used in the CRUSADE Registry from July 2001 to March 2005 (Figure 6)[36].

In light of these favorable comparisons, the patients in this study received a higher rate of evidence-based pharmaceutical therapy at discharge than expected. Therefore, the initially high prescription rates observed might have attenuated any further benefit that would be conferred by the addition of algorithm-driven care by physician extenders, leading to similar rates between groups in both primary and secondary endpoints at 3 months and 1 year.

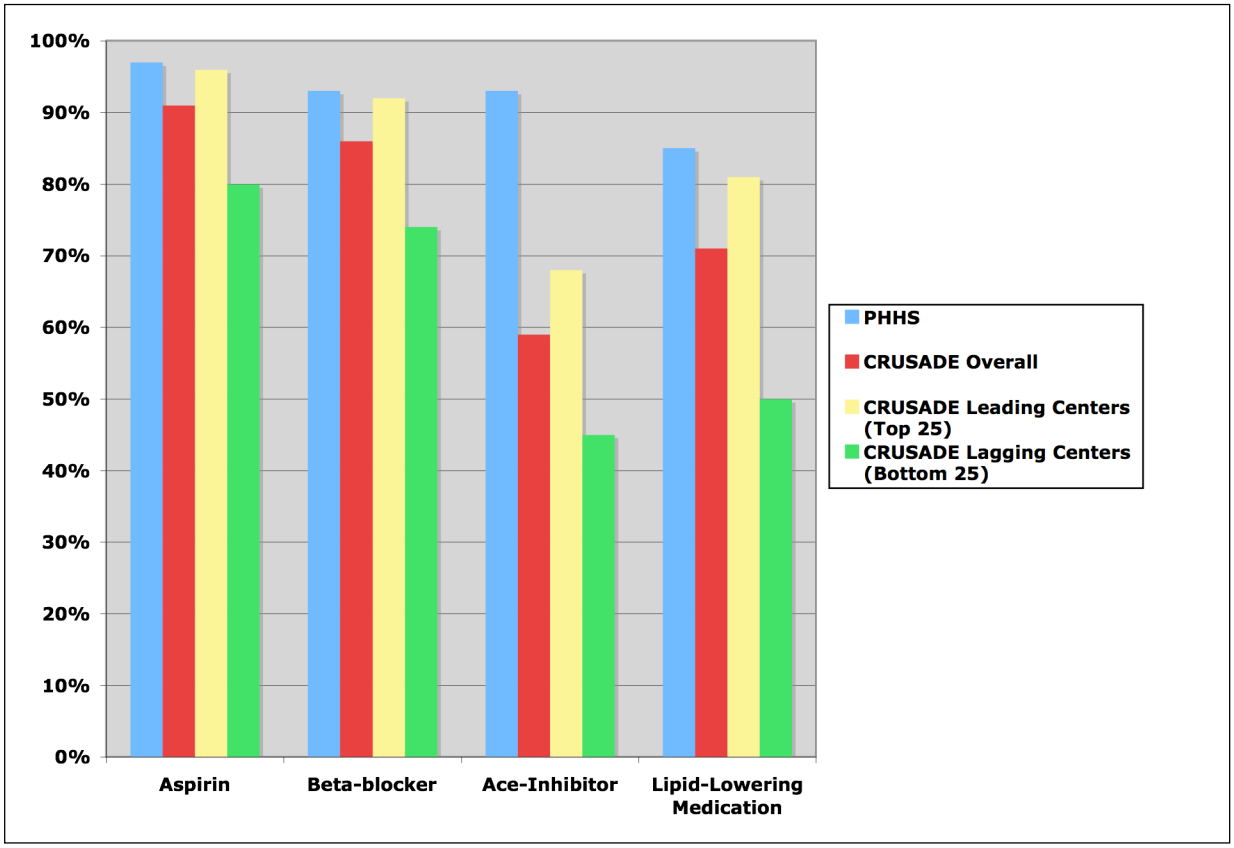


Figure 6. Rates of evidence-based medication at discharge, PACE-Rx versus CRUSADE July 2001-March 2005.

A second possibility is that subjects in the present study differ from those in previous studies. The majority of prior studies examined individuals in community-based ambulatory practices with already-established primary care[29, 31, 32], while those in the present study came from an urban academic institution following an inpatient admission for an ACS event. As a tax-supported urban county hospital, Parkland Memorial Hospital serves a socio-economically underprivileged and racially diverse population. Thus, since the present study specifically examined a higher-risk population as compared with those examined in prior studies, higher rates of visit non-adherence were seen at both 3-month and 1-year measurements (Table 4).

Table 4. Comparison of Visit Adherence at Follow-Up Appointments.

	PACE-Rx at 3 Months	PACE-Rx at 1 Year	SPLINT at 1 Year	WHITTINGTON at 6 Months
Combined	111/140 (79.3)	92/140 (65.7)	1462/1697 (86.2)	115/120 (95.8)
Nurse Led	57/72 (79.2)	47/72 (65.3)	723/851 (85.0)	59/60 (98.0)
Usual Care	54/68 (79.4)	45/68 (66.2)	739/846 (87.4)	56/60 (93.0)

This phenomenon may have diminished the effectiveness of additional physician extender visits in the present study, as individuals at highest risk may have been lost to follow-up. These findings suggest that a significant source of the "treatment gap" observed in this population may arise in part from an inability to maintain patient follow-up despite a high initial rate of evidence-based therapies implemented at discharge.

There are many other varied reasons why patients in our study were non-adherent with clinic visits. After completion of the one-year study period, non-adherent patients were contacted by telephone to try and find possible reasons why they did not participate in the study. Six patients died in each arm of the study, which is to be expected in a post-ACS population. Five patients in the physician extender arm and one patient in the usual care claimed that they were unable to afford clinic visits. It is possible that patients who did not attend either the post-ACS visit or other usual care visits did so because they could not afford to attend. Another possible reason for low visit adherence was lack of transportation, as many patients in this population only have access to a bus system that requires them to make several transfers throughout the city to get to Parkland. Several patients in each study arm moved which reflects our migrant population. Time was also an issue as wait times at clinics is lengthy with patients having to

devote at least half a day to one visit. All these help explain the high rate of non-adherence in this population and possibly why the results of the study were overwhelmingly negative.

This challenge in maintaining adherence in at-risk populations is further illustrated by the discrepancy observed between evidence-based medication use and participation in therapeutic lifestyle modifications. The number of patients participating in lifestyle modifications was low in both treatment groups, and only dietary changes were improved significantly by the addition of a physician extender. Although therapeutic lifestyle modifications and participation in cardiac rehabilitation decrease risk of future events[37-40], actual implementation of these changes still remains a challenge. A possible strategy to improve adherence to lifestyle recommendations in clinical practice is to designate time at each visit for education about the benefits of lifestyle modifications, and to formulate an achievable action plan for each patient[40]. However, this strategy is still limited by visit non-adherence, as implementation of many lifestyle modifications require added visits, for example, to a nutritionist, a smoking cessation class, or cardiac rehabilitation. In our study approximately 21% of the overall cohort was lost to follow up at 3 months, which increased to 34% at one-year. Potential solutions to address this limitation may involve a combination of these programs into a multidisciplinary post-ACS clinic, in which a patient would be able to follow-up with a physician, meet with a nutritionist, and participate in cardiac rehabilitation and smoking cessation class in one visit. Alternatively, given the success of medications prescribed at discharge, further efforts could be placed on assisting patients with starting lifestyle modifications during the patient's initial hospital stay.

Limitations

Although the present study was a prospective, randomized controlled trial, there are specific limitations. First, there was a high overall rate of visit non-adherence. Although this effect was similarly high between the two treatment arms, this reduced the number of patients we were able to follow for three-month and one-year data and is a potential source of bias. Second, the present study only examined the prescription rates of evidence-based therapies and did not evaluate actual use of medications. It would be of interest to evaluate if there are significant discrepancies between prescription rates and actual use in this and other similar underserved populations.

Conclusion

The addition of a physician extender to usual care in the management of post ACS patients did not improve significantly the attainment of LDL and blood pressure goals, prescription of evidence-based medications, or most lifestyle modifications at three months and one-year following an ACS event. This is likely due to a high level of adherence to ACS treatment guidelines at discharge in our study population, and a low rate of adherence to clinical and study follow-up visits. Efforts should now be made to increase adherence with lifestyle modifications and follow-up visits.

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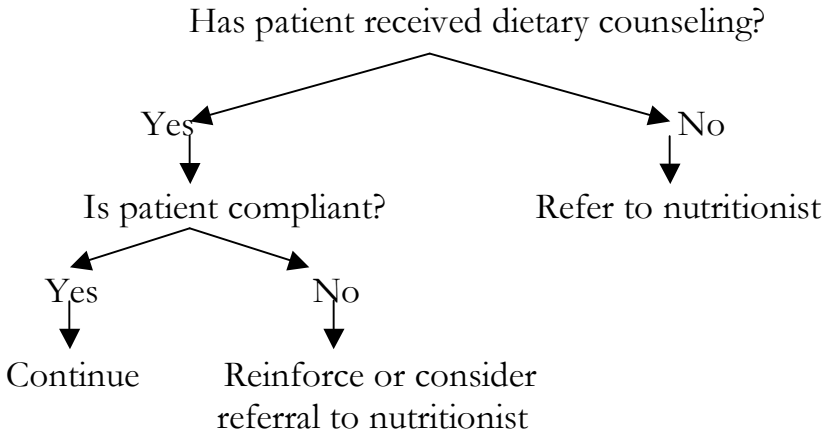
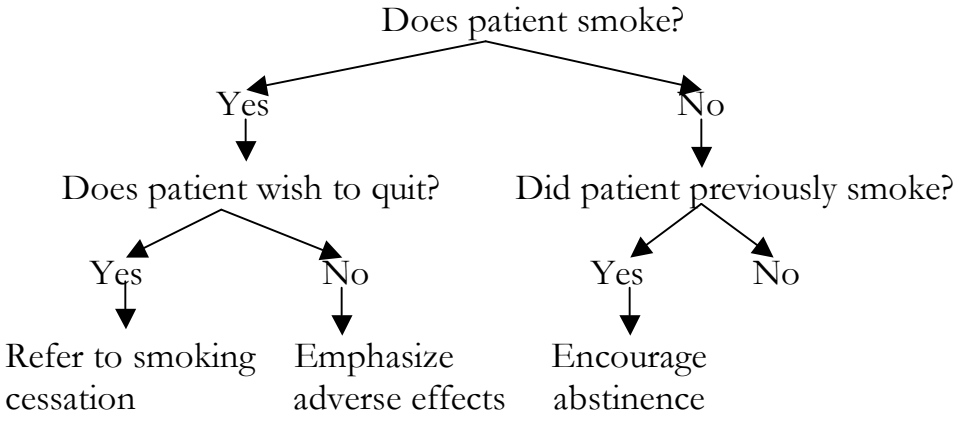
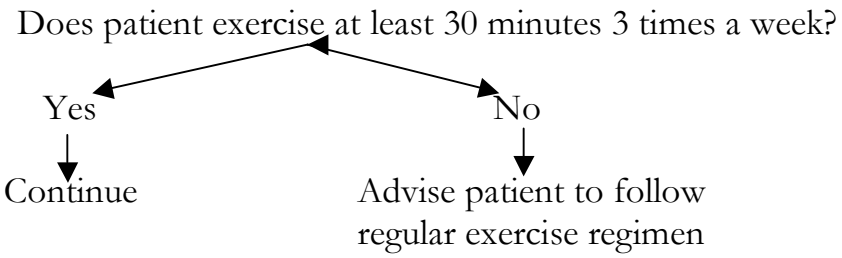
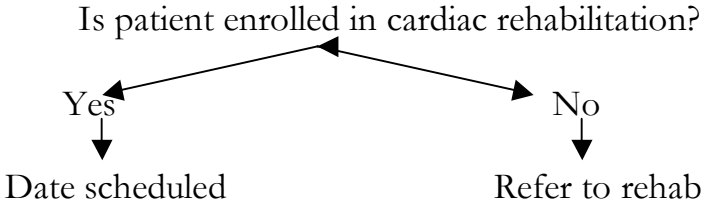
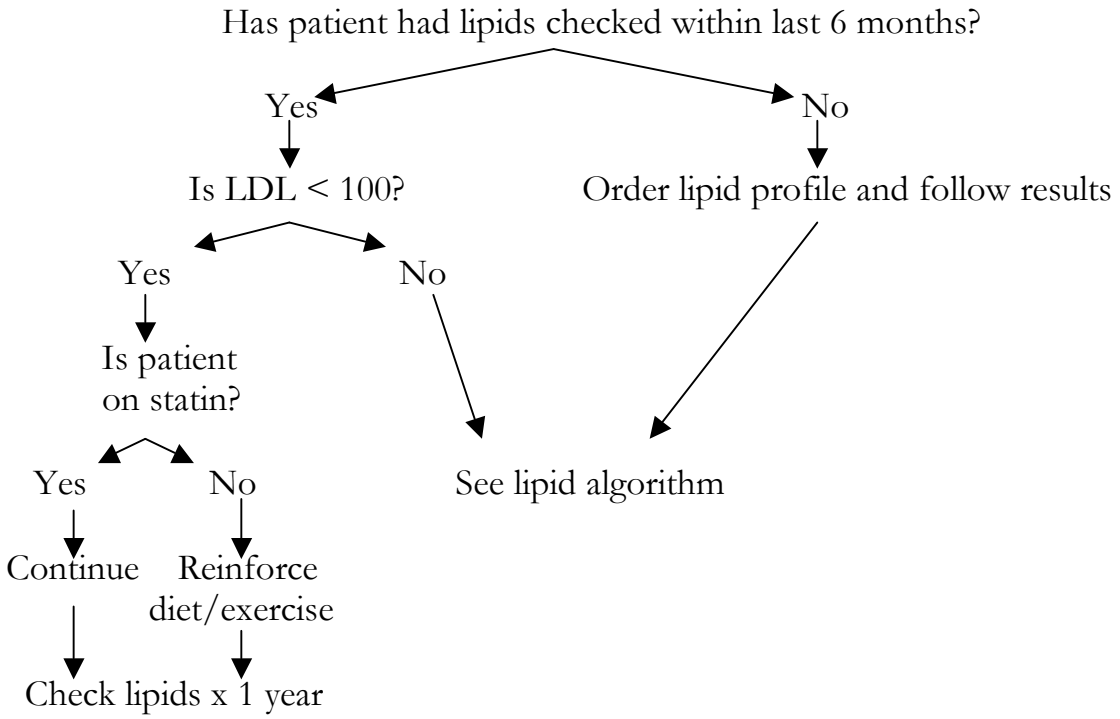
APPENDIX A
Post-ACS Clinic Algorithm



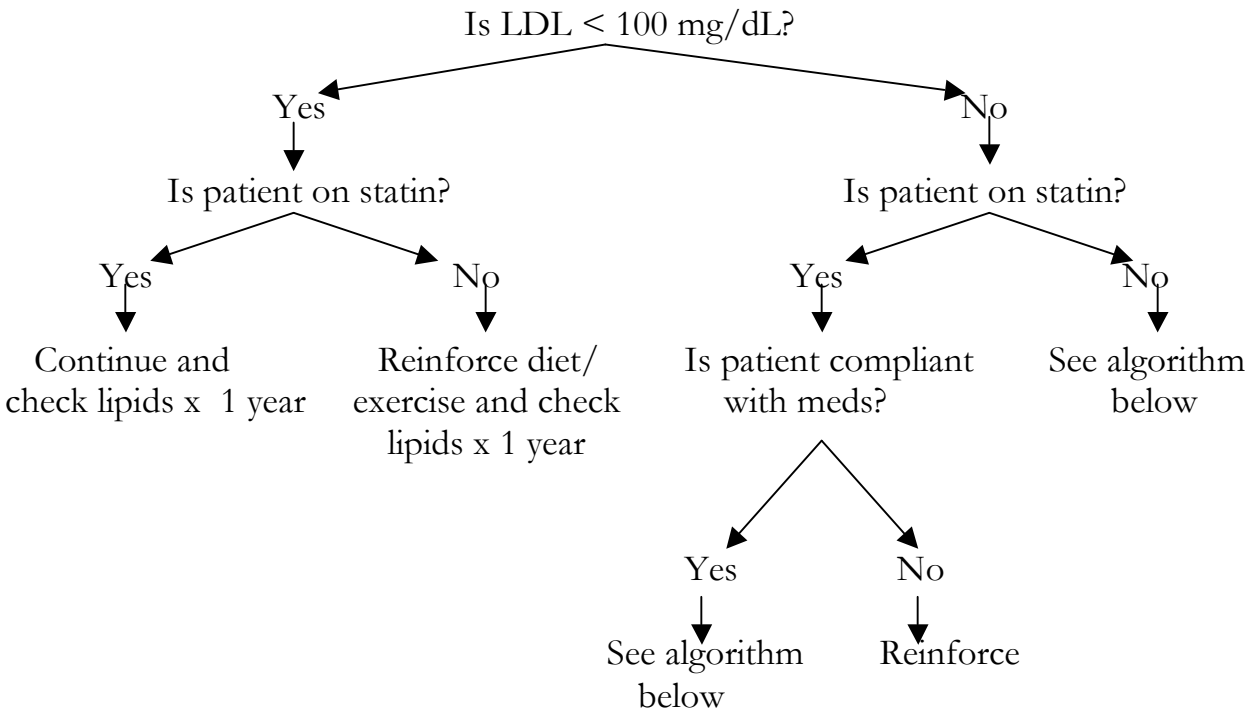


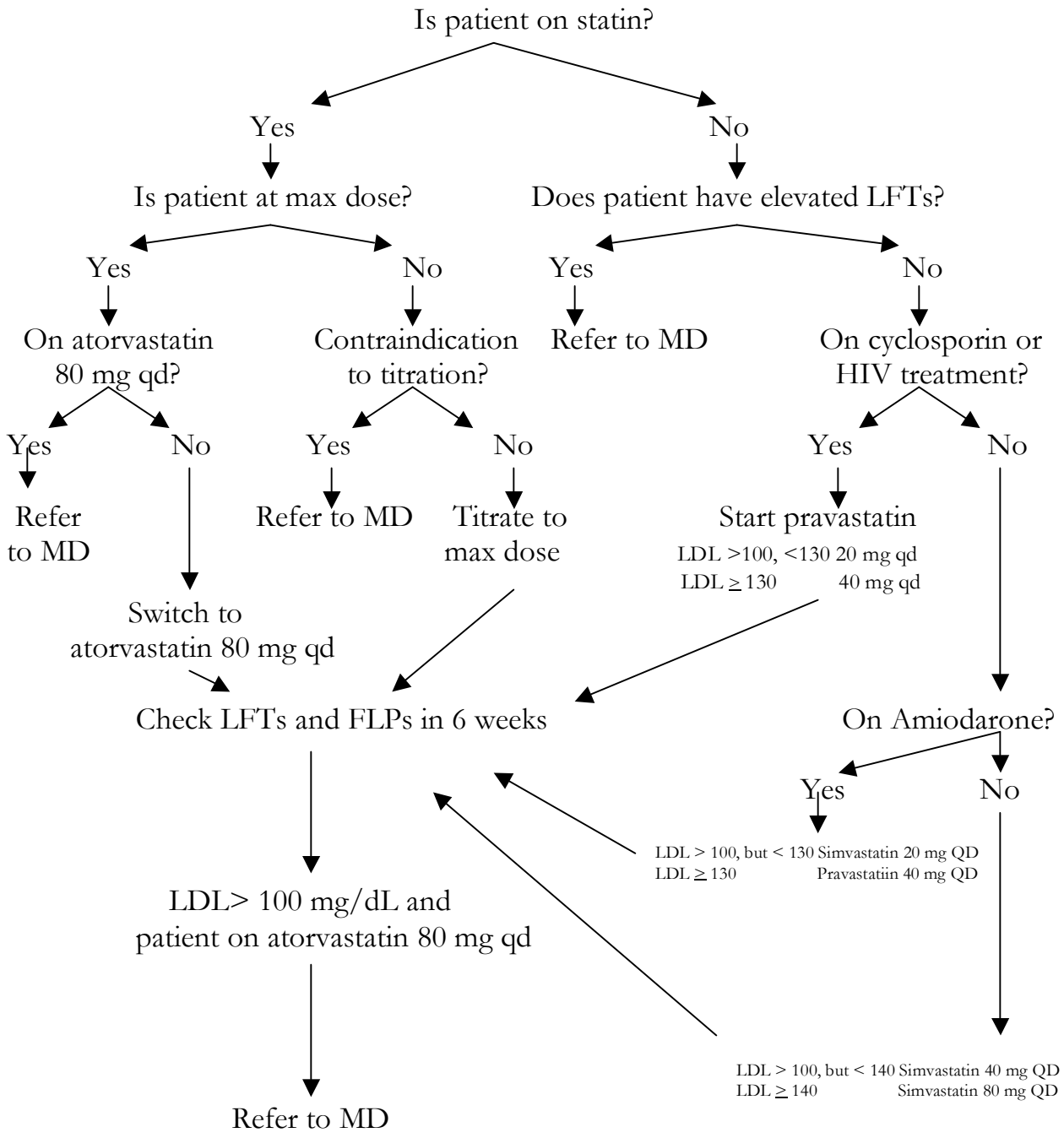




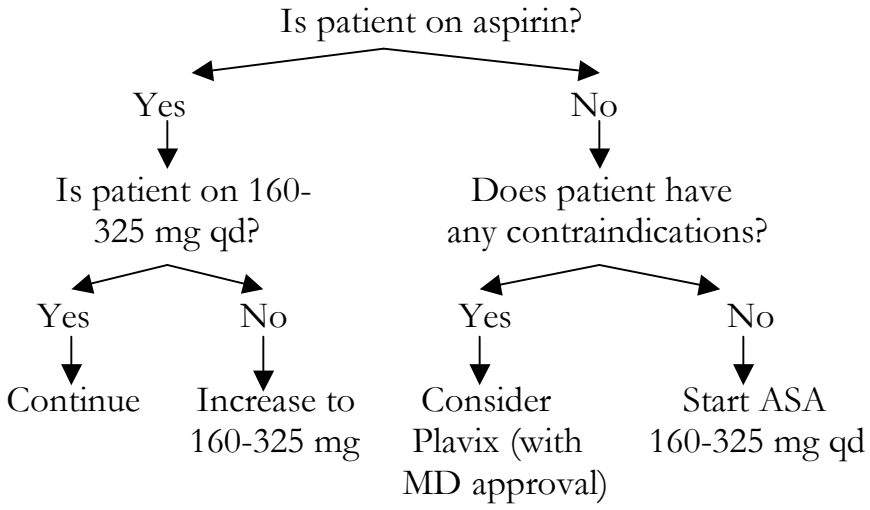

Has patient had lipids checked within last 6 months?
Yes
No
Is LDL < 100?
Order lipid profile and follow results
Yes
No
Is patient on statin?
See lipid algorithm
Yes
No
Continue
Reinforce diet/exercise
Check lipids x 1 year

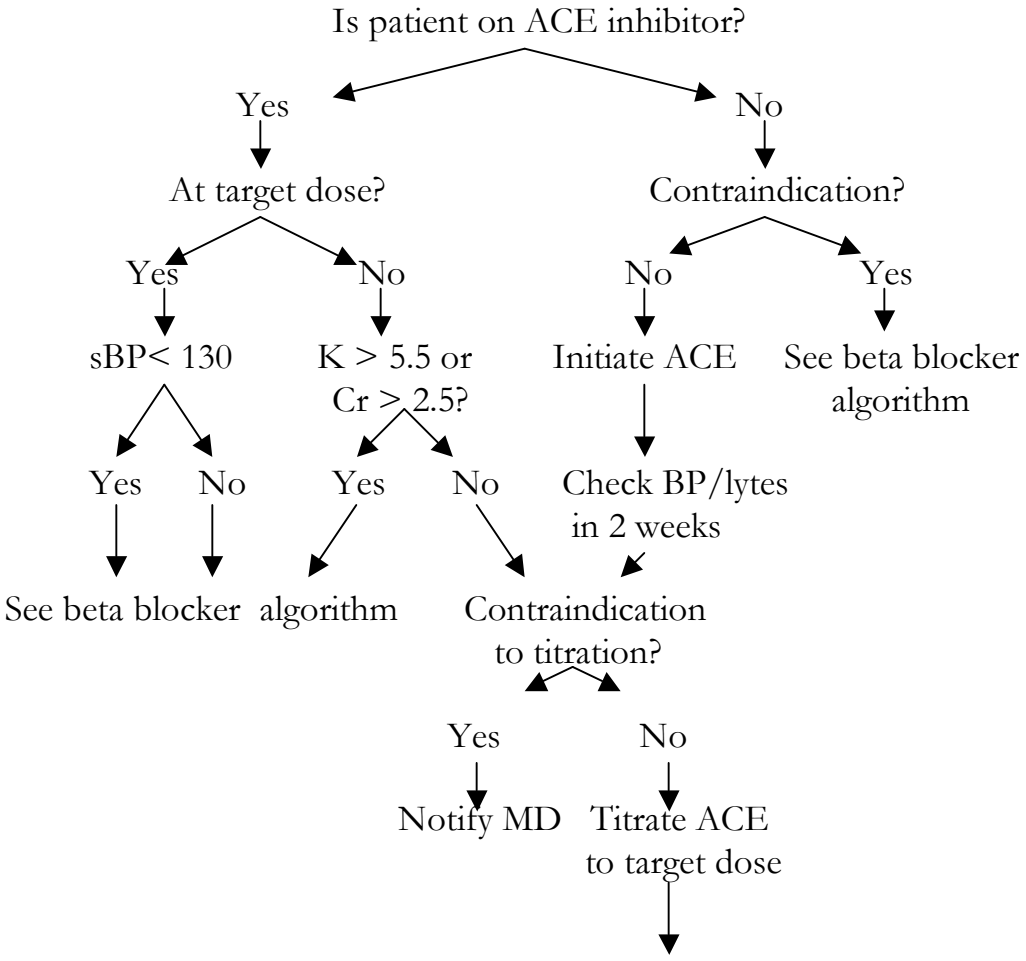
Lipid Algorithm

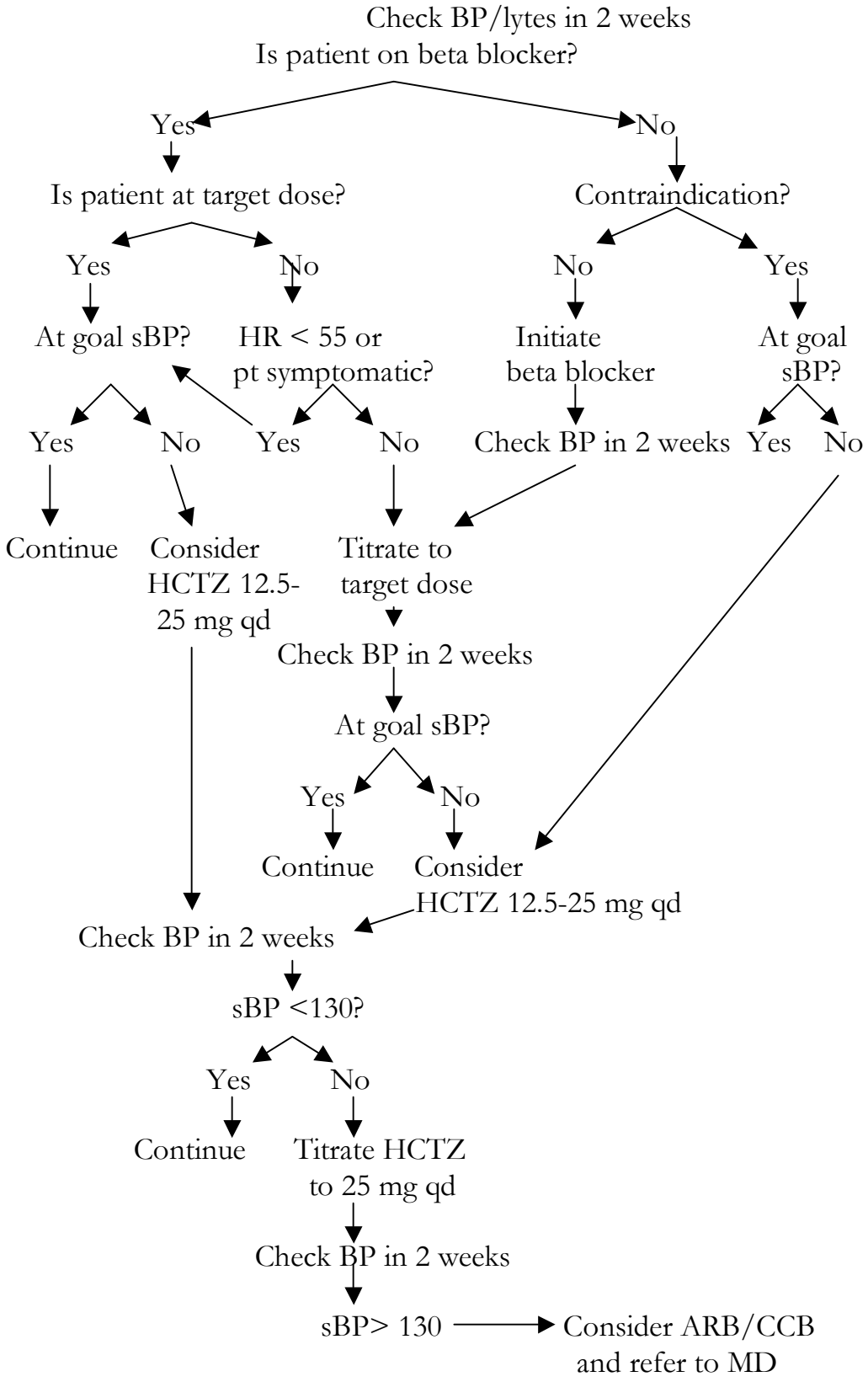




- Check fasting lipids and LFTs after initiation of statin and each subsequent dose adjustment.
- Titrate statin to max dose for goal LDL < 100 mg/dL
- Switch to atorvastatin 80 mg if LDL > 100mg /dL despite max simvastatin
- If LDL > 100 mg/dL on atorvastatin 80 mg, refer to MD


Is patient on aspirin?
Yes
No
Is patient on 160-325 mg qd?
Does patient have any contraindications?
Yes
No
Yes
No
Continue
Increase to 160-325 mg
Consider Plavix (with MD approval)
Start ASA 160-325 mg qd


Is patient on ACE inhibitor?
Yes
No
At target dose?
Contraindication?
Yes
No
No
Yes
sBP< 130
K > 5.5 or Cr > 2.5?
Initiate ACE
See beta blocker algorithm
Yes
No
Yes
No
Check BP/lytes in 2 weeks
See beta blocker algorithm
Contraindication to titration?
Yes
No
Notify MD
Titrate ACE to target dose


Check BP/lytes in 2 weeks
Is patient on beta blocker?
Yes
No
Is patient at target dose?
Contraindication?
Yes
No
No
Yes
At goal sBP?
HR < 55 or pt symptomatic?
Initiate beta blocker
At goal sBP?
Yes
No
Yes
No
Check BP in 2 weeks
Yes
No
Continue
Consider HCTZ 12.5-25 mg qd
Titrate to target dose
Check BP in 2 weeks
At goal sBP?
Yes
No
Continue
Consider HCTZ 12.5-25 mg qd
Check BP in 2 weeks
sBP <130?
Yes
No
Continue
Titrate HCTZ to 25 mg qd
Check BP in 2 weeks
sBP> 130
Consider ARB/CCB and refer to MD

- **ACE inhibitors:**
  Prescribe indefinitely to all post MI patients, unless contraindicated.

  Contraindications:
  K > 5.5 mEq/L
  Cr > 2.5 mg/dL
  Symptomatic hypotension
  Pregnancy
  Renal artery stenosis
  Inability to tolerate ACE

  Precautions and close monitoring:
  sBP < 90 mmHg
  Cr > 2.5 mg/dL

- **Beta blockers:**
  Prescribe indefinitely to all post-MI patients, unless contraindicated. Advise patients that side effects may occur during initiation of therapy but do not prevent long term use; abrupt discontinuation should be avoided; to self monitor for evidence of hyptonsion and bradycardia

  Contraindications:
  Overt heart failure
  Heart rate < 55 and patient symptomatic
  sBP < 90
  Second or third degree AV block
  PR interval > 0.24 ms
  Severe COPD/asthma
  Sick sinus syndrome

  Precautions and close monitoring:
  Heart rate < 60 bpm

- **Aspirin:**
  Prescribe 160-325 mg/day indefinitely unless contraindicated.

  Relative contraindications:
  Blood dyscrasia
  Severe hepatic disease

  Absolute contraindication:
  Hypersensitivity to salicylates

  Consider antiplatelet therapy (clopidogrel, ticlopidine, dipyridamole) for patients who experience subsequent cardiovascular events despite aspirin, or those with salicylate hypersensitivity.

	Starting dose	Titration	Target dose
ACE-inhibitors:			
Captopril	12.5 mg tid	double dose	50 mg tid
Enalapril	5 mg qd	double dose	20 mg bid
Fosinopril	10 mg qd	double dose	40 mg qd
Lisinopril	10 mg qd	double dose	40 mg qd
Quinapril	10 mg qd	double dose	40 mg qd
Ramipril	2.5 mg qd	double dose	10 mg qd
Beta blockers:			
Atenolol	12.5 -25 mg qd	double dose	50 mg qd
Metoprolol	12.5-25 mg bid	double dose	50 mg bid
Toprol XL	12.5 mg qd	double dose	50 mg qd
Carvedilol	6.25 mg bid	double dose	25 mg bid
ARBs:			
Valsartan	80 mg qd	double dose	160 mg qd
Losartan	25 mg qd	double dose	100 mg qd
HCTZ:	12.5-25 mg qd	double dose	25 mg qd
CCB:			
Amlodipine	2.5 mg qd	double dose	10 mg qd

- After initiation of antihypertensive and each dosage adjustment, check BP within 2-3 weeks.
- Consult MD if significant change in labs
- If patient cannot tolerate antihypertensive or has significant adverse effect, consult MD

VITAE

Sundeep Viswanathan was born in Buffalo, NY and completed high school in Houston, TX. Sundeep's interest in research started at an early age when he spent summers in high school working at the Research Institute on Addictions in New York. He attended the University of Texas at Austin earning a Bachelor of Science in Biochemistry and participating in the Dean's Scholars Honors Program. While at UT, Sundeep continued his interest in clinical research, completing a summer research fellowship at the National Institute of Aging in Baltimore, MD studying the effects of cancer chemotherapeutic agents on a novel large B cell lymphoma cell line. He also spent time working on a thesis project as part of his degree in organic chemistry synthesis in Organic Chemistry lab at UT. Sundeep graduated Summa Cum Laude from UT Austin with a perfect 4.0 GPA.

In August of 2003, Sundeep matriculated into the University of Texas Southwestern Medical School at Dallas. He spent two formal summers and additional time during medical school working with fellow student Jeffrey Yorio and mentor Darren McGuire, MD on the PACE-Rx study. He also spent time working in the Department of Radiology at Texas Childrens Hospital in Houston studying the efficacy of cardiac MRI in evaluating anatomical changes of children with congenital heart disease undergoing a staged Fontan procedure. He will graduate with a Doctorate in Medicine with a Distinction in Research in May of 2008. Sundeep will continue training in Internal Medicine at Barnes-Jewish Hospital in St. Louis where he plans on specializing in Cardiology or Oncology.

VITAE

Jeff Yorio was born in Fort Worth, Texas and grew up in Burleson, Texas. During the summer of 1995, Jeff participated in the START (Student Teacher Applied Research Training) Program at UNT Health Science Center, where he worked for eight-weeks in the lab of Dan Dimitrijevich, Ph.D. He graduated from Burleson High School in May 1997. He attended The University of Texas at Austin and graduated in May 2001 with a Bachelor of Science in Advertising with High Honors. After college, Jeff moved to New York City, where he worked as an advertising copywriter for GWHIZ Advertising for clients such as Food Network, Dairy Queen, W Hotels, Majesco Games, TOPPS and Furnished Quarters. In June 2003, Jeff went back to The University of Texas at Austin to complete premedical post-baccalaureate work.

Jeff matriculated at The University of Texas Southwestern Medical School in 2004. He worked on the PACE-Rx research study for two formal summers and throughout medical school with fellow student, Sundeep Viswanathan, and mentor, Darren McGuire, M.D. He received the NIH T-35 Training Grant for Medical Student Research to fund his participation. Sundeep and Jeff presented posters at the 43rd and 44th UT Southwestern Medical Student Research Forum, as well as the 5th & 6th Annual Cardiovasular Symposium at UTSW. They were also co-first authors on a paper that was published in the Journal of Internal Medicine in January 2008.

In the spring of 2008, Jeff began working on a lung cancer research project on the association between intervals in diagnosis and treatment and outcomes with David Gerber, MD. He will graduate with a Doctorate in Medicine with a Distinction in Research in May of 2008. He will begin his postgraduate training in Internal Medicine at The University of Texas Southwestern Medical School in July 2008, and will most likely pursue a fellowship in oncology after his residency. He is married to Andi Yorio and they have one son, Eli.