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Acute Pharmacological Treatment given to Older Adults with Acute Myocardial Infarction: A Nationwide Emergency Department Study, 1992-2010

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Acute Pharmacological Treatment Given to Older Adults with Acute Myocardial Infarction: A Nationwide Emergency Department Study, 1992–2010

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

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DEDICATION

To my Husband

Without you this would only be a dream

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ABSTRACT

ACUTE PHARMACOLOGICAL TREATMENT GIVEN TO OLDER ADULTS WITH ACUTE MYOCARDIAL INFARCTION: A NATIONWIDE EMERGENCY DEPARTMENT STUDY, 1992–2010

Maryam S. Alowayesh, MSc

Virginia Commonwealth University, 2013

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

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OBJECTIVE: To determine the pattern and predictors of use of antiplatelet agents and beta-blockers given in the emergency department (ED) to older adults with acute myocardial infarction (AMI) and its effects on in-hospital mortality and length of hospital stay (LOS) and to determine the effect of computerized ED guideline reminders on their utilization.

METHODS: A cross-sectional study using the National Hospital Ambulatory Medical Care Survey (NHAMCS) ED data for years 1992 to 2010 was conducted. Patients were included if they had an admission diagnosis of AMI (ICD-9-CM code 410.xx) and were ≥55 years. Survey logistic regression was used to examine whether there was a trend in the use of antiplatelet agents and beta-blockers across the years and to explore the association between various predictor variables and their utilization rates. The chi-square test was used to see whether users of these drugs were different from non-users in their rates of in-hospital mortality. Survey linear regression was used to explore the effect of utilization of these drugs on LOS. All the visits were

weighted to get national estimates. All of the analyses were carried out with SAS 9.3 statistical package.

RESULT: A total of 1,771 visits (weighted frequency = 6.1 million) by patients were selected for this study. Both anti-platelet agents and beta-blockers were shown to have a positive trend across the years. Age, sex, chest pain, triage, using an ambulance, and metropolitan region were all found to be significant predictors of either antiplatelet agent or beta-blocker utilization. Use of beta-blockers was associated with lower in-hospital mortality. Neither drug class had an effect on LOS. Finally, patients who were treated in EDs with computerized guideline reminders were twice as likely to get an antiplatelet agent, but this was not seen with beta-blockers.

CONCLUSION: This study displayed a positive pattern across the years in the use of antiplatelet agents and beta-blockers given to older AMI patients. It also showed that age, sex, and other important variables were significant predictors of their utilization. The use of beta-blockers yielded lower in-hospital mortality. Finally, the use of ED reminders increased antiplatelet agent utilization.

CHAPTER 1

Introduction

Acute Myocardial Infarction Statistics

Heart disease is the number one cause of death in the United States; accounting for 617,000 deaths in 2008.[1] Almost 1.2 million older adults, defined as those adults aged 65 years and older, were discharged from a hospital with heart disease in 2008-2009. Approximately half of those were discharged with acute myocardial infarction (AMI).[2-3] Older adults represent about 13% of the US population, yet account for 60% of hospital discharges for AMI and almost 90% of AMI in-hospital deaths.[3-4] Cardiovascular morbidity and mortality rates rise even more rapidly in patients 75 years or older.[5]

Despite the high prevalence of AMI morbidity and mortality in the older adult population, limited randomized clinical trial data is available to guide their care.[5] Although explicit age-based exclusions in clinical trials have become less frequent since 1990, age-based exclusions still appear.[6-8] Even when age-based exclusions are eliminated from these clinical trials, implicit age-based exclusions are still a concern.[9] For example, physician/investigator preference or the types of sites involved in the recruitment process may create implicit exclusion criteria that affect the type of patients enrolled, which may in turn affect the generalizability of the findings.[9]

AMI Treatment Timeliness

AMI treatment is a timely matter, so delay in evidence-based acute therapies may put patients at risk.[10] Hence, there is emphasis in the literature on the importance of initiating AMI

treatment in the emergency department (ED).[11-12] The ED is considered to be a critical setting for measuring AMI care since therapies started in the ED are more likely to be continued during hospitalization with a lasting impact on patient outcomes.[11-12] The Institute of Medicine has identified the ED as the part of the health care system in most need of improvement.[13] The ED faces a lot of challenges like boarding of admitted patients in the ED, crowding, and ambulance diversion. AMI is considered an ideal disease for studying ED quality of care since it is initially treated in the ED and its therapies are time-sensitive and may impact mortality.[12,14] Despite its importance, quite few resources have been directed at studying AMI care in the ED.[12]

AMI management in the ED is related to the "3 T's"—triage, treatment, and timeliness of specialty consultation.[10] Initial triage effectiveness governs patient outcomes because empiric therapy often will be started (e.g. aspirin) and patients will be risk stratified. It is challenging to triage patients in the ED, as it has to be done in a short time period with limited information.[10] Triaging older patients is even more challenging since they frequently present with atypical symptoms like no chest pain, dizziness, and shortness of breath, often called a silent MI.[15] Receiving care by a multidisciplinary specialist team in the ED (i.e. primary care physician, emergency medicine physician, cardiologist, and an ED nurse) is considered to be a class Ib recommendation in the American Heart Association (AHA) guidelines; however, it is not always feasible.[16] In this same recommendation, it is also suggested to have written protocols for triaging and managing AMI patients in the ED.[16] Part of these protocols provide the content of the admitting orders and must indicate that aspirin and a beta-blocker were given in the ED, and if not, what was the reason.[16]

AMI Guidelines

A large body of evidence supports the early treatment of AMI with antiplatelet agents and beta-blockers.[17-23]Treatment with early administration of beta-blockers is becoming more controversial, specifically intravenous (IV) beta-blockers.[24-26] It has been shown that the early IV administration of a beta-blocker to patients who are hemodynamically unstable or show signs of heart failure may cause cardiogenic shock.[26] The early administration of an oral beta-blocker is still considered safe and recommended.[20,24] In this case, practice guidelines are considered to be the best tool to guide health professionals' decisions on AMI treatment by utilizing the strongest body of evidence from randomized clinical trials (RCTs) and large observational studies.

The American College of Cardiology and the American Heart Association (ACC/AHA) have used a joint committee since 1980 to guide AMI treatment and other cardiovascular diseases.[27] Approximately every two years they publish a new guideline or update one of the existing guidelines.[27-34] Since 2006, they started publishing performance measures for AMI treatment. An update of these measures was published in 2008.[35-36] These performance measures aim to assist in the measurement of AMI care quality and increase the uptake of AMI guidelines.[35] In the 2006 performance measures, beta-blockers were recommended to be given upon ED arrival; however, this recommendation was omitted from the 2008 update.[36] They argue that since there is a distinction between IV beta-blockers and oral beta-blockers and there is a list of patient factors that need to be checked before administering a beta-blocker, early beta-blockers were not fit to be a performance measure because of the complexity of its implementation.[36]

AMI Initiatives

AMI is one of the most extensively studied medical condition in the literature.[37] In the last two decades, AMI mortality decreased by 33%, which is believed to be the result of improved AMI treatment.[38] Numerous quality improvement (QI) initiatives and AMI registries contributed to this improvement by enabling the provision of consistent care and the quick adoption of clinical advances.[38] These initiatives aided in the constant measurement of AMI quality of care by creating continuous opportunities for improvement.[38] One of the most well-known AMI registries is the Global Registry of Acute Coronary Events (GRACE). It is a prospective observational project aimed to improve the acute and long-term care in AMI. Patient data has been collected in 14 countries since 1999.[39]

There are many US-based QI initiatives and AMI registries. A well-known governmental QI initiative is the Cooperative Cardiovascular Project (CCP). It was initiated in 1992 by the Health Care Financing Administration (HCFA, now the Centers for Medicare and Medicaid Services) to benefit Medicare patients.[40] It is a nationwide program that aims to improve quality of AMI care received by Medicare beneficiaries.[40] The American College of Cardiology (ACC) has developed a program called Guidelines Applied in Practice (GAP) with a goal of facilitating the use of the ACC/AHA guidelines in practice.[41] The American Heart Association (AHA) has a similar initiative to GAP called the Get With the Guidelines (GWTG) initiative. The ACC and the AHA share the same goals in their QI initiatives.[38] The National Cardiovascular Data Registry (NCDR) had the initiative in year 2007 to merge two large AMI registries into one large national AMI registry.[38] The National Registry of Myocardial Infarction (NRMI) and "Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines" (CRUSADE) QI initiative merged into one

registry called the Acute Coronary Treatment and Intervention Outcomes Network (ACTION).[38] Afterwards, the NCDR still perceived a need for a more unified registry; hence, it facilitated a merger in 2008 between the ACTION registry and the GWTG initiative to create the ACTION Registry-GWTG (AR-G).[38]

Conceptual Framework

When studying the quality of care in a certain disease (e.g. AMI), it is best to use a framework that has been developed to measure and assess clinical practice. The most utilized and widely accepted framework in this area is the Donabedian model, or the structure-process-outcome model, a simple and persuasive model that combines all aspects of health care.[42]

To best understand and use the Donabedian model, it is important to explain this triad "structure-process-outcome" in more detail. Structure in this model represents material resources, human resources, and organizational characteristics, such as the presence of teaching and research functions and integrated computer systems. Process, on the other hand, constitutes all the activities performed in patient health care, like diagnosis, treatment, and prevention. Outcome is the end result of a health care service or activity and reflects any desirable or undesirable change in the patient. Outcomes may include clinical, economic, and humanistic outcomes.[42]

There are certain rules or conditions that govern how we use this model. It is important to know that structure, process, and outcome are not considered aspects of quality. We can only infer that quality is good or bad by the information available to us. Another pivotal rule is that without a predetermined relationship between the structure, process, and outcome, no inferences can be made. This relationship should be supported by well-established evidence. The stronger

this relationship is the stronger the inferences being made. Finally, this model is developed to assess clinical practice, so it may not work as well in other settings.[42]

Choosing the right outcome to assess clinical care is a pivotal step. Donabedian provided some guidelines to follow when choosing the outcome. The outcome must be relevant, achievable by good care, attributed to health care, and available to collect.[42] Also, it is important to consider the magnitude and duration of the outcome, and when tracking the consequences of taking an action, it is also important to track the consequences of not taking action.[42]

Overview of the study

This study is designed to assess the acute pharmacological treatment given in the ED to older adults with AMI from a "structure-process-outcome" approach. The structure component is the ED computerized guideline reminders. The process component is the utilization of anti-platelet agents and beta-blockers in the ED. Finally, the outcome component is in-hospital mortality and length of hospital stay. Our study is an exploratory study that is aimed to generate hypotheses for future study.

Significance

This study gives national estimates about older adult AMI care in the ED from 1992 to 2010, which is the first to capture this long period of time of ED AMI care for older adults. Using the Donabedian model as a conceptual framework gave a holistic view of AMI care in older adults. The impact of having a computerized ED guideline reminder on the usage of antiplatelet agents and beta-blockers in the ED was evaluated, which is also a first. It also did describe the percentages of antiplatelet agents and beta-blockers used only in the ED, which was only done in few studies. Our study attempted to see the effect of AMI care in the ED on hospital outcomes, like in-hospital mortality and LOS. Finally, this study may help in increasing the

awareness of the ED health care professionals of older adults AMI care and the importance of incorporating computerized clinical decision support (CCDS) systems in the ED to remind health professionals about using guideline recommended therapies.

Study Objectives

This study had four primary objectives.

1. Examine the temporal trend in the ED use of anti-platelet agents and beta-blockers in older adults with AMI in the US from 1992 to 2010
2. Explore the association between a variety of predictor variables (demographic, clinical, visit, and hospital variables) and the ED use of anti-platelet agents and beta-blockers in older adults with AMI
3. Evaluate the association between the ED use of anti-platelet agents and beta-blockers in older adults with AMI and the rate of in-hospital mortality and length of hospital stay
4. Evaluate the association between the use of ED computerized guideline reminders and the ED utilization of anti-platelet agents and beta-blockers in older adults with AMI

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CHAPTER 2

Literature Review

AMI overview

AMI definition and classification

The literal meaning of myocardial infarction is the death of cardiac myocytes caused by prolonged ischemia.[1] The World Health Organization (WHO) defined myocardial infarction in the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) project published in 1994;[2] however, this definition was updated by the European Society of Cardiology (ESC) and the American College of Cardiology (ACC) in 2000 because the WHO definition erroneously diagnosed patients with non-myocardial infarction even when actual cardiac damage had occurred.[1,3] The updated definition of AMI is summarized in Figure 2.1.

Criteria for acute, evolving, or recent MI
Either one of the following criteria satisfies the diagnosis for an acute or recent MI:

(1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:
- (a) ischemic symptoms;
- (b) development of pathologic Q waves on the ECG;
- (c) ECG changes indicative of ischemia (ST segment elevation or depression); or
- (d) coronary artery intervention (e.g., coronary angioplasty).

(2) Pathologic findings of an acute MI.

Figure 2.1: AMI definition of the European Society of Cardiology and the American College of Cardiology (Adapted from Ref. 1**)**

MI: Myocardial infarction; CK-MB: Creatine kinase-MB; ECG: Electrocardiogram

Acute Coronary Syndromes (ACS) encompass a number of cardiovascular presentations which differ by the extent and duration of coronary occlusion, and include unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).[1] Both NSTEMI and STEMI are known collectively as AMI.[5] Classification of AMI is made according to the changes found in the ECG. Figure 2.2 illustrates the differences between the two.[4] AMI may be further classified according to the pathologic Q-waves. Patients with STEMI are more likely to have Q-waves in their ECG findings, or Q-wave MI (QMI). NSTEMI patients are less likely to have them, thus non-Q-wave MI (NQMI).[5] The pathophysiology of ACS starts with the rupture of an atherosclerotic plaque followed by platelet adherence, aggregation, and activation of the clotting cascade, which will end in the formation of a clot filled with fibrin and platelets. [4]

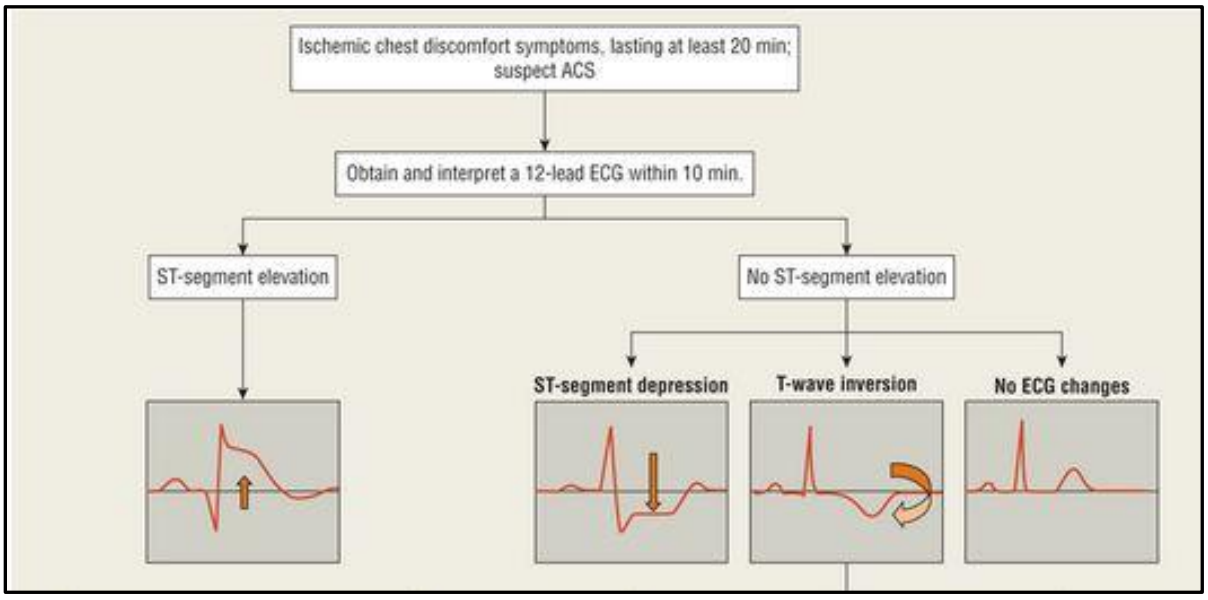

Figure 2.2: Differences in ECG between STEMI and NSTEMI (Adapted from Ref. 4**)**

AMI diagnosis and risk stratification

The typical symptom of AMI is chest pain, or more formally a midline anterior anginal chest discomfort that may radiate to the shoulder, down the left arm, to the back, or to the jaw. There are other symptoms that may accompany chest pain, like nausea, vomiting, and shortness of breath. There are no specific signs of AMI; hence, on physical examination, there will be no suggestive signs of AMI. The main diagnostic procedure in detecting AMI is the 12-lead ECG, followed by a laboratory test of troponin and CK-MB, which are biochemical markers of myocardial cell death, to confirm AMI diagnosis. The 12-lead ECG should be done within 10 minutes of patient's presentation in the ED.[4] More recent studies are recommending the 12-lead ECG to be done in the ambulance by the EMS staff.[6] It is important to check the troponin and CK-MB level at least 3 times (in the ED, at 12 hours, and at 24 hours) because some patients may present to the ED with values below the level of detection. At 12 or 24 hours, they may have positive values of troponin or CK-MB.[4] Figure 2.3 illustrates CK-MB and troponin levels in the blood across the days around AMI.[7]

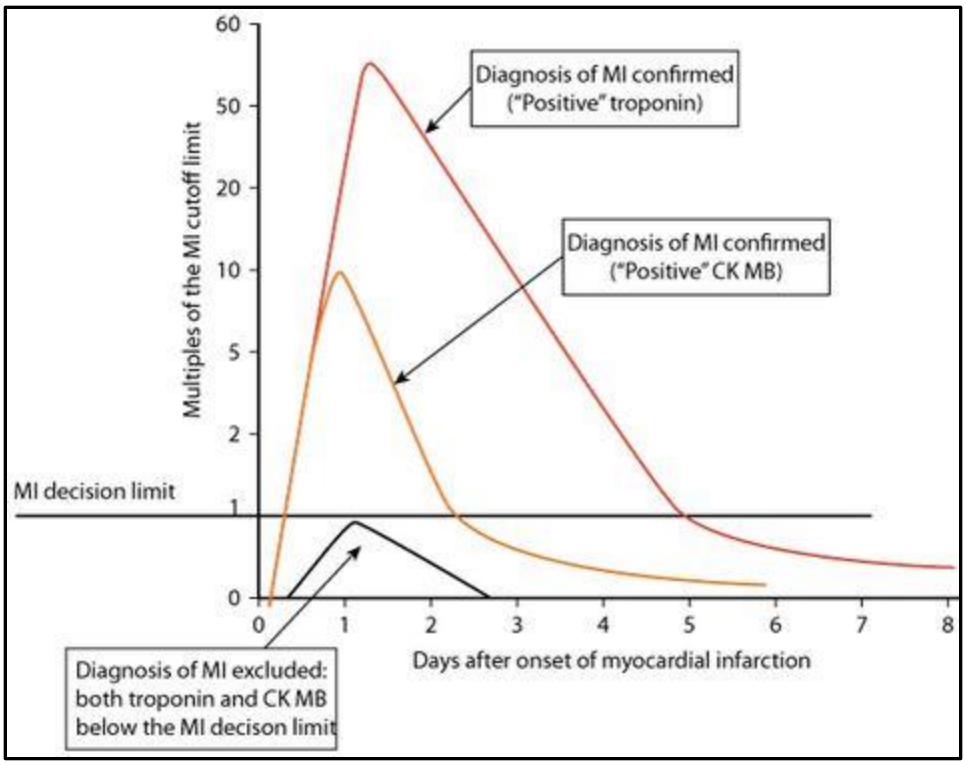

Figure 2.3: Troponin and CK-MB levels in AMI patients

Risk stratification in AMI is very important, as patients will be treated according to their risk stratification.[4] Patients are stratified according to their symptoms, medical history, ECG readings, and troponin or CK-MB levels. Patients experiencing a STEMI are considered to be at high risk of mortality. On the other hand, when patients are experiencing a NSTEMI, their risk level is dependent on many factors. The Thrombolysis in Myocardial Infarction (TIMI) risk score is used to stratify NSTEMI patients[4-5,8] and is presented in Figure 2.4. Low risk patients are usually monitored either in the ED or in a general ward. If values of troponin and CK-MB are still negative, they could be discharged. Moderate risk patients will be admitted either to the coronary care unit (CCU) or the step-down unit (SDU) to be monitored and treated. High risk patients should get early coronary angiography, which will be done in the cardiac catheterization laboratory.[4]

<table>
<tr><td>Past medical history
Age ≥ 65 years
≥ 3 risk factors for CAD
• Hypercholesterolemia
• HTN
• DM
• Smoking
• Family history of positive CHD
Known CAD (≥50% stenosis of coronary artery)
Use of aspirin within the past 7 days</td><td>Clinical presentation
ST- segment depression(≥0.5)
2 episodes of chest discomfort within the past 24 hours
Positive biomedical marker for infection.</td></tr>
<tr><td colspan="2">Using the TIMI Risk Score
One point is assigned for each of the seven medical history and clinical presentation findings.
The score (point) total is calculated, and the patient is assigned a risk for experiencing the composite end point of death, myocardial infarction, or urgent need for revascularization as follows</td></tr>
<tr><td>High Risk
TIMI risk score 5 – 7 points</td><td>Medium Risk
TIMI risk score 3 –4 points</td><td>Low Risk
TIMI risk score 0 – 2 points</td></tr>
<tr><td colspan="2">Other Ways to identify High – Risk Patients
Other findings that alone or in combination may identify high – risk patients:
• ST- segment depression.
• Positive biomedical marker for infection.
• Deep symmetric T- wave inversions (≥ 2mm).
• Acute heart failure.
• DM.
• Chronic kidney disease.
• Refractory chest discomfort despite maximal pharmacotherapy for ACS.
• Recent MI within the past 2 weeks.</td></tr>
</table>

Figure 2.4: TIMI score for NSTEMI (Adapted from Ref. 4)

Risk factors of getting an AMI are actually the same factors that are responsible of developing and progressing of atherosclerosis.[9] There are established risk factors which have clear evidence that their modification is associated with a decrease in the risk of cardiovascular disease (CVD).[3] These include dyslipidemias (high Low-Density Lipoprotein (LDL) or low High-Density Lipoprotein (HDL)), smoking, and hypertension.[3,9] There are other established risk factors, but it is less clear if their modification is associated with a decrease in the risk of CVD.[3] These include diabetes mellitus, obesity, and physical inactivity.[3,9] More recently, there are

emerging risk factors, which are mostly inflammatory markers like C-reactive protein and interleukins, but it is not clear whether their modification is associated with a decrease in the risk of CVD.[3]

Most AMI complications are life-threatening. The larger the infarct area, the higher the chance of experiencing complications. Also, the more ruptured plaques and the more coronary arteries involved, the worse the prognosis will be.[10] The most life-threatening complication is cardiogenic shock. Almost 2-6% of AMI patients experience it. Patients presenting with STEMI are more likely to develop cardiogenic shock compared to patients with NSTEMI.[11-12] Mortality almost reaches 60% when patients experience cardiogenic shock.[13] Other complications are pericarditis, ventricular and atrial tachyarrhythmia, venous thromboembolism, heart block, valvular dysfunction, left ventricular (LV) free-wall rupture, bradycardia, stroke secondary to LV thrombus embolization, and heart failure. Many patients experience those complications even before reaching the hospital. For example, almost 25% of patients with AMI die before reaching the hospital because of ventricular fibrillation.[14]

AMI treatment

AMI acute interventional treatment

Time is a crucial factor in AMI treatment. Minutes can mean the difference between a patient's death and survival. Early restoration of blood flow to prevent further expansion of the infarct area is one of the most important short-term treatment goals.[4] This can be achieved either by fibrinolysis or primary percutaneous coronary intervention (PCI). According to the ACC/AHA recommendations, STEMI patients should receive fibrinolysis within 30 minutes or primary PCI within 90 minutes.[15] Both timely fibrinolysis and timely PCI are considered to be quality performance measures. Time to fibrinolysis is called "door-to-needle-time," and time to

PCI is called "door-to-balloon-time".[15] STEMI patients should be transferred directly from the ED to the cardiac catheterization unit to undergo a coronary angiography with either a balloon angioplasty, placement of bare-metal stent, or drug-eluting intracoronary stent.[4] PCI has been proven to be safer and more effective than fibrinolysis and also has fewer contraindications and side effects.[15-17] Patients may undergo rescue PCI during their hospitalization if the fibrinolysis was unsuccessful, which is superior to repeated fibrinolysis.[18] High risk NSTEMI patients should also be revascularized early either by a primary PCI or coronary artery bypass surgery (CABG).[5,17]

AMI acute medical treatment

Early pharmacotherapy is a pivotal component of AMI patients' treatment. Both STEMI and NSTEMI patients receive the same pharmacological treatment. The standard treatment that should be given in the ED is intranasal oxygen (if oxygen saturation was less than 90%), morphine (for anginal pain), sublingual nitroglycerin, aspirin, a beta-blocker, and anti-coagulants (ex. unfractionated heparin or enoxaparin).[5,15] It has been well established that both aspirin and beta-blockers improve survival.[19-20] Hence, it was recommended that aspirin should be given as early as within 10 minutes of experiencing chest pain.[21] Beta-blockers should also be given early either IV or orally.[5-15] There has been some controversy around the IV administration of beta-blockers because of the risk of cardiogenic shock when given to hemodynamically unstable patients.[22-23] Early administration of aspirin and beta-blockers are both considered Class I recommendations in the ACC/AHA guidelines.[5,15,23] Early administration of aspirin prevents thrombotic occlusion during the PCI procedure.[21]

AMI secondary prevention

The main therapeutic goal in AMI treatment is to prevent ventricular remodeling, which will lead to cardiac failure and ultimately death.[4,24] Drugs that prevent ventricular remodeling improve survival. [24] Both beta-blockers and angiotensin converting enzyme (ACE)-inhibitors are well established to improve survival because both of them help prevent ventricular remodeling.[20, 25-27] Both should be continued indefinitely after their initiation in the hospital.[5,15,23] Also, aspirin should be continued indefinitely after AMI, because it decreases the risk of death, recurrent MI, and stroke.[5,15,19,23] Statins could be started in the hospital regardless of patient's LDL cholesterol levels and also continued indefinitely because of their benefits in preventing total mortality, CV mortality, and stroke.[5,28-29] Finally, most patients should also take clopidogrel as secondary intervention, but the duration of treatment differs according to how the patient was managed in the hospital.[4] It should be administered indefinitely if the patient has aspirin allergy. It should only be administered for 9-months post AMI if the patient was managed medically and for 12-months if the patient underwent PCI.[4]

Older adults

Challenges of treating AMI in older adults

Chronological age alone has been shown to be an independent predictor of medical decision-making potentially impacting clinical care.[30] One of the consequences of advanced age in AMI is the atypical clinical presentation of AMI in older adults, such as shortness of breath, functional and cognitive decline, fatigue, and non-diagnostic electrocardiogram (ECG). More importantly, chest pain, which is the landmark symptom of AMI, is seen less commonly in this population.[31,32] This may lead to difficulty in facilitating early triage and diagnosis, which will in turn lead to a delay or underuse of recommended care.[31] Additionally, older adults are known to

have a higher prevalence of comorbid conditions, which may further complicate their care.[31] Patients presenting with comorbidities cause a challenge to physicians because they need to consider the contraindications and drug interactions and also weigh the risks and benefits before prescribing any drug. Another possible problem that may lead to the delay of care of older adults is the potential for inappropriate risk stratification. Since most older adults have a low prevalence of traditional, widely known, risk factors like ischemic heart disease, smoking, and family history of cardiovascular (CV) diseases, their risks of negative outcomes may be underestimated leading to a lower estimated urgency in care.[33]

It is important to mention that advanced age in and of itself is considered to be an independent predictor of increased mortality after AMI.[34] There are several physiologic and structural changes in older adults that may yield negative outcomes.[35] These include an increase in LV mass index, abnormalities of LV function, and decrease in systemic vascular compliance.[36-42] Furthermore, there may be an increase in coagulation factors (VII, VIII, and IX) compared to the anticoagulation factors (antithrombin III and Protein C) that may lead to a greater risk of thrombosis, hence a greater infarct size.[42] Older adults have increased risk of experiencing in-hospital AMI complications including congestive heart failure, atrial fibrillation, cardiogenic shock, and complete heart block.[30] All of these complications may contribute to a longer hospital stay. As one study reported, older adults have hospital stays almost two times longer than younger adults.[33] Another study found that the older the patient is the higher the mortality risk from AMI.[30]

Challenges of pharmaceutical care in older adults

Older adults (i.e., those ≥65 years) represent about 13% of the US population yet account for 32% of all prescription drugs.[43,44] Older patients are more likely to experience adverse drug events (ADEs). This is due to several factors, including overuse of medications, medication errors, non-adherence to medications, and inappropriate drug use.[45] It has been reported that the incidence of ADEs in older patients varied from 5% to 35%, depending on the method used to define ADEs.[46,47] ADEs may result in the need for additional medications, disability, decrease in quality of life, hospitalization, or death.[48] One way of preventing ADEs in older patients is to avoid the use of potentially inappropriate medications (PlMs).[49]

PIMs are drugs that have a poor risk-benefit profile due to aging-related physiologic or pharmacokinetic changes or have been correlated with poor outcomes in older patients.[49-51] Specific criteria for appropriateness of drugs in older adults were developed to identify these PIMs. The National Committee for Quality Assurance (NCQA) established a list of drugs to be avoided in the elderly (DAE) as part of the Healthcare Effectiveness Data and Information Set (HEDIS) measures.[52] The NCQA HEDIS measures are based on the Beers list and the 2003 update of that.[53,54] In 2012, the American Geriatrics Society (AGS) updated Beers criteria for PIMs use in older adults.[55]

Prescription of PIMs in older patients is highly prevalent ranging from 12% in community-dwelling elderly to 40% in nursing home residents.[56] PIMs in older adults are associated with drug-related problems like hip or femur fracture, falls, hypoglycemia, as well as an increase in overall health care costs.[57] Older adults are more vulnerable to PIM exposure in the ED because of the patients acuity and physician unfamiliarity with the patient.[58]

ED utilization by older adults

Older adults (≥65 years) are the fastest growing segment in the US population.[59,60] As with any other health service, ED utilization by older adults will increase with this increase in population.[61] It was found in a study using the NHAMCS database that older adults' rate of ED utilization increased by 34% from 1993 to 2003.[61] This will increase the problem of ED crowding, which will further complicate the ED management of the older adults.[61] It will also increase the problem of ED boarding, ED boarding happens when patients are admitted to the hospital but are still awaiting their bed space, so they get boarded in the ED corridors until they get admitted, especially since most older adults coming to the ED will eventually be admitted to the hospital.[59,60,62] ED crowding plus ED boarding may cause a delay in treatments and decline in the quality of care provided.[62] Sadly, older adults may be significantly affected by this delay since they present with more severe conditions, more comorbidities, and higher levels of acuity.[63] It was found that older adults are five times more likely to get a high-priority triage than younger adults.[62,64]

The time from ED arrival to ED disposition is longer in older adults compared to younger adults. Elderly patients were three times more likely to stay more than 1 day in the ED than younger patients (14.0% vs. 4.7%, $p < 0.001$).[63] This may be attributed to the difficulty older adults face in trying to explain their clinical condition or history, plus the ambiguity of their physiological signs or symptoms.[63,65] An older adult ED visit costs twice more than a younger adult because of higher drug charges, higher treatment charges, and more diagnostic procedures.[63,66-67] The old-old (≥85) age group was found to have higher ED utilization.[63,68] This was due to their lack of social support, poor living arrangements, and limited mobility.[63]

Previous investigations

ED treatment of AMI

Few studies have documented ED utilization of aspirin and beta-blockers in AMI patients.[69-76] A couple of studies defined drug use to be limited to ED administration only.[69-70, 74-76] Some of those studies considered that as a limitation because they were not able to capture pre-hospital use of aspirin.[70,74,76] Another study was only interested in the ED use of beta-blockers, so they did not need information about pre-hospital administration of drugs, because beta-blockers are not given by paramedics.[75] Interestingly, in a Brazilian study, the documented average length of stay in the emergency room was 6.7 days.[69] This suggests that emergency rooms there may be treated like an official ward. Hence, use of drugs in the ED in that study may not mean early use because a drug may have been started on the 5th day of the stay in the ED. The other studies documented drug administration to be in the ED or 24 hours before ED arrival.[71-73] Those studies aimed to capture aspirin administration by the EMS or by the patient at home.

Several studies had detailed clinical information about study patients.[71-73,75-76] Patients who had contraindications to aspirin and beta-blockers could thus be excluded. Their utilization percentages were more accurate in comparing percentages across studies (see Table 2.1). Utilization varies greatly between studies primarily because they were done in different years. Earlier years had lower utilization rates compared to more recent years. The definition of administration and the depth of their clinical information can all affect utilization rates. The Brazilian study included an educational intervention for the ED staff about the implementation of clinical guidelines, so pre-intervention utilization rates and post-intervention utilization rates were available.[69] In Table 2.1, the pre-intervention rates are reported for the sake of consistency with other studies. Only one study was nationally representative, but it was almost 10 years old.[74]

Finally, only one study was specifically designed to study older adults, but the focus was beta-blocker administration.[75] All these studies examining ED treatment of AMI are summarized in Table 2.1.

Table 2.1: Summary of studies documenting ED utilization of aspirin and beta-blockers in AMI patients

Reference	Study setting	Time frame	Total no. of AMI patients	Mean age or Median age	N(%) treated with ASA&BB	Conclusion
Escosteguy (2011)[69]	1 Hospital in Brazil	2005-2006	78	Not mentioned	(Pre-intervention) ASA: 68 (87%), BB: 40 (51%) (Post-intervention) ASA: 63 (96%), BB: 62 (94%)	ED educational interventions increased ASA& BB utilization
Takakuwu (2010)[70]	1 Hospital in Pennsylvania	1999-2002	4,470	52.2 ± 15.8	ASA: 2,498 (56%), BB: NA	ASA utilization was not affected by age, race, sex
Tsai (2010)[71]	58 Hospitals across 20 states	2003-2006	3,819	65 (54 – 76)**	ASA: 2,980 (83%), BB: 945 (55%)	Utilization of ASA&BB was not ideal in ED
Vinson (2007)[72]	5 Hospitals in California and Colorado	2000-2002	2,215	74.3 ± 13.6 (women) 66.8 ± 11.9 (men)	ASA: 1,639 (80.5%), BB: 552 (60.3%)	ASA&BB utilization was suboptimal in ED
Magid (2005)[73]	5 Hospitals in California and Colorado	2000-2002	2,215	74.3 ± 13.6 (women) 66.8 ± 11.9 (men)	ASA: 1,639 (80.5%), BB: 552 (60.3%)	Older adults receive less ASA&BB in ED
Pham (2007)[74]	NHAMCS	1998-2004	1,492	62 (aspirin users)*** 64 (BB users)	ASA: 596 (40%), BB: 231 (17%)	ED use of ASA &BB was below expected goals
Vega (2006)[75]	1 Hospital in Pennsylvania	2001-2003	385	68 ± 14	ASA: NA, BB: 129 (47%)	Older STEMI patients receive less BB in ED
Saketkhou (1997)[76]	4 Hospitals in Rhode Island	1994	2,383	66 ± 14	ASA: 712 (30%), BB: NA	ASA in the ED is underutilized

*BB = beta-blockers, **Median was provided with IQR, ***SD was not provided, ED= Emergency department, AMI= Acute myocardial infarction

Inpatient treatment of AMI

Several studies have documented inpatient use of aspirin and beta-blockers in AMI patients.[77-90] Two studies looked at the trend of aspirin and beta-blockers utilization across time (1992-2002) with both noting an upward trend in utilization.[77,81] Other studies were carried out to examine the effect of sex or race on aspirin or beta-blocker utilization.[79,81,82,90] Their results varied. One study was interested to know if diabetic AMI patients had different utilization rates of aspirin compared to non-diabetic AMI patients.[83] The authors found that patients who had diabetes were less likely to get aspirin compared to patients who did not have diabetes.[83] Another study examined the effect of type of insurance on the utilization of aspirin and beta-blockers.[88] It found that patients in health maintenance organizations were more likely to receive aspirin and beta-blockers than fee-for-service patients.[88]

Most of the studies examined the effect of age on utilization of aspirin and beta-blockers, and all hypothesized older patients were less likely to receive aspirin or beta-blockers.[80,84-87,90] All studies found evidence supporting their hypothesis. Utilization rates in all of these studies were very similar. Aspirin rates were generally above 80%, and beta-blockers were between 60% and 70%.[77,79-84,88] Some of the older studies (1990-1996) had lower beta-blocker utilization rates.[85-87, 89-90] During that time period there was not much emphasis on beta-blocker use for secondary prevention in AMI patients. Studies examining inpatient use of aspirin and beta-blockers are summarized in Table 2.2.

Table 2.2: Summary of studies documenting inpatient utilization of aspirin and beta-blockers in AMI patients

Reference	Study setting	Data years	Total no. of AMI patients	Mean age or Median age	% treated with ASA & BB	Conclusion
Gottlieb (2007)[77]	25 Hospitals in Israel	1992-2002	1,475	80.8 ± 5.1*	ASA: 87, BB: 70*	ASA&BB utilization had a positive trend across 1992-2002
Marti (2007)[78]	1 Hospital in Spain	2000-2004	Not mentioned	Age range (80-97)	ASA: 55, BB: 4	very low use of ASA &BB in patients ≥85
Mehta (2006)[79]	GUSTO and ASSENT trials	1992-2000	32,419	61.1±12.2 (Whites) 57.0±12.1 (Blacks)	(Whites) ASA: 93.2, BB: 80.8 (Blacks) ASA: 93.7, BB: 82.6	ASA&BB utilization was not different between white and black patients
Avezum (2005)[80]	102 hospitals in 14 countries	1999-2002	24,165	50% of the sample are 55-74 years**	(age = 65-74) ASA: 92, BB: 78 (age ≥85) ASA: 88, BB: 65***	ASA&BB utilization was suboptimal in older adults
Vaccarino (2005)[81]	NRMI† database	1994-2002	598,911	66.4 (White men) 74.0 (White women) 61.3 (Black men) 67.3 (Black women)	(White men) ASA: 84, BB: 67 (White women) ASA: 79, BB: 63 (Black men) ASA: 84, BB: 68 (Black women) ASA: 78, BB: 65	Use of ASA&BB did not vary according to race and sex
Blomkalns (2005)[82]	CRUSADE†† database	2000-2002	35,875	68 (56-78) †††	(Males) ASA: 91.6, BB: 77.7 (Females) ASA: 89.6, BB: 75.9	Use of ASA&BB did not vary according to sex
Collinson (2004)[83]	PRAIS-UK‡ database	1998-1999	1,046	66 ± 12	(Diabetics) ASA: 81, BB: NA (non-Diabetics) ASA: 88, BB: NA	Diabetics had lower ASA utilization than non-diabetics

Stern (2004)[84]	26 Hospitals in Israel	2000	2,133	70 ± 2 (65-74) 81 ± 5 (≥75)	(age = 65-74) ASA: 96, BB: 76 (age ≥75) ASA: 95, BB: 64	Older adults are less treated with ASA&BB than youngers adults
Rathore (2003)[85]	CCP‡‡ database	1994-1996	146,718	76 ± 7	(age = 65-69) ASA: 78, BB: 55 (age ≥85) ASA: 64, BB: 38	Older adults are less treated with ASA&BB than youngers adults
Ruiz-Bailen (2002)[86]	119 Hospitals in Spain	1995-2001	17,761	65.2 ± 12.3	ASA: 97, BB: 44	ASA&BB were underutilized in older adults
Mehta (2001)[87]	CCP‡‡ database	1994-1996	163,140	Not mentioned	(age = 65-69) ASA: 84, BB: 52 (age ≥85) ASA: 69, BB: 33	Older adults had lower utilization rates of ASA&BB
Soumerai (1999)[88]	20 Hospitals in Minnesota	1992-1996	2,340	50% of the sample are ≥75 years	(HMO) ASA: 88, BB: 73 (FFS) ASA: 83, BB: 62	HMO patients were more likely to get ASA&BB than FFS patients
Marciniak (1998)[89]	Hospitals in AL, CN, IO, WS	1992-1996	23,535	75.3	ASA: 84, BB: 47	ASA&BB were suboptimaly used
Stone (1996)[90]	TIMI III ‡‡‡ Registry	1990-1993	3,318	63.8	ASA: 82, BB: 45	Older adults are less treated with ASA& BB than younger adults

*Numbers are of most recent year (2002), **No mean age was reported, ***NRMI= National Registry of Myocardial Infarction, †Youngest and oldest groups were only reported, ††CRUSADE= Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines initiative, ††† Median and IQR, ‡ PRAIS-UK= Prospective Registry of Acute Ischemic Syndromes in the United Kingdom, ‡‡ CCP= Cooperative Cardiovascular Project, ‡‡‡ TIMI= Thrombolysis In Myocardial Infarction, AMI = Acute myocardial infarction, BB = beta-blockers

AMI treatment effect on mortality

Several studies examined the effect of aspirin and beta-blockers on mortality, but none looked at their effect on length of hospital stay (LOS).[91-100] Most of studies were interested in the effect of aspirin and beta-blockers on in-hospital mortality.[91,92,95,96,98,99] The results from these studies varied. A couple of studies looked at the effect of aspirin on 30-day mortality post-AMI.[94,100] Both found that aspirin significantly lowered 30-day mortality.[94,100] Another studies looked at the effect of aspirin or beta-blockers on mid-to-long-term mortality. One study examined the effect of beta-blockers on midterm mortality (mean follow-up almost 2 years) and found that patients receiving a beta-blocker had a lower midterm mortality.[93] The other study evaluated 1-year mortality post-AMI and found that both aspirin and beta-blockers administration resulted in lower 1-year mortality rates.[97]

Some studies looked at the cumulative effect of all acute treatment given to the patient on in-hospital mortality.[95,98] One examined the cumulative effect of acute medical treatment (aspirin, beta-blockers, oral anti-coagulants, and oral anti-platelets) and found that patients treated acutely with these drugs had lower in-hospital mortality.[95] The other examined the cumulative effect of both acute medical and interventional treatment (e.g. PCI) finding that patients had lower in-hospital mortality rates when they were treated acutely by those drugs.[98]

Several studies were interested in the effect of acute treatment of aspirin and beta-blockers on mortality, which was defined by most studies to be administered in the first 24 hours.[91,92,95,96,98,99] These studies all evaluated the effects of aspirin and beta-blockers on in-hospital mortality, which may explain why they only looked at acute treatment. All these studies are summarized in Table 2.3

Table 2.3: Summary of studies documenting the effects of utilization of aspirin and beta-blockers in AMI patients on mortality

Reference	Study setting	Data years	Total no. of AMI patients	Mean ± SD age or Median (IQR) age	Effect of aspirin on mortality	Effect of BB on mortality
Filardo (2011)[91]	14 Hospitals in Texas	2002-2008	6,826	65.3 ± 14.7*	OR=0.37 (95% CI: 0.22-0.65)	OR=0.24 (95% CI: 0.11-0.52)
Medina (2011)[92]	GWTG-CAD database***	2000-2009	156,677	66.4 ± 14.7	OR=0.88 (95% CI: 0.76-1.02)**	OR=0.87 (95% CI: 0.77-0.98)
Kashima (2010)[93]	1 Hospital in Japan	2002-2008	77	86 ± 4	NA	HR=0.34 (95% CI: 0.12-0.99) †
Radcliff (2010)[94]	CCP database	1994-1995	120,032	76.7 ± 7.4	OR=0.57 (95% CI: 0.54-0.60) ††	NA
Peterson (2008)[95]	NRMI database	1990-2006	2,515,106	65.5 ± 14 †††	OR=0.980 (95% CI: 0.975-0.984) ‡ for both aspirin and beta-blockers	
Wienbergen (2007)[96]	MITRAPLUS‡‡ German registry	1994-2005	17,809	65.3 ± NA	NA	OR=0.70 (95% CI: 0.61-0.81)
Yan (2006)[97]	9 provinces in Canada	1999-2001	4,627	46% of the sample is less than 65 years	OR=0.48 (95% CI: 0.36-0.65)	OR=0.72 (95% CI: 0.56-0.93)
Alexander (2005)[98]	CRUSADE database	2001-2003	56,963	58% of the sample is older than 65	Acute aspirin and BB associated with lower rates of hospital mortality (OR not provided)	
Krumholz (1999)[99]	CCP database	1994-1995	58,165	75.1± NA	NA	OR=0.81 (95% CI: 0.75-0.87)
Krumholz (1995)[100]	CCP database	1992-1993	10,018	NA	OR=0.73 (95% CI: 0.65-0.82)	NA

*Results of year 2008, **Comparison between (65-79) age group and (<65) age group, *** GWTG-CAD= Get with the Guidelines-Coronary Artery Disease, †Results of the non-PCI group, †† Results of the community-dwelling older adults, ††† Results of most recent years 2003-2006, ‡This OR represents the effect of all acute treatment (aspirin, beta-blockers, anti-coagulants, and anti-platelets) on mortality, ‡‡ MITRA= Maximal Individual Therapy of Acute Myocardial Infarction registry, ‡‡‡ No SD available, the mean age is for the beta-blocker users, CI= Confidence intervals, CCP= Cooperative Cardiovascular Project, OR= Odds ratio, NRMI= National Registry of Myocardial Infarction, CRUSADE= "Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines", NA= Not available, SD= Standard deviation

ED structure effect on AMI treatment

Only two studies evaluated ED structure effects on AMI treatment.[101-102] Both studies used national databases: CRUSADE[101] and CCP[102]. One study conducted a survey on 316 CRUSADE participating hospitals from 2001 to 2003.[101] This survey targeted ED physicians and nurse coordinators to answer certain questions about the ED structure. Only 136 hospitals (representing 20,856 patients) replied with both the physician and the nurse response. This study had valuable input about the relationship between ED structure and ACC/AHA guidelines concordance (ECG within 10 minutes, aspirin and beta-blockers at arrival, use of heparin and glycoprotein IIb/IIIa inhibitors within 24 hours). They found that the strongest determinant of guideline concordance was having an ED administration highly committed to quality initiatives (OR: 1.58, 95% CI: [1.45-1.72]). They also found that having adequate nursing in the ED yields better concordance with the guidelines (OR: 1.09, 95% CI: [1.04-1.15]) because it allows more time with each patient. Finally, their most relevant result to the current study is that one of the main determinants of guideline concordance is having an algorithm, not specified whether it is computerized or not, available in the ED for AMI care (OR: 1.08, 95% CI: [1.03-1.12]).

The other study was only interested in aspirin and beta-blocker administration.[102] It examined the organizational infrastructure of 44 hospitals in Kansas participating in the CCP project to see whether organizational infrastructure affects administration of aspirin and beta-blockers. They found that almost 68% of hospitals have an ED protocol, where 43% of those protocols specified aspirin and 18% specified beta-blockers. Having protocols that specified aspirin and beta-blockers in the ED significantly affected beta-blocker administration on admission (OR: 2.14, 95% CI: [1.25-3.77]), but it did not affect aspirin on admission (OR: 1.31, 95% CI: [0.87-2.00]). They also found that almost 54% of the hospitals had an ED standardized

order set where 34% of those sets specified aspirin and 20% specified beta-blockers. Having those standardized sets in the ED significantly affected aspirin administration on admission (OR: 1.57, 95% CI: [1.01-2.48]), but it did not affect beta-blocker administration on admission (OR: 1.57, 95% CI: [0.87-2.93]). Unlike the previous study, they did not find that having an ED administration committed to quality was a determinant of aspirin or beta-blocker administration.[102]

No studies examined the effect of computerized clinical decision support (CCDS) systems in the ED on AMI treatment. Several studies have looked at the effect of CCDS in other disease states and in different settings. [103-106] Few studies have examined the effect of CCDS system in the ED.[107-108] One study used the CCDS system in the ED to screen for HIV. They found that using the CCDS for this purpose increased the detection rate of HIV and hence helped in treating undetected HIV cases[107] The other study found that when incorporating pneumococcal vaccination reminders in the CCDS system in the ED, it helped to overcome existing barriers that the health professionals had towards pneumococcal vaccination.[108]

Literature gap and significance

Based on this extensive literature review, most of the studies were not specifically focused on older adults (>65). Also, very few studies evaluated care in the ED where the AMI patient is first evaluated and treated. Several studies examined the effect of acute (ED plus inpatient) AMI care on mortality, but none looked specifically at the effect of ED care on mortality. None of these studies looked at the effect of ED care on length of hospital stay. Finally, only two studies looked at the effect of ED structure on AMI care in the ED, but none looked at the effect of CCDS in the ED on AMI care.

This study will give national estimates about older adult AMI care in the ED from 1992 to 2010. This is the first study to capture this long period of time of ED AMI care for older adults. This study uses the Donabedian model for quality measurement, which gives a holistic view of AMI care in older adults. This study will evaluate the impact of having a computerized reminder to prompt ED staff to use guidelines, on the usage of guideline concordance therapy in the ED. This study will also reveal the percentages of drugs use only in the ED, which was only done in few studies. This study will also attempt to see the effect of care in the ED on hospital outcomes, like in-hospital mortality and LOS. Finally, this study may help increase ED health care professionals' awareness of older adults AMI care and the importance of incorporating CCDS systems in the ED to remind health professionals about using guideline recommended therapies.

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CHAPTER 3

Methods

Data source

The National Hospital Ambulatory Medical Care Survey (NHAMCS), one of the databases available from the National Center for Health Statistics (NCHS), was used for this study. NHAMCS was selected instead of the National Ambulatory Medical Care Survey (NAMCS) because ED data is only available in the NHAMCS database. NHAMCS includes a national probability sample of visits to the emergency and outpatient departments of noninstitutional general and short-stay hospitals in the 50 States and the District of Columbia.[1]

The survey design is a four-stage probability sampling approach with samples of primary sampling units (PSUs), hospitals within PSUs, clinics and emergency service areas within hospitals, and patient visits within clinics and emergency service areas.[1] The PSU consists of a county, a group of counties, county equivalents (such as parishes and independent cities), towns, townships, minor civil divisions (for some PSUs in New England), or a metropolitan statistical area (MSA).[2] The PSUs are comprised of a probability subsample of the PSUs used in the 1985-94 National Health Interview Survey (NHIS).[2] The hospitals are divided into 16 subsamples; each subsample has a data collection period of 4 weeks. In year 2010, the most recent year available, about 112 PSUs, 488 hospitals, 388 EDs, and 100 visits in each ED were sampled. The validity and quality of this survey and database have been assessed in more than 100 previous publications.[2]

Given the sampling method, the results from NHAMCS should be nationally representative. All of the analyses should be weighted to get national estimates. In order to get

reliable national estimates, the estimates must be based on at least 30 cases and the estimates should have a relative standard error of less than 30%.[1]

Data in NHAMCS are abstracted from patient records by a trained nurse who works in the hospital. A nurse is chosen because she/he is more acquainted with the hospital's records, which makes it easier to abstract the information. A field representative then checks on the quality of the data collection and is concerned mostly with the completeness of the form. Incomplete data items are sometimes imputed using a hot deck procedure by assigning a value from a randomly selected patient record form with similar characteristics. Then, the data is sent to be coded by a trained medical coding personnel from the Division of Data Processing at the NCHS computer facility in Research Triangle Park North Carolina.[2]

Study population

Data for this study were obtained from1992 to 2010. Patients who were included in this study had to have an admission diagnosis of AMI (ICD-9-CM code 410.xx) and be at least 55 years of age. Admission diagnosis was chosen instead of discharge diagnosis because this study is interested in the medications given in the ED, which are prescribed based on the patient's admission diagnosis. To ensure the accuracy of the admission diagnosis, patients were excluded if their diagnosis was considered questionable (rule-out). It is important to note here that from year 1992 to 1996 the variable indicating whether the diagnosis is probable or not was not available, hence these years had larger numbers of participants; meaning it is probable that some of these cases did not have a confirmed AMI diagnosis. Another reason for choosing the admission diagnosis is for consistency purposes; the admission diagnosis was available in all the years but discharge diagnosis was only available from year 2005 onwards.

Study design

This study used a cross-sectional design for all of the aims. The first aim explored the trend in the utilization of antiplatelet agents and beta-blockers from 1992-2010. The second aim explored the bivariate associations between receiving antiplatelet agents or beta-blockers and demographic, clinical, visit, and hospital characteristics. The third aim determined whether an association existed between receiving antiplatelet agents or beta-blockers and in-hospital mortality and length of hospital stay. In this aim, only years 2005 onwards were used because these are the only years that have discharge data. Moreover, only patients who are admitted to the hospital will be used in this aim, meaning patients who died in the ED or patients who were transferred to other hospitals will be excluded. The fourth aim evaluated the association between the use of a computerized guideline reminder in the ED and the ED usage patterns of antiplatelet agents and beta-blockers.

Data extraction and manipulations

Drug data variables

The drugs of interest in this study are: antiplatelet agents (aspirin, clopidogrel, ticlopidine, and dipyridamole) and beta-blockers (all beta-blockers available in NHAMCS, summarized in Table 3.1). These drugs were chosen because they were recommended as part of acute medical care for an AMI in the ACC/AHA guidelines. In these guidelines, the use of aspirin and beta-blockers in the first 24 hours is considered a quality indicator. It was also mentioned in the guidelines that if aspirin was contraindicated, clopidogrel, ticlopidine, or dipyridamole can be used instead. An important matter to note here is that in 2006, NHAMCS switched from the Food and Drug Administration's (FDA) National Drug Code Directory (NDC) to Lexicon Plus®, a proprietary database of Cerner Multum, Inc., to code characteristics of drugs

listed on the patient record.[3] A drug conversion file and a SAS program were supplied by NHAMCS team in order to recode the years before 2006 to Lexicon Plus® for researchers interested in merging data before 2006 with year 2006 and after. The drug codes used in this study are summarized in Table 3.1.

Table 3.1: Drug codes

Drug group	Drug name and codes	
Antiplatelet agents	Aspirin (d00170) Clopidogrel (d04258) Ticlopidine (d00514) Dipyridamole (d00213)	
Beta-blockers	Metoprolol (d00134) Atenolol (d00004) Carvedilol (d03847) Nadolol (d00018) Metipranolol (d00297) Betaxolol (d00176) Bisoprolol (d00709)	Propranolol (d00032) Acebutolol (d00128) Pindolol (d00137) Timolol (d00139) Esmolol (d00224) Carteolol (d00708)

Demographic data variables

Age was a continuous variable that was recoded into a categorical variable. This variable grouped patients into older or equal to 65 and younger than 65. Sex was coded into males and females. Ethnicity was originally coded as Hispanic and non-Hispanic. For patient race, NHAMCS had a recode for all years that defined race as white, black, and other, which was used for this study. Patient residence was defined as private, nursing home, institutions, and homeless beginning in 2005; however, the years earlier defined patient residence as nursing home or not nursing home. For consistency purposes, the nursing home and not nursing home coding was the one chosen to be used for this study. The source of payment variable was recoded into the following categories: Medicare, Medicaid, private insurance, and other. The "other" category included workers compensation, charity, and self-pay.

Clinical data variables

Systolic blood pressure (SBP) and heart rate (HR) were continuous variables that were recoded to categorical variables. For the SBP variable, patients who had a SBP that is less than or equal to 90 mmHg were considered to be hypotensive; more than 90 mmHg was not hypotensive. For the HR variable, patients who had an HR that is less than or equal to 60 bpm were considered to be bradycardic; more than 60 bpm was not bradycardic. These variables were defined this way to identify patients who had a potential contraindication to beta-blockers. The clinical presentation of interest for these patients is whether or not they had chest pain. NHAMCS has a variable that specifies the patients' reason for visit, which coded the patients' verbatim of why they are visiting the ED. The chest pain code was looked up, and then a variable specific to chest pain was created.

The triage variable presented some challenges as the coding changed three times across the study period. A new variable was created to put all these changes into consideration by grouping triage into two categories: high and low. High triage patients were given a priority to be seen within 1 hour or less; low triage patients were given a priority to be seen within 1-2 hours. The number of procedures done and number of diagnostic services done were continuous variables. Cardiac enzyme test and cardiac monitor test variables were both coded as yes/no variables, the actual result of the test is not provided.

Visit Data variables

The time variable was recoded to three categories: day, evening, and night. Day was considered to be 8:00 am to 3:59 pm; evening was considered to be 4:00 pm to 11:59 pm; and night was considered to be 12:00 am to 7:59 am. The variable representing the day of the week of the visit was recoded to weekday and weekend. Mode of arrival variable coding changed

across the years, some years had more than one transport category and others had only ambulance or not. Hence, it was recoded into arrival by ambulance or not, for consistency purposes throughout the years. The provider seen variable was also collected differently across the years with different variable names, so it was defined into the following categories; physician, physician assistant, resident physician, nurse practitioner, and nurse (RN/LPN). The provider seen variable is coded in a way that you can select all that apply. For example, a patient can be seen by a nurse, a physician, and resident. Patients' discharge variables were only available starting year 2005. Discharge status was defined as alive or dead. Length of hospital stay (LOS) was a continuous variable expressed in days.

Hospital Data Variables

Hospital ownership and Metropolitan Statistical Area (MSA) variables had different names across the years, so they had to be recoded for consistency purposes. Hospital ownership had 3 categories: proprietary (for-profit), government (non-federal), and voluntary (not-profit). MSA was two categories: MSA and non-MSA. Hospital region was expressed as Northeast, Midwest, South, and West. The computerized guideline reminder variable was only available starting year 2005 and was a simple yes/no variable, there was no further explanation of that variable to show its actual content.

Design variables

In order to get national estimates and to account for the four-stage survey sampling design, design variables provided from NHAMCS must be used in all analyses. The first design variable is patient weight (PATWT), the second is stratum weight (CSTRATM), and the third is PSU weight (CPSUM). Years prior to 2002 did not have these design variables; hence,

NHAMCS has provided a SAS program to add these design variables to those years for researchers interested in merging data before 2002 with year 2002 and after.

Outcome Variables

For aims 1, 2, and 4, the outcome variables of interest are antiplatelet agent utilization and beta-blocker utilization. Utilization for each drug class is expressed by yes/no for each visit, so they it is visit-level data. For aim 3, the outcome variables are in-hospital mortality and length of hospital stay.

Predictor Variables

Predictors will be grouped into patient demographics (sex, race, ethnicity, residence, and source of payment), patient clinical characteristics (triage level, SBP, HR, clinical presentation, number of procedures done in ED, number of diagnostic services done, whether they did a cardiac enzyme test, and whether they had cardiac monitoring), visit characteristics (time and day of arrival, provider seen, transport used to get to the hospital), hospital characteristics (hospital region, hospital ownership, MSA, and availability of computerized guideline reminders). Predictor variables summary and coding are presented in Table 3.2.

Table 3.2: Predictor Variables

Predictor Variables	Coding
Patient Demographics	
Sex	Male, Female
Race	White, Black, Other
Ethnicity	Hispanic, Not Hispanic
Patient residence	Nursing home, Other
Expected source of payment	Medicare, Medicaid, Private, Other
Patient Clinical Characteristics	
Systolic blood pressure (SBP)	Hypotensive "≤ 90mmHg" (Yes/No)
Heart rate (HR)	Bradycardic "≤60bpm" (Yes/No)

Number of procedures done during the ED visit	Actual number.
Number of diagnostic services done during the ED visit	Actual number.
Patient clinical presentation	Chest pain (Yes/No)
Triage level	High priority (1-60 min), Low priority (>60 min)
Cardiac Enzyme test	Yes, No
Cardiac Monitor test	Yes, No
Visit Characteristics	
Time of arrival	Day (8am-3:39pm), Evening (4pm-11:59pm), Night (12am-7:59am)
Day of Arrival	Weekday, Weekend
Mode of transport	Ambulance, Other
Provider seen	Physician, Physician Assistant, Resident, Nurse Practitioner, Nurse (RN/LPN)
Hospital Characteristics	
Hospital region	Northeast, Midwest, South, West
Hospital ownership	Proprietary, Government, Nonprofit
Metropolitan Statistical Area	MSA, non-MSA
ED Computerized guideline reminders	Yes, No

Patient Demographics

Several studies have shown that patient demographics such as gender and race can be important predictors of AMI treatment. Females and black patients have been shown to be undertreated.[4-7] Patient's residence also acts as a predictor of AMI treatment. A recent study showed that patients admitted from nursing homes were less likely to receive treatment for AMI.[8] Furthermore, the effect of source of payment is also of importance on AMI care. A nationally representative study has shown that patients with private insurance were more likely to have appropriate AMI care.[9]

Patient Clinical Characteristics

Patient clinical characteristics can be considered important predictors of AMI treatment. A recent study showed that if a patient with AMI was given a low-priority triage level, it was associated with delay in treatment, longer hospital stay, and higher mortality.[10] A multi-center study that looked at chest pain in older adults found that it is more difficult to diagnose acute chest pain in older adults, so this may lead to a lower-priority triage and hence delayed care.[11]

Visit Characteristics

The timing of the ED visit, both time of day and the day of the week, has been shown to be an important consideration. A recent study showed that patients admitted off-hours (i.e., 4pm to 7:30am on weekdays or all day on weekends) were more likely to have in-hospital mortality and also experience a delay in AMI care.[12] From the standpoint of day of arrival, a study showed that patients admitted during the weekend had higher in-hospital mortality, which may be explained by the disparities in resources and expertise of healthcare providers working during weekends when compared to weekdays.[13]

Hospital Characteristics

Some hospital characteristics like, hospital region and hospital ownership may have an effect on AMI care. A study found that patients in the northeast region were more likely to get better quality of AMI care.[9] In the same study, it was shown that patients who were in governmental hospitals were less likely to receive appropriate treatment for AMI.[9]

Statistical analysis

Descriptive statistics were used to describe the baseline characteristics for our patients. Continuous variables were expressed as the weighted mean ± standard deviation (SD) and the 95% confidence intervals (CI) of the mean. The SURVEYMEANS procedure will be used for continuous variables. Categorical variables were expressed as the weighted frequency and the row percent and 95% CI of the row percent. The SURVEYFREQ procedure was used for categorical variables. The *a priori* significance level is set to two-sided p-value of 0.05. SAS version 9.3 was used for all analyses.

In this study, the aim was to generate hypotheses, so predictive model building strategies were not used. Given the exploratory nature of this study, the focus is on adjusting for potential confounders and providing insight for further studies in this area.

For the first aim, which was to examine the temporal trend in receiving antiplatelet agents and beta-blockers, the SURVEYLOGISTIC procedure was used to conduct a logistic regression analysis. Two models will be used, one for antiplatelet agents as the outcome variable, and the other with beta-blockers as the outcome variable. The predictor variable for both models was year as a continuous variable, ranging from 1992 to 2010. The odds ratio was used to explain the magnitude and direction of the trend.

For the second aim, the effect of demographic, clinical, visit, and hospital characteristics on receiving antiplatelet agents and beta-blockers was examined. A bivariate logistic regression was carried out using the SURVEYLOGISTIC procedure between the outcome variables, which was the utilization of antiplatelet agents or beta-blockers, and the predictor variables. The odds ratio was used to express the magnitude and direction of the relationship. Then, if the relationship is significant, a multivariate logistic regression will be carried out controlling for

age, sex, race, and year. These variables were chosen because they have strong evidence confirming their effect on anti-platelet agent and beta-blocker utilization rates, plus they are available most of the time for all patients.[4-7]

For the third aim, the first outcome examined was in-hospital mortality. Given the low mortality rate, only 15 cases of mortality, it was not possible to carry out a Kaplan-Meir Survival Analysis nor a logistic regression analysis. Hence, a chi-square test was used to determine whether the patients who took an antiplatelet agent or beta-blocker were different from the ones who did not in their rate of in-hospital mortality. The SURVEYFREQ procedure with CHISQ option was used to carry out the chi-square test. The second part of the third aim is looking at whether guideline-concordant therapy has an effect on length of hospital stay. Since the dependent variable in this analysis is continuous, the SURVEYREG procedure was used to carry out a linear logistic regression between LOS and antiplatelet agents or beta-blockers. The regression coefficient was used to express the magnitude and direction of the relationship.

For the last aim, the association between the availability of a computerized guideline reminder in the ED and the ED utilization of antiplatelet agents and beta-blockers was evaluated. Like the first aim, a bivariate logistic regression was conducted using the SURVEYLOGISTIC procedure in SAS. The odds ratio was used to express the magnitude and direction of the relationship. If the relationship is significant, then a multivariate logistic regression was carried out adjusting for age, sex, race, and race.

All the analyses were weighted to get national estimates. In order to get reliable national estimates, our estimates must be based on at least 30 cases. The other requirement for reliability is that estimates should have a relative standard error of less than 30%, was not achievable in this study. We reached this conclusion after long discussions with NHAMCS statisticians. We

concluded that our data may be highly clustered because only a very few EDs may account for most visits for our specific diagnosis, which will mean that our standard errors will always be high because of that clustering. The SAS code for the data manipulation and data analysis is provided in Appendix A.

Human subject protection and data privacy

Data files were available from the National Center for Health Statistics, which codes and encrypts the data to prevent identifiability resulting in a dataset compliant with the Health Insurance Portability and Accountability Act of 1996. This study qualified for exemption according to 45 CFR 46.101(b) Category 4 at Virginia Commonwealth University internal review board (IRB). (VCU IRB#: HM14455). A copy of the IRB Approval form can be found in Appendix B.

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CHAPTER 4

Results

Descriptive Results

A total of 1771 visits (weighted: 6.1 million visits) were eligible for this study. Almost 3.33 million (54%) [95% CI: 51.7% to 57.1%] of our population were females with a mean age of 72.1 (±13.7) years. This population is 87% (5.32 million) white [95% CI: 84.9% to 89.1%] and 94% (5.33 million) non-Hispanic [95% CI: 91.8% to 95.3%]. A summary of patients' demographics is presented in Table 4.1.

Table 4.1: Patient Demographics

Patients' Demographics *Total population = 6,118,050*	Unweighted Frequency	Weighted Frequency (%)	95% CI of the %
Age	---	72.1 (±13.7)*	[71.4 – 72.7]
Sex			
- Female	951	3,329,349 (54.4)	[51.7 – 57.1]
- Male	820	2,788,701 (45.6)	[42.9 – 48.3]
Race			
- White	1,519	5,323,371 (87.0)	[84.9 – 89.1]
- Black	179	589,075 (9.6)	[7.9 – 11.4]
- Other**	73	205,604 (3.4)	[2.1 – 4.6]
Ethnicity			
- Non-Hispanic	1,558	5,328,722 (93.6)	[91.8 – 95.3]
- Hispanic	105	365,550 (6.4)	[4.7 – 8.2]
Source of payment**			
- Private	251	853,526 (20.2)	[16.8 – 23.7]
- Medicare	689	2,690,918 (63.7)	[59.7 – 67.7]
- Medicaid	91	327,806 (7.8)	[5.9 – 9.6]
- Other†	94	350,091 (8.3)	[6.1 – 10.5]
Patients' residence††			
- Nursing home	50	168,520 (7.9)	[4.9 – 10.8]
- Other †††	575	1,971,606 (92.1)	[89.2 – 95.0]

* The numbers represent the mean and the calculated standard deviation.

** The other race category included Asian, Native Hawaiian/other Pacific Islander, American Indian/Alaska Native, and more than one race reported.*** Sources of payment data started to be collected in year 1995.

† The other source payment category included worker's compensation, self-pay, and no charge/charity.

†† Patient residence data started to be collected in year 2001.

††† The other residence category included private residence, other institution, other residence, and homeless.

Patients' clinical characteristics, diagnostic services, and procedures were available in NHAMCS database. Patients who had chest pain in this older adult population were 3.7 million, almost 89% of the population. Patients who had a contraindication to beta-blockers were around 20%: 11% hypotensive, and 15% bradycardic. A summary of patients' clinical characteristics, diagnostic services, and procedures is presented in Table 4.2.

Table 4.2: Patient Clinical Characteristics

Clinical Characteristics *Total population = 6,118,050*	Unweighted Frequency	Weighted Frequency (%)	95% CI of the %
Chest pain			
- Yes	1,055	3,666,299 (88.9)	[86.4 – 91.4]
- No	123	457,443 (11.1)	[8.6 – 13.6]
Hypotension*			
- Yes	70	252,549 (10.7)	[7.7 – 13.6]
- No	624	2,116,200 (89.3)	[86.4 - 92.3]
Bradycardia*			
- Yes	107	354,49 (14.9)	[11.6 – 18.4]
- No	587	2,014,2527 (85.1)	[81.6 – 88.4]
Triage**			
- High (0-60mins)	1,567	5,341,873 (94.5)	[92.9 – 96.0]
- Low (>60mins)	83	312,314 (5.5)	[3.9 – 7.1]
Cardiac Enzymes test***			
- Yes	252	992,945 (68.9)	[62.9 – 74.9]
- No	108	448,036 (31.1)	[25.0 – 37.1]
Cardiac monitor†			
- Yes	791	2,996,405 (68.4)	[64.5 – 72.4]
- No	374	1,382,190 (31.6)	[27.6 – 35.5]
Electro-cardio-gram			
- Yes	1,582	5,473,217 (89.5)	[87.4 – 91.5]
- No	189	644,833 (10.5)	[8.5 – 12.6]
Total procedures done†,††	---	1.16 (±1.65)	[1.1 – 1.2]
Total diagnostic services done †	---	6.67 (±4.85)	[6.4 – 6.9]

*Data about blood pressure and heart rate were first collected in 2001.
**The high triage category represents urgent and emergent cases, the low triage category represent not urgent cases.
*** Data about cardiac enzyme test was first collected in 2005.
† Data about cardiac monitor, total procedure done, and diagnostic services done was first collected in 1995.
†† The numbers represent the mean and the calculated standard deviation.

The day and time the patient arrived to the ED, the mode of their arrival, the providers' seen, the type of ward they were admitted to, number of drugs taken, and their discharge status were all collected. A majority of patients were admitted on a weekday (almost 70%). Also, a majority of patients were seen by an attending physician and a nurse (91% and 90%, respectively). Patients visit characteristics are summarized in Table 4.3.

Table 4.3: Patient visit characteristics

Patients' Visit Characteristics *Total population = 6,118,050*	Unweighted Frequency	Weighted Frequency (%)	95% CI of the %
Time*			
- Day (08:00-15:59)	501	1,817,897 (41.9)	[38.2 – 45.8]
- Evening (16:00-23:59)	394	1,506,112 (34.8)	[31.6 – 38.0]
- Night (00:00-7:59)	256	1,006,024 (23.2)	[20.0 – 26.5]
Day			
- Weekday	807	2,858,609 (70.4)	[67.2 – 73.7]
- Weekend	336	1,199,857 (29.6)	[26.3 – 32.8]
Arrival**			
- Ambulance	252	958,184 (54.8)	[48.6 – 60.9]
- Other	238	791,567 (45.2)	[39.1 – 51.4]
Provider seen***			
- Attending physician	1,622	5,570,978 (91.1)	[89.1 – 93.0]
- Physician assistant	42	144,812 (2.4)	[1.3 – 3.4]
- Resident/intern	308	889,955 (14.5)	[12.1 – 17.0]
- Nurse practitioner	23#	66,814 (1.5)	[0.7 – 2.3]
- RN/LPN nurse	1,588	5,515,296 (90.1)	[87.9 – 92.3]
Admission ward†			
- Critical Care Unit	97	388,635 (40.7)	[32.9 -28.5]
- OR/Cath lab/SDU	62	256,438 (26.7)	[20.0 – 33.7]
- Other wards	79	309,764 (32.4)	[24.1 – 40.8]
Discharge status††			
- Alive	222	902,868 (95.6)	[93.0 – 98.2]
- Dead	15#	41,310 (4.41)	[1.8 – 6.9]
Number of drugs†††			
- (0-2 drugs)	174	603,248 (32.5)	[26.3 – 38.7]
- (3-5 drugs)	208	754,666 (40.7)	[34.6 – 46.7]
- (6-8 drugs)	135	498,175 (26.8)	[21.1 – 32.6]

* Data about time of arrival was first collected in 1995. # It was less than 30 row cases, so not reliable estimates
** Data about arrival mode was first collected in 2003.
*** Numbers of providers seen is not mutually exclusive (i.e. a patient can be seen by multiple providers).
† OR = Operation Room, Cath lab = Catheterization lab, SDU = Step Down Unit, Data about admission was first collected in 2005.
††Data about whether the patient was discharged from any hospital within the last 7 days and data about discharge status was first collected in 2005. ††† Data about number of drugs from 2003 to 2010

Hospital characteristics are summarized in Table 4.4. Data specific to the ED structure (i.e. computerized guideline reminders) were only collected beginning in 2005. Almost 52% of the EDs had computerized guideline reminders.

Table 4.4: Hospital Characteristics

Hospital Characteristics *Total population = 6,118,050*	Unweighted Frequency	Weighted Frequency (%)	95% CI of the %
Region			
- Northeast	525	1,507,271 (24.6)	[20.5 – 28.8]
- Midwest	421	1,651,986 (27.0)	[21.9 – 32.1]
- South	496	1,926,372 (31.5)	[26.9 – 35.9]
- West	329	1,032,421(16.9)	[13.8 – 19.9]
Metropolitan Statistical Area			
- MSA	1,455	4,615,904 (75.4)	[68.2 – 82.7]
- Non-MSA	316	1,502,146 (24.6)	[17.3 – 31.8]
Hospital Ownership			
- Voluntary/non-profit	1,405	4,751,702 (77.7)	[74.1 – 81.2]
- Government/non-federal	175	657,327 (10.7)	[8.2 – 13.3]
- Proprietary	191	709,021 (11.6)	[8.9 – 14.2]
Guideline reminders*			
- Yes	104	435,149 (52.2)	[42.1 – 62.3]
- No	95	398,398 (47.8)	[37.7 – 57.9]

* Data about computerized guideline reminders was first collected in 2005.

Results by objective

Objective 1: Trend in use of anti-platelet agents and beta-blockers across 1992-2010

Both anti-platelet agents and beta-blockers showed a positive trend across the years (OR = 1.09 [95% CI: 1.07 to 1.19] and OR = 1.16 [95% CI: 1.13 to 1.19], respectively) as shown in Figure 4.1. The lowest antiplatelet agent utilization was in 1992 at 13% and highest in 2010 at almost 59%. For beta-blockers, the lowest was in 1994 at around 2% and the highest in 2007 at 38%. There was a gradual increase in the use of both anti-platelet agents and beta-blockers.

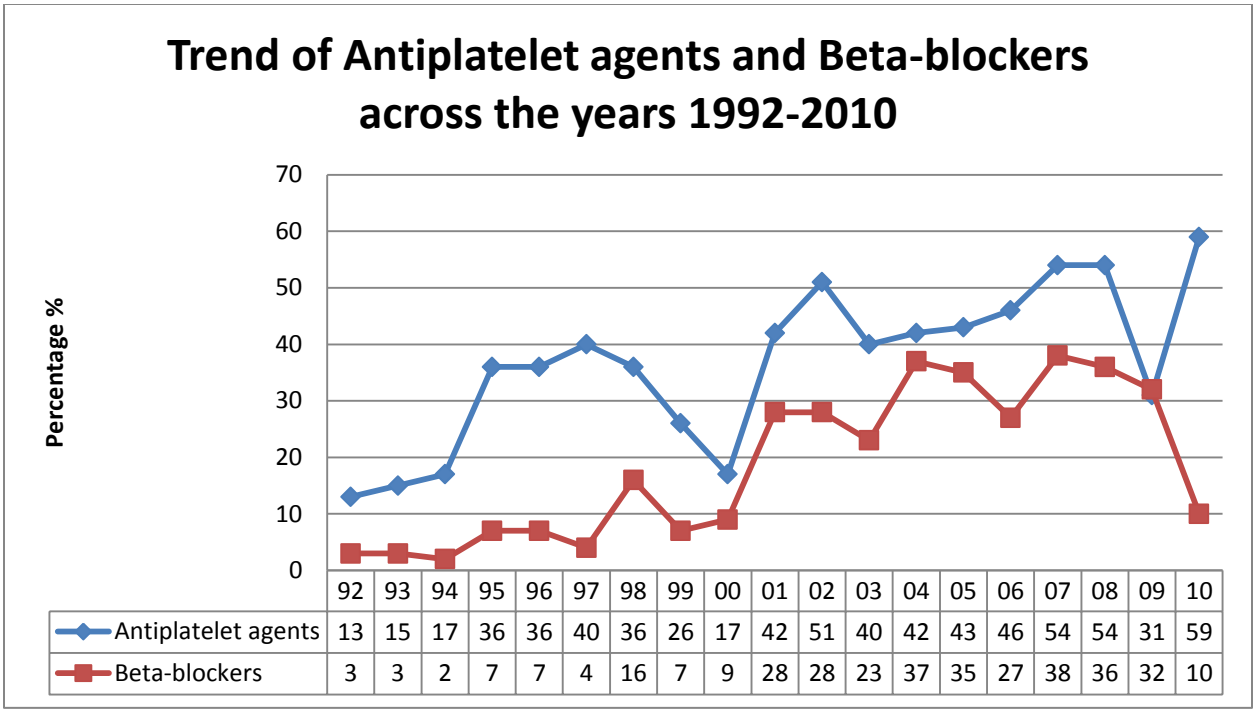

Figure 4.1: Trend of antiplatelet agents and beta-blockers utilization across the years

Objective 2: Predictors of anti-platelet agents and beta-blocker use

Age was a significant predictor of anti-platelet agents use. Younger adults (i.e., <65 years old) were more likely to receive an anti-platelet agent than older adults (OR = 1.316 [95% CI: 1.077 to 1.609]); however, age was not found to be a significant predictor of beta-blocker use. Sex, on the other hand, was considered to be a significant predictor of beta-blocker use. Females were almost 70% less likely to receive a beta-blocker compared to males (OR = 0.699 [95% CI: 0.471 to 0.950]). Sex was not considered a significant predictor of antiplatelet agents use. Race and ethnicity were not significant predictors for either antiplatelet agents or beta-blockers. Patients not living in nursing homes were almost 2.5 times more likely to get antiplatelet agents (OR = 2.477 [95% CI: 1.254 to 4.894]); however, there was no significant relationship between a patient's residence and beta-blocker use. The source of payment was not considered to be a significant predictor for either antiplatelet agents or beta-blockers use.

Several patient clinical characteristics were significant predictors of medication use. Those patients with no chest pain were less likely to get a beta-blocker (OR = 0.330 [95% CI: 0.132 to 0.827]). Patients with high triage were almost 2.5 times more likely to get an antiplatelet agent (OR = 2.483 [95% CI: 1.284 to 4.801]); however, triage did not have a significant relationship with beta-blockers use. Interestingly, for every 1 point increase in the number of diagnostic services the patients received in the ED, the more likely he/she got an antiplatelet agent (OR= 1.145 [95% CI: 1.089 to 1.205]) or a beta-blocker (OR = 1.074 [95% CI: 1.000 to 1.153]).

Patients who did not arrive in an ambulance were more likely to receive anti-platelet agents (OR = 1.652 [95% CI: 1.072 to 2.545]); however, arrival by ambulance was not a significant predictor of beta-blocker utilization. The time and day of arrival were not significant predictors for either antiplatelet agents or beta-blocker use. Patients who were seen by a nurse practitioner were 8% less likely to get an antiplatelet agent (OR = 0.082 [95% CI: 0.022 to 0.307]). Patients who were treated in a hospital that is located in a Metropolitan Statistical Area (MSA) were more likely to get an antiplatelet agent (OR = 1.825 [95% CI: 1.331 to 2.502]). The summary of all these bivariate associations are presented in Tables 4.5 and 4.6.

After adjusting for demographic characteristics (age, sex, and race) and year, all significant predictors of the use of antiplatelet agents remained significant, but for beta-blockers only chest pain remained to be a significant predictor of utilization. Results of the multivariate analysis are summarized in Tables 4.7 and 4.8. All unadjusted and adjusted analyses are summarized in Figure 4.2 and 4.3.

Table 4.5: Bivariate associations between patients' demographic, clinical, visit, and hospital characteristics and the use of antiplatelet agents

Predictor variables	Odds ratio (OR)	95% CI of OR
Demographic		
- Age (younger than 65 vs. 65 and older)	*1.316	[1.077 - 1.609]
- Sex (females vs. males)	0.815	[0.649 – 1.024]
- Race (referent: black)		
- Other	0.881	[0.434 – 1.786]
- White	0.692	[0.461 – 1.038]
- Ethnicity (Hispanic vs. non-Hispanic)	1.184	[0.712 – 1.970]
- Payment (referent: Medicaid)		
- Other	1.732	[0.855 – 3.508]
- Private	1.364	[0.767 – 2.424]
- Medicare	0.934	[0.542 – 1.611]
- Residence (other residence vs. nursing homes)	*2.477	[1.254 – 4.894]
Clinical		
- Chest pain (no chest pain vs. chest pain)	0.792	[0.490 – 1.280]
- Triage (high vs. low)	*2.483	[1.284 – 4.801]
- Total diagnostic services	*1.145	[1.089 – 1.205]
Visit		
- Time (referent: night)		
- Day	0.897	[0.596 – 1.350]
- Evening	0.943	[0.628 – 1.413]
- Day (weekend vs. weekday)	1.061	[0.768 – 1.466]
- Arrival (other transport vs. ambulance)	*1.652	[1.072 – 2.545]
- Provider seen		
- Physician (no vs. yes)	0.733	[0.465 – 1.155]
- Resident (no vs. yes)	0.745	[0.507 – 1.093]
- Nurse RN/LPN (no vs. yes)	0.693	[0.447 – 1.077]
- Physician assistant (no vs. yes)	1.037	[0.412 – 2.606]
Hospital		
- Region (referent: West)		
- Northeast	0.842	[0.594 – 1.192]
- Midwest	0.747	[0.538 – 1.038]
- South	0.807	[0.569 – 1.144]
- MSA (MSA vs. non-MSA)	*1.825	[1.331 – 2.502]
- Ownership (referent: Proprietary)		
- Voluntary/non-profit	1.152	[0.784 – 1.695]
- Government/non-federal	1.016	[0.565 – 1.827]

*p<0.05

Table 4.6: Bivariate associations between patients' demographic, clinical, visit, and hospital characteristics and use of beta-blockers

Predictor variables	Odds ratio (OR)	95% CI of OR
Demographic		
- Age (younger than 65 vs. 65 and older)	1.221	[0.892 – 1.670]
- Sex (females vs. males)	*0.669	[0.471 – 0.950]
- Race (referent: black)		
- Other	1.269	[0.462 – 3.483]
- White	0.863	[0.517 – 1.442]
- Ethnicity (Hispanic vs. non-Hispanic)	1.870	[0.992 – 3.524]
- Payment (referent: Medicaid)		
- Other	0.993	[0.392 – 2.520]
- Private	1.817	[0.877 – 3.765]
- Medicare	1.344	[0.702 – 2.575]
- Residence (other residence vs. nursing homes)	1.798	[0.621 – 5.203]
Clinical		
- Chest pain (no chest pain vs. chest pain)	*0.330	[0.132 – 0.827]
- Triage (high vs. low)	1.604	[0.656 – 3.922]
- Total diagnostic services	*1.074	[1.000 – 1.153]
Visit		
- Time (referent: night)		
- Day	0.860	[0.520 – 1.424]
- Evening	1.128	[0.685 – 1.859]
- Day (weekend vs. weekday)	1.164	[0.803 – 1.686]
- Arrival (other transport vs. ambulance)	1.384	[0.850 – 2.254]
- Provider seen		
- Physician (no vs. yes)	1.030	[0.560 – 1.894]
- Resident (no vs. yes)	1.014	[0.612 – 1.682]
- Nurse RN/LPN (no vs. yes)	1.723	[0.993 – 2.988]
- Physician assistant (no vs. yes)	1.293	[0.457 – 3.653]
Hospital		
- Region (referent: West)		
- Northeast	1.248	[0.723 – 2.156]
- Midwest	0.675	[0.361 – 1.263]
- South	0.866	[0.492 – 1.524]
- MSA (MSA vs. non-MSA)	1.555	[0.874 – 2.767]
- Ownership (referent: Proprietary)		
- Voluntary/non-profit	*2.263	[1.129 – 4.534]
- Government/non-federal	2.148	[0.945 – 4.882]

* $p<0.05$

Table 4.7: Multivariate analysis of predictors of antiplatelet agent use*

Predictor Variables	Odds Ratio (OR)	95% CI of OR
Age (younger than 65 vs. 65 and older)	1.261	[1.012 – 1.572]
Residence (other residence vs. nursing homes)	2.231	[1.017 – 4.892]
Triage (high vs. low)	2.833	[1.329 – 6.038]
Total diagnostic services	1.136	[1.078 – 1.196]
Arrival (other transport vs. ambulance)	1.618	[1.018 – 2.571]
MSA (MSA vs. non-MSA)	1.692	[1.205 – 2.375]

*adjusted for age, sex, race, and year

Table 4.8: Multivariate analysis of predictors of beta-blocker use*

Predictor Variables	Odds Ratio (OR)	95% CI of OR
Sex (females vs. males)	0.725	[0.504 – 1.042]
Chest pain (no chest pain vs. chest pain)	0.339	[0.131 – 0.880]
Total diagnostic services	1.014	[0.974 – 1.085]

*adjusted for age, sex, race, and year

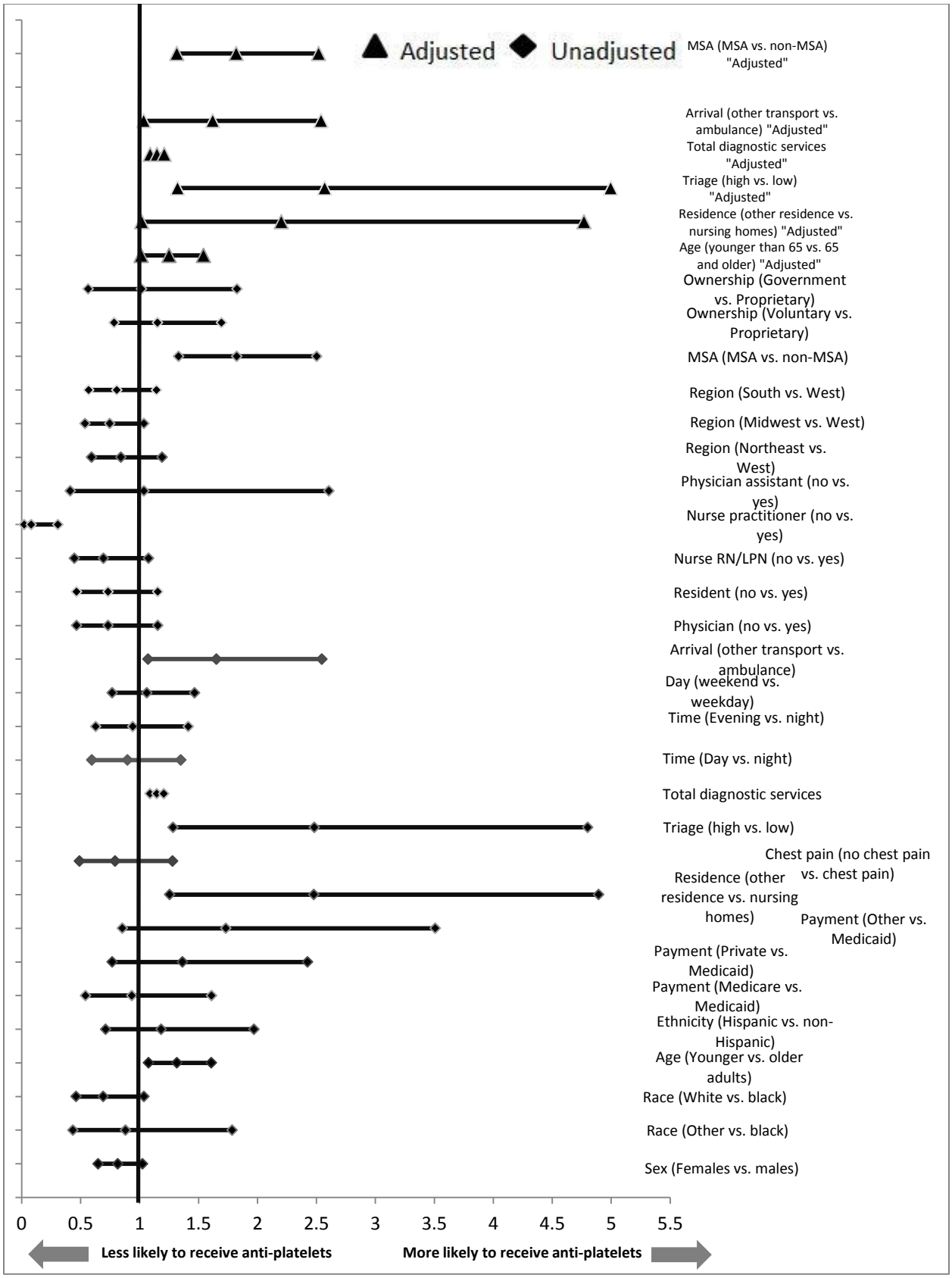

Figure 4.2: Forest plot of bivariate associations between predictors and anti-platelets use

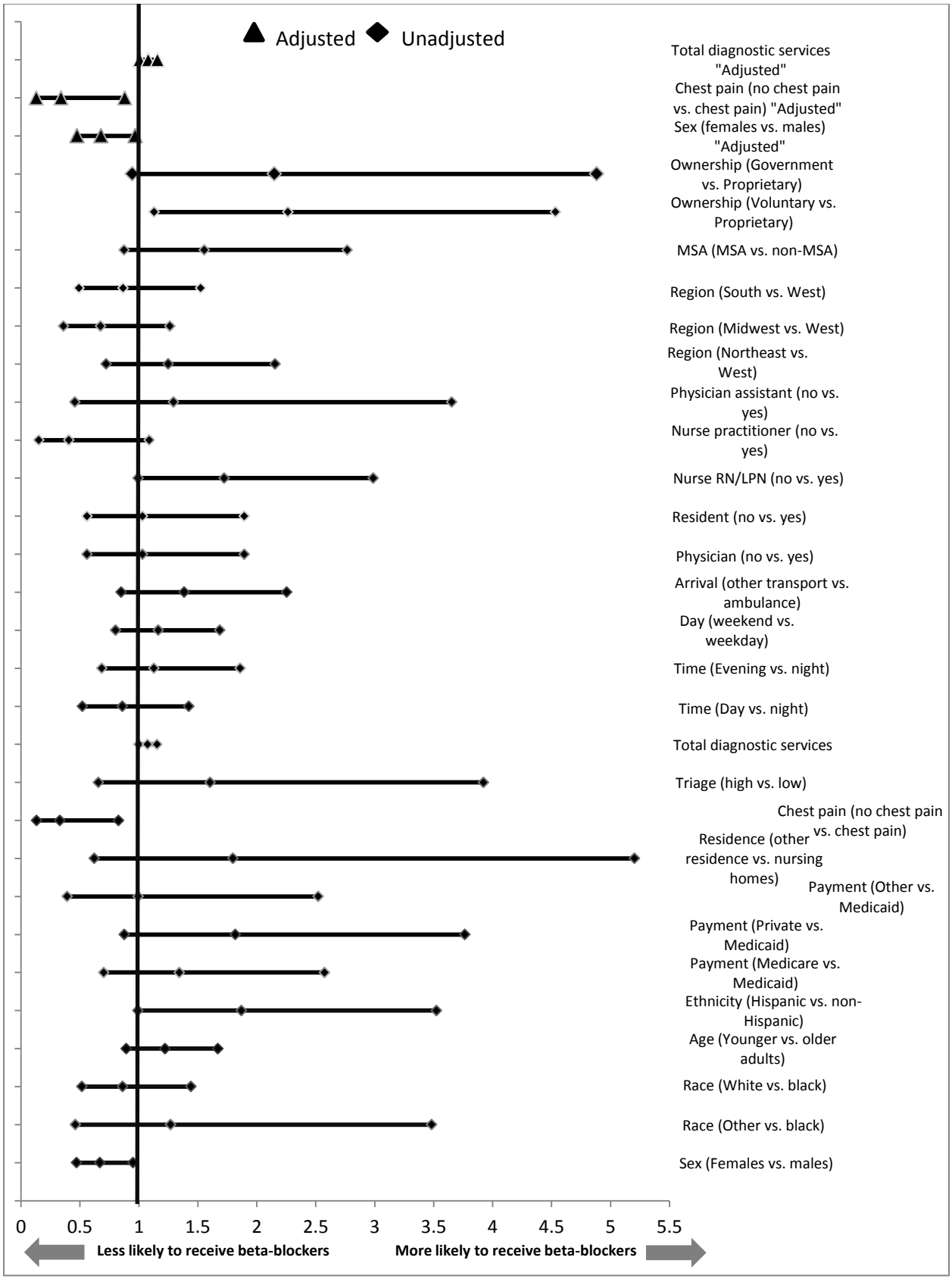

Figure 4.3: Forest plot of bivariate associations between predictors of beta-blocker use

Objective 3: The effect of the use of anti-platelet agents and beta-blockers on in-hospital mortality and length of hospital stay

In-hospital mortality in this population was around 4%. After a chi-square test between the utilization of antiplatelet agents and beta-blockers and in-hospital mortality, there was no significant difference between patients receiving anti-platelet agents and patients who did not in their in-hospital mortality ($\chi^2 = 0.008$, p= 0.909). However, there was a significant difference between patients receiving beta-blockers and patients who did not in their in-hospital mortality ($\chi^2 = 2.518$, p= 0.041).

The mean length of hospital stay was 6.6 (±8.2) days. A linear regression between the utilization of antiplatelet agents and beta-blockers and length of hospital stay indicated that there was no statistically significant relationship between antiplatelet agents and beta-blockers use and length of hospital stay ($\beta = 0.937$, p = 0.411) and ($\beta = -0.045$, p = 0.967) respectively.

Objective 4: The effect of ED guideline reminders on the use of anti-platelet agents and beta-blockers

Almost 52% hospitals had computerized guideline reminders. A bivariate logistic regression showed that patients who were treated in EDs that had a computerized guideline reminder were twice as likely to get an antiplatelet agent (OR = 2.004 [95% CI: 1.052 to 3.815]). Computerized reminders were not significantly associated with beta-blocker use (OR = 0.594 [95% CI: 0.304 to 1.162]).

CHAPTER 5

Discussion

Discussion of descriptive results

The representation of females in our study is highly consistent with the literature.[1,2] We found that the older the age group the higher percentage of females (χ^2= 104.5, p < 0.001). It has been suggested that women present with AMI at older ages.[1] The percentage of patients who were admitted from a nursing home in our population was around 7.9%, which is similar to the proportion of nursing home residents in other studies (6.4%).[3]

Chest pain is the hallmark symptom of AMI. In our study almost 89% of our patients experienced chest pain. This was consistent with the older adult literature.[1,2] However, when dividing older adults into different age groups, we found that the older the age group, the less likely they were to experience chest pain (younger adults (55-64 years) was 90% and older old adults (≥85 years) was 78%, χ^2 = 15.54, p = 0.045). This was also found in other studies that looked at the differences by age in AMI presentation.[2,4]

Less than 20% of our patients had a contraindication to beta-blockers. Approximately 11% had bradycardia and almost 15% had hypotension, some patients had both hypotension and bradycardia. These percentages were similar to a study that looked at the percentage of patients who had a contraindication to beta-blockers.[5]

In our study, about 70% of the patients visited the ED during the day or evening shift. This is consistent with other studies where the percentage of patients who arrived during the day and evening shift was 69-74% and during the night shift was 26-32%.[1,6] Almost half of our patients arrived by an ambulance, which is also similar to the previous study (45%).[1]

Discussion of results by objective

Objective 1: Trend in use of anti-platelet agents and beta-blockers across 1992-2010

This study showed a positive trend in both antiplatelet agents and beta-blockers use. This also was seen in another study.[7] One study found that administration of aspirin and beta-blockers within the first 24 hours of admission showed a positive trend from years 1990 to 2006.[7] Another study that looked at in-hospital use of aspirin and beta-blockers from years 1992 to 2002 also found a significant positive increase in both treatments over time.[8]

In our study, underuse of both antiplatelet agents and beta-blockers in the ED is evident. Our utilization percentages are hard to compare with other studies in the literature, because most of the studies reported in-patient utilization rates.[2,9,10] Interestingly, even among the studies that intended to look only at ED care, their definition of acute care was the receipt of medication within the first 24 hours of admission, which actually may have been in the ED or in the in-patient setting.[1,4]

This study showed that beta-blockers were highly underused in the ED (overall use = 14%). This underuse may be attributed to the fact that beta-blockers are more often administered once the patient is admitted to the hospital. Because beta-blockers have a long list of contraindications that the physician has to check before administration, early use may be hard to accomplish given the time constraints in the ED.[5] Furthermore, whether some of these are absolute or relative contraindications may be unclear to the physicians, such as non-acute asthma, COPD, and chronic heart failure.[5]

The strong drop in beta-blockers use noticed in our study, from 32% in 2009 to 10% in 2010, may be explained by the 2008 changes in ACC/AHA performance measures that omitted the recommendation of administering beta-blockers at arrival.[11] This change was likely a result of findings from the COMMIT trial, which found that intravenous beta-blockers administered at arrival may cause cardiogenic shock for patients with history of heart failure.[12] The ACC/AHA guidelines still consider beta-blockers to be class I indication for many patients.[11] Oral beta-blockers are still useful and effective for a wide range of patients,[13] but it was omitted from the AMI performance measures because of safety concerns.[11] This change was widely adopted by hospitals because this measure was also removed from the AMI measures list common to the Centers for Medicare & Medicaid Services (CMS) and The Joint Commission in March 2009.[14] This wide adoption may be explained by the fact that, If a hospital does not comply to JCAHO/CMS, it will lose 2.0 percent of their annual market basket update, only hospitals who are enrolled in the inpatient prospective payment system (IPPS).[14]

Objective 2: Predictors of anti-platelet agents and beta-blocker use

Age

There is overwhelming evidence for the underuse of effective AMI treatments in the older adult population.[4,7] Our study supported these previous findings since we found older adults were less likely to receive an antiplatelet agent; however, no significant relationship was found with beta-blockers. The older adult population is known to have more contraindications to medications than their counterparts due to their increased comorbidities. For example, gastrointestinal bleeding is a common problem in older adults that may prevent the administration of an antiplatelet agent. A previous study found a 15% reduction in the likelihood of getting aspirin and 21% with beta-blockers, respectively for every 10-year increase in age.[4]

The TIMI III Registry study found that older adults were less likely to receive aspirin and beta-blockers ($p = 0.04$).[15] This was also confirmed by GRACE global registry, which found that the older the age group the less likely was the utilization of aspirin and beta-blockers.[10] Another study found that one of the strongest determinants against receiving a beta-blocker was age older than 65 years.[16] Moreover, a study using NRMI database found that older adults (>75) were consistently less likely to receive beta-blockers within 24 hours of admission across the years 1990 to 2006.[7]

Sex

There is contradicting evidence about the effect of patient's sex on the receipt of AMI treatment. Our study found that females were less likely to receive a beta-blocker in the bivariate logistic regression analysis; however, after adjusting for age, sex, race, and year, the relationship did not remain significant, also there was no significant relationship with antiplatelet agents. One study found that the relationship between sex and AMI treatment was not significant after adjusting for age.[1] They suggested that women were less likely to receive AMI treatment just because they were generally older at presentation with AMI.[1] Several other studies found that women were consistently older than men when presenting with AMI, and they presented with atypical symptoms of AMI, like no chest pain, that may also explain the lower use of evidenced based drugs in females.[1,17-23] Four studies using the largest databases of AMI (NRMI, CRUSADE, TIMI, and CCP) found that women were less likely to receive aspirin and beta-blockers.[7,23-25] Another study found that one of the strongest determinants against receiving a beta-blocker is female gender.[16] Furthermore, a study using the NRMI database found that females were consistently less likely to receive beta-blockers within 24 hours of admission across the years 1990 to 2006.[7]

Race and ethnicity

In our study we found that race and ethnicity were not associated with receipt of both antiplatelet agents and beta-blockers. This was consistent with other studies that also found no significant relationships between race and ethnicity and AMI treatment.[26-28] However, in the TIMI registry, they found that blacks were less likely to get beta-blockers, but there was no significant relationship with aspirin.[15] In a Medicare study, they found that white people are more likely to get early beta-blockers (OR, 1.14; 95% CI, 1.04 to 1.23).[13] Interestingly, a study using the NRMI database found that blacks were less likely to receive beta-blockers within 24 hours of admission in the earlier years of the study (1994-1996) but in the later years (2003-2006) they were more likely to get beta-blockers.[7]

Payment

There was no significant relationship between the source of payment and receipt of antiplatelet agents and beta-blockers. This result was expected because more than 60% of our patients were covered by Medicare, so it is hard to find the effect of payment in this kind of distribution. Plus, there could be a spill-over effect from the Medicare patients on the other patients especially that Medicare emphasizes a lot on quality. A previous study looked at the relationship between source of payment and AMI care, but it only looked at private payment by differentiating between patients who had an HMO plan and FFS plan. The authors found that patients with HMO plans were more likely to receive aspirin and beta-blockers comparing to patients with FFS plan.[29]

Residence

In our study, patients admitted from nursing homes were less likely to be administered an antiplatelet agent. This may be attributed to the possibility that nursing home residents may be

given aspirin by the nursing home staff when AMI is expected (i.e. experiencing chest pain). This was confirmed by another study, which found that getting aspirin and being admitted from a nursing home is negatively correlated (Rho = -0.069 ($p < 0.001$)).[3]

Chest pain

In our study, patients who did not have chest pain were less likely to receive beta-blockers, but there was no significant association between antiplatelet agents and chest pain. This is similar to another study which found that people who experienced chest pain within < 48 hours of admission were more likely to get beta-blockers (OR, 1.71; 95% CI, 1.58 to 1.84).[13] Another study found that patients who experienced chest pain are more likely to get aspirin.[25]

Hospital Region, Ownership, and MSA

Our study found no significant relationship between hospital region and receipt of antiplatelet agents or beta-blockers. Some previous studies have found that hospitals in the Northeast region did better on various AMI performance measures.[6,30]

Objective 3: The effect of the use of anti-platelet agents and beta-blockers on in-hospital mortality and length of hospital stay

In-hospital mortality

Our study found that there was a significant difference in the in-hospital mortality rate between patients who received beta-blockers and patients who did not. The majority of patients who took a beta-blocker lived (99%). However, there was no significant difference in the in-hospital mortality rate between patients who received an antiplatelet agent and patients who did not. At 4%, in-hospital mortality in our population was very similar to other studies that looked at AMI in-hospital mortality (4-7%).[16,31-35] The 4% in our study only represents 15 actual cases of AMI mortality, hence it is not necessarily comparable to the 4% in other studies. We also

noticed that older age groups in our population had higher in-hospital mortality than the younger age groups, but it was not significantly different. Other studies found this relationship to be significant, the older the age group the higher the in-hospital mortality rate.[10,32-34] Similar to our findings, three studies found that beta-blockers were associated significantly with lower in-hospital mortality rates.[16,31,35] Another study found that the early use of guideline-recommended therapies (aspirin, beta-blockers, glycoprotein IIb/IIIa inhibitors, heparin, and catheterization) were associated with lower in-hospital mortality rates.[34]

Length of hospital stay

Mean LOS was 6.6 (±8.2) days. It was similar to other studies who had hospitalized older adults with AMI.[36] We did not find a significant relationship between receipt of antiplatelet agents or beta-blockers and length of hospital stay. It may be expected that medical treatment (i.e. antiplatelet agents and beta-blockers) may not have a significant effect on LOS like interventional treatments may have (e.g. PCI, CABG, and fibrinolysis). Krumholz et al. found that patients who received aspirin had a shorter LOS than patients who did not; however, it was not mentioned if they were significantly different or not.[25]

Objective 4: The effect of ED guideline reminders on the use of anti-platelet agents and beta-blockers

Almost 52% of hospitals had computerized guideline reminders. A bivariate logistic regression showed that patients who were treated in EDs that had a computerized guideline reminder were twice as likely to get an antiplatelet agent, but it was not significantly associated with beta-blockers use. As mentioned before, beta-blockers are harder to administer in an ED setting, so it is not expected that ED reminders may increase their use in the ED. Plus, aspirin could be prescribed by a nurse or a physician in the ED, unlike beta-blockers which are only

prescribed by a physician. We cannot compare our results to other studies, since no studies to our knowledge examined the effect of computerized clinical decision support (CCDS) systems in the ED on AMI treatment. However, several studies have looked at the effect of CCDS in other disease states and in different settings.[37-40] Few studies have examined the effect of CCDS system in the ED.[41-42] One study used the CCDS system in the ED to screen for HIV. They found that using the CCDS for this purpose increased the detection rate of HIV and hence helped in treating undetected HIV cases.[41] The other study found that when incorporating pneumococcal vaccination reminders in the CCDS system in the ED, it helped to overcome existing barriers that the health professionals had towards pneumococcal vaccination.[42]

Limitations

The lack of detailed clinical information in the database prevents us from excluding ineligible subjects for drug therapy, which is especially important for beta-blockers. Only blood pressure and heart rate were available for us to identify patients who were hypotensive or bradycardic, which is considered a contraindication to beta-blockers administration. Also, because of the lack of data on out-of-hospital management, we were unable to determine if patients received therapy before hospital arrival. This is more relevant with respect to aspirin, as it may be given in the ambulance or taken at home by the patient. Both of these misclassifications may have overestimated the percentage of underuse in our study.

If the database shows that a patient was prescribed a drug that does not necessarily mean that the patient has actually taken the drug. Even when a drug is mentioned to be given in the emergency department, it does not necessarily mean that the patient was administered the drug. In our case, there is little that we can do to overcome that, because there is no other way that we

could find this information other than the emergency department form. We can only acknowledge this as a limitation, which is common in most database research.

A researcher is limited by the information collected. It is important to have in mind that the database is not specifically built to answer the research question. Hence, not all the information needed to carry out the research maybe available. Sometimes the incompleteness of data would be a minor issue that can be acknowledged, but sometimes it is a major issue that may cause us to reconsider using this data source. For example, we are limited by the number of drugs available in each visit record in NHAMCS. From 2003 to 2010, there are 8 drugs available, from 1995 to 2002, there are 6 drugs available, and from 1992 to 1994, there are 5 drugs available. This may cause us to miss some of the utilization of anti-platelet agents and beta-blockers, especially in patients with a lot of comorbidities, which may likely receive a large number of drugs. Another important matter to note here that from year 1992 to 1996 the variable indicating whether the diagnosis is probable or not was not available. These years had larger numbers of participants, meaning it is probable that some of these cases did not have a confirmed AMI diagnosis. We chose to add these years because of our need to meet sample size requirements for national estimates and acknowledge it as a limitation.

In our study, there was some important information that was not available in order to describe the population better. For example, the patient's medical history was not available. If a patient had a previous AMI in a different setting, which is considered a cardiac risk factor, we were unable to account for it. Also, a patient's drug history is not available, so previous usage of anti-platelets or beta-blockers will not be known. This is important because it could affect the ED use for these drugs. Furthermore, the patient's social history, such as smoking status, is not available, which is also considered to be a cardiac risk factor. Furthermore, sociodemographic

patient factors are not available such as education, income, primary language spoken, and employment. Having this information better describes our population, and their risks to outcomes.

Data may be subject to many types of inaccuracies. There could be miscoding practices, either deliberately or just by human error. In our database it is more likely to be human error than deliberate miscoding. Since NHAMCS does not represent administrative claims data and there is no incentive to deliberately miscode the diagnosis or procedures to get higher reimbursements, this would be highly unlikely. Diagnosis codes are the only way to identify our population, to confirm our diagnosis; only visits with unquestionable diagnosis were used. Some studies can confirm the diagnosis by available clinical information, but in our case it was not possible.

Some limitations arise from our relatively small sample size. We were not able to control for all available covariates in our multivariate regression analysis. Hence, we only controlled for important demographic variables, such as age, sex, and race. We were also not able to carry out a Kaplan-Meir survival analysis to examine in-hospital mortality or a logistic regression analysis, because we only had 15 cases of mortality across 2005-2010.

Practical implications

Delivering time-sensitive therapies in the ED should be a priority by the hospital staff; this may be facilitated by forming a system that ensures receipt of these therapies before the patient is discharged from the ED.[43] Having ED clinical pathways and protocols that promote use of guideline-recommended therapies in the ED is a good approach to ensuring receipt of antiplatelet agents. These clinical pathways and protocols may be incorporated in a CCDS to increase their efficiency. Also, it is important to maximize the provision of these effective medications to AMI patients, irrespective of age and sex.[1] When emergency physicians work

together with other health care providers (e.g., cardiologists and EMS) this will facilitate a better provision of care in the ED to AMI patients.[6] Also, this is an area where ED pharmacists could best help in, improving the provision of guideline-concordant treatment to older AMI patients presenting to the ED. A recent literature review have shown that pharmacists have a great role in the ED in increasing medication safety and improving patient drug reconciliation.[44]

Future Directions

Research about the care given in the ED setting needs more attention. It is important to look at other guideline-recommended therapies that should be given in the ED, like fibrinolysis and PCI in the older adult population. Conducting a study to be at the ED-level could give another perspective on ED care. Another acute care setting that needs attention is the EMS. More studies are needed to quantify the actual use of aspirin in EMS, plus other care guidelines like, 12-led-ECG and fibrinolysis in the ambulance. Furthermore, clinical guidelines should create and validate performance measures that are ED-specific and that merit more research.[37] Also, there are other structure components that are not collected in NHAMCS that may be looked at in future research, like the effect of being treated with a cardiologist in the ED.

Conclusion

This is the first study to capture this long period of time of ED AMI care for older adults. It provided national estimates about older adults ED use of antiplatelet agents and beta-blockers from 1992 to 2010, which showed that both had a positive trend in utilization across the years. This study confirms the finding that older adults and females have lower utilization rates of AMI treatment than their counterparts. This study also reveals new relevant associations, like the effect of chest pain and triage on utilization rates of antiplatelet agents and beta-blockers. This study attempted to evaluate the impact of having a computerized reminder to prompt ED staff to

use guidelines, on the usage of antiplatelet agent therapy in the ED. Our results showed that having a computerized guideline reminder increase the utilization of antiplatelet agents but not beta-blockers. This study also attempted to see the effect of ED utilization of antiplatelet agents and beta-blockers on hospital outcomes, like in-hospital mortality and LOS. We only found that beta-blockers were significantly associated with lower in-hospital mortality. Finally, this study may help in increasing the awareness of the ED health care professionals of older adults AMI care.

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APPENDIX A

SAS code

SAS code of data manipulation (example of year 2010)

```
/*work program for year 2010*/
data nhamcs.nhamcs10work;
set nhamcs.nhamcs10;

if substr(DIAG1,1,3) = '410' then AMI1adm = 1;
else AMI1adm = 0;

if substr(DIAG2,1,3) = '410' then AMI2adm = 1;
else AMI2adm = 0;

if substr(DIAG3,1,3) = '410' then AMI3adm = 1;
else AMI3adm = 0;

if AMI1adm = 1 and prdiag1 = 0 then participant1 = 1;
else participant1 = 0;

if AMI2adm = 1 and prdiag2 = 0 then participant2 = 1;
else participant2 = 0;

if AMI3adm = 1 and prdiag3 = 0 then participant3 = 1;
else participant3 = 0;

if seen72 = 1 then seen = 1;
else seen = 0;

if AGE>=55 then older =1;
else older=0;

if (participant1 = 1 or participant2 = 1 or participant3= 1) and older = 1
and seen= 0 then participant = 1;
else participant= 0;

if age >=55 then agecat = 3;
if age >=65 then agecat = 2;
if age >=75 then agecat = 1;
if age >=85 then agecat = 0;

if substr(HDDIAG,1,3) = '410' then AMIdisch = 1;
else AMIdisch = 0;

antiplatelet = 0;
if drugid1 = '' and drugid2 = '' and drugid3 = '' and drugid4 ='' and drugid5
='' and drugid6 ='' and drugid7 = '' and drugid8 = '' then antiplatelet = .;
if drugid1 = 'd04258' or 'd00514' or 'd00213' or drugid2 = 'd04258' or
'd00514' or 'd00213' or drugid3 = 'd04258' or 'd00514' or 'd00213' or drugid4
= 'd04258' or 'd00514' or 'd00213' or drugid5 = 'd04258' or 'd00514' or
'd00213' or drugid6 = 'd04258' or 'd00514' or 'd00213' or drugid7 = 'd04258'
```

```
or 'd00514' or 'd00213' or drugid8 = 'd04258' or 'd00514' or 'd00213' then
antiplatelet= 1;

aspirin = 0;
if drugid1 = '' and drugid2 = '' and drugid3 = '' and drugid4 ='' and drugid5
='' and drugid6 ='' and drugid7 = '' and drugid8 = '' then aspirin = .;
if drugid1 = 'd00170' or drugid2 = 'd00170' or drugid3 = 'd00170' or drugid4
= 'd00170' or drugid5 = 'd00170' or drugid6 = 'd00170' or drugid7 = 'd00170'
or drugid8 = 'd00170' then aspirin= 1;

betablocker = 0;
if drugid1 = '' and drugid2 = '' and drugid3 = '' and drugid4 ='' and drugid5
='' and drugid6 ='' and drugid7 = '' and drugid8 = '' then betablocker = .;
if drugid1 = 'd00134' or 'd00004' or 'd03847' or 'd00709' or 'd00128' or
'd00018' or 'd00176' or 'd05265' or 'd00032' or drugid2 = 'd00134' or
'd00004' or 'd03847' or 'd00709' or 'd00128' or 'd00018' or 'd00176' or
'd05265' or 'd00032' or drugid3 = 'd00134' or 'd00004' or 'd03847' or
'd00709' or 'd00128' or 'd00018' or 'd00176' or 'd05265' or 'd00032' or
drugid4 = 'd00134' or 'd00004' or 'd03847' or 'd00709' or 'd00128' or
'd00018' or 'd00176' or 'd05265' or 'd00032' or drugid5 = 'd00134' or
'd00004' or 'd03847' or 'd00709' or 'd00128' or 'd00018' or 'd00176' or
'd05265' or 'd00032' or drugid6 = 'd00134' or 'd00004' or 'd03847' or
'd00709' or 'd00128' or 'd00018' or 'd00176' or 'd05265' or 'd00032' or
drugid7 = 'd00134' or 'd00004' or 'd03847' or 'd00709' or 'd00128' or
'd00018' or 'd00176' or 'd05265' or 'd00032' or drugid8 = 'd00134' or
'd00004' or 'd03847' or 'd00709' or 'd00128' or 'd00018' or 'd00176' or
'd05265' or 'd00032' then betablocker= 1;

if vdayr = 1 or vdayr = 7 then day = 0;
if vdayr >=2 & vdayr <7 then day = 1;

/*change in arrtime unknown coding for 2009*/
if arrtime >=0000 then hours= 0;
if arrtime >=0800 then hours = 1;
if arrtime >=2201 then hours = 0;
if arrtime = (-9) then hours =.;

/*change in rfv unknown coding for 2009*/
chestpain = 0;
if (rfv1 >=89900 & rfv1 <=90000) or (rfv2 >=89900 & rfv2 <=90000) or (rfv3
>=89900 & rfv3 <=90000) or rfv1 = (-9) or rfv2 = (-9) or rfv3 = (-9) then
chestpain =.;
if rfv1 = 10501 or rfv2 = 10501 or rfv3 = 10501 then chestpain = 1;

/*change in residnce coding for 2009*/
if residnce = 2 then ptresidnce = 1;
if residnce = 1 or (residnce >=3 & residnce <=5) then ptresidnce = 0;
if residnce = (-8) or residnce = (-9) then ptresidnce = .;

/*change in ptrace coding for 2009*/
if racer = 1 then ptrace = 1;
if racer = 2 then ptrace = 2;
if racer = 3 then ptrace = 0;

/*change in paytype unknown coding for 2009*/
if paytyper = 1 then payment = 1;
if paytyper = 2 then payment = 2;
```

```
if paytyper = 3 then payment = 3;
if paytyper >=4 & paytyper <=7 then payment = 0;
if paytyper = (-8) or paytyper = (-9) then payment = .;
/*change arrival coding in 2009*/
if arrems = 1 then arrival = 1;
if arrems = 2 then arrival = 0;
if arrems = (-8) or arrems = (-9) then arrival = .;

/*change in admission coding in 2009*/
if admit = 1 then admission = 1;
if admit = 2 or admit = 3 or admit = 4 then admission = 2;
if admit = 5 or admit = 6 then admission = 0;
if admit = (-7) or admit = (-8) or admit = (-9) then admission = .;

/*change in triage coding for 2009*/
if immedr = 1 or immedr = 2 or immedr = 3 then triage = 1;
if immedr = 4 or immedr = 5 then triage = 2;
if immedr = 7 then triage = .;

if dieded = 1 then deathed = 1;
if dieded = 0 then deathed = 0;

if tranoth = 1 then transferhospital = 1;
if tranoth = 0 then transferhospital = 0;

if ethun = 1 then ethnicity = 1;
if ethun = 2 then ethnicity = 2;
if ethun = (-9) then ethnicity = .;

if pulse =<60 then bradycardia = 1;
else bradycardia = 0;

if bpsys =<90 then hypotension = 1;
else hypotension = 0;

if bradycardia = 1 or hypotension = 1 then Contraindication = 1;
else Contraindication = 0;

if attphys = 0 then physcian = 0;
if attphys = 1 then physcian = 1;

if rnlpn = 0 then nurse = 0;
if rnlpn = 1 then nurse = 1;

if msa = 1 then metro = 1;
if msa = 2 then metro = 2;

if owner = 1 then ownership = 1;
if owner = 2 then ownership = 2;
if owner = 3 then ownership = 3;

if arrtime >=0800 & arrtime =< 1559 then time= 1;
if arrtime >=1600 & arrtime =< 2359 then time = 2;
if arrtime >=0000 & arrtime =< 0759 then time = 3;
if arrtime = (-9) then time = .;

options nofmterr;
```

```
run;

/*check the keep list for every year*/
data nhamcs.nhamcs10small;
set nhamcs.nhamcs10work;
keep betablocker aspirin antiplatelet drugid1 drugid2 drugid3 drugid4 drugid5
drugid6 drugid7 drugid8 seen AMIdisch older participant participant1
participant2 participant3 agecat chestpain day time ptresidnce ptrace arrival
admission payment triage waittime physcian resint nursepr nurse physasst
deathed transferhospital ethnicity age sex pulse bradycardia bpsys
hypotension contraindication disch7da cardenz cardmon ekg totdiag totproc los
hdstat patwt region metro ownership hospcode patcode cstratm cpsum year edwt
ereminde;
run;
```

SAS code for the analysis program

```
/*Analysis program for Maryam Alowayesh Dissertation, last modified April 8th
2013*/

/*Demographic Descriptives*/

/*Descriptive age*/
proc surveymeans data=nhamcs.nhamcs10ed_opdappend_end;
var age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive age';
options nofmterr;
run;

/*Descriptive demographic: sex race ethnicity payment residence*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*sex participant*ptrace participant*ethnicity
participant*payment participant*ptresidnce/ row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive demographics';
options nofmterr;
run;

/*Clinical Descriptives: totproc totdiag*/
proc surveymeans data=nhamcs.nhamcs10ed_opdappend_end;
domain participant;
var totdiag totproc;
cluster cpsum;
strata cstratm;
weight patwt;
title 'totdiag totproc Descriptives';
options nofmterr;
run;
```

```
/*Clinical Descriptives: chestpain triage hypotension bradycardia cardenz
cardmon ekg*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*chestpain participant*triage participant*hypotension
participant*bradycardia participant*cardenz participant*cardmon
participant*ekg  /row CL CLWT ;
cluster cpsum;
strata cstratm;
weight patwt;
title 'clinical descriptive';
options nofmterr;
run;

/*Visit Descriptives: arrival day time disch7da hdstat physcian resint
nursepr nurse physasst*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*arrival participant*day participant*disch7da
participant*hdstat participant*physcian participant*resint
participant*nursepr participant*nurse participant*physasst/row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'visit Descriptives';
options nofmterr;
run;

/*Hospital Descriptives: region metro ownership ereminde*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*region participant*metro participant*ownership
participant*ereminde/row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'hospital Descriptives';
options nofmterr;
run;

/*AIM 1: trend of aspirin_antiplatelet across years*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
model aspirin_antiplatelet (event ='1')= year;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'trend of aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 1: trend of betablocker across years*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
model betablocker (event ='1')= year;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'trend of betablocker';
options nofmterr;
```

```
run;


/*Associations with Demographic Characteristics*/

/*AIM 2: age (older_65) and aspirin_antiplatelet (new_participant)*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class older_65 sex ptrace;
model aspirin_antiplatelet (event ='1')= older_65 sex ptrace;
domain new_participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'older_65 and new_participant and aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: age (older_65) and betablocker (new_participant)*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class older_65;
model betablocker (event ='1')= older_65;
domain new_participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'older_65 and new_participant and betablocker';
options nofmterr;
run;

/*AIM 2: sex and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class sex;
model aspirin_antiplatelet (event ='1')= sex;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'sex+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: sex and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class sex ptrace;
model betablocker (event ='1')= sex ptrace age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'sex+ betablocker';
options nofmterr;
run;

/*AIM 2: race and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ptrace;
model aspirin_antiplatelet (event ='1')= ptrace;
```

```
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ptrace+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: race and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ptrace;
model betablocker (event ='1')= ptrace;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ptrace+ betablocker';
options nofmterr;
run;

/*AIM 2: ethnicity and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ethnicity;
model aspirin_antiplatelet (event ='1')= ethnicity;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ethnicity+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: ethnicity and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ethnicity;
model betablocker (event ='1')= ethnicity;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ethnicity+ betablocker';
options nofmterr;
run;

/*AIM 2: payment and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class payment;
model aspirin_antiplatelet (event ='1')= payment;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'sex+ aspirin_antiplatelet';
options nofmterr;
run;
```

```
/*AIM 2: payment and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class payment;
model betablocker (event ='1')= payment;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'payment+ betablocker';
options nofmterr;
run;

/*AIM 2: residnce and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ptresidnce sex ptrace;
model aspirin_antiplatelet (event ='1')= ptresidnce sex ptrace age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ptresidnce+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: residnce and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ptresidnce;
model betablocker (event ='1')= ptresidnce;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ptresidnce+ betablocker';
options nofmterr;
run;

/*Association with Clinical Characteristics*/

/*AIM 2: chestpain and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class chestpain;
model aspirin_antiplatelet (event ='1')= chestpain;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'chestpain+ aspirin_antiplatelet';
options nofmterr;
run;
```

```
/*AIM 2: chestpain and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class chestpain ptrace sex;
model betablocker (event ='1')= chestpain age ptrace sex;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'chestpain+ betablocker';
options nofmterr;
run;

/*AIM 2: triage and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class triage sex ptrace;
model aspirin_antiplatelet (event ='1')= triage age sex ptrace;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'triage+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: triage and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class triage;
model betablocker (event ='1')= triage;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'triage+ betablocker';
options nofmterr;
run;

/*AIM 2: totproc and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
model aspirin_antiplatelet (event ='1')= totproc;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'totproc+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: totproc and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
model betablocker (event ='1')= totproc;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
```

```
title 'totproc+ betablocker';
options nofmterr;
run;
/*AIM 2: totdiag and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ptrace sex;
model aspirin_antiplatelet (event ='1')= totdiag sex age ptrace;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'totdiag+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: totdiag and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class sex ptrace;
model betablocker (event ='1')= totdiag sex ptrace age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'totdiag+ betablocker';
options nofmterr;
run;

/*Association with Visit Characteristics*/

/*AIM 2: time and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_endingf;
class time;
model aspirin_antiplatelet (event ='1')= time;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'time+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: hours and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_endingf;
class time;
model betablocker (event ='1')= time;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'time+ betablocker';
options nofmterr;
run;
```

```
/*AIM 2: day and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class day;
model aspirin_antiplatelet (event ='1')= day;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'day+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: day and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class day;
model betablocker (event ='1')= day;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'day+ betablocker';
options nofmterr;
run;

/*AIM 2: arrival and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class arrival sex ptrace;
model aspirin_antiplatelet (event ='1')= arrival sex ptrace age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'arrival+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: arrival and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class arrival;
model betablocker (event ='1')= arrival;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'arrival+ betablocker';
options nofmterr;
run;
```

```
/*AIM 2: physcian and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class physcian;
model aspirin_antiplatelet (event ='1')= physcian;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'physcian+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: physcian and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class physcian;
model betablocker (event ='1')= physcian;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'physcian+ betablocker';
options nofmterr;
run;

/*AIM 2: resint and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class resint;
model aspirin_antiplatelet (event ='1')= resint;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'resint+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: resint and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class resint;
model betablocker (event ='1')= resint;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'resint+ betablocker';
options nofmterr;
run;
```

```
/*AIM 2: nurse and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class nurse;
model aspirin_antiplatelet (event ='1')= nurse;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'nurse+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: nurse and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class nurse;
model betablocker (event ='1')= nurse;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'nurse+ betablocker';
options nofmterr;
run;

/*AIM 2: nursepr and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class nursepr ptrace sex;
model aspirin_antiplatelet (event ='1')= nursepr ptrace sex age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'nursepr+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: nursepr and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class nursepr;
model betablocker (event ='1')= nursepr;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'nursepr+ betablocker';
options nofmterr;
run;
```

```
/*AIM 2: physasst and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class physasst;
model aspirin_antiplatelet (event ='1')= physasst;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'physasst+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: physasst and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class physasst;
model betablocker (event ='1')= physasst;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'physasst+ betablocker';
options nofmterr;
run;

/*Association with Hospital Characteristics*/

/*AIM 2: region and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class region;
model aspirin_antiplatelet (event ='1')= region;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'region+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: region and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class region;
model betablocker (event ='1')= region;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'region+ betablocker';
options nofmterr;
run;
```

```
/*AIM 2: Metro and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class metro sex ptrace;
model aspirin_antiplatelet (event ='1')= metro sex ptrace age;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'metro+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: metro and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class metro;
model betablocker (event ='1')= metro;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'metro+ betablocker';
options nofmterr;
run;

/*AIM 2: ownership and aspirin_antiplatelet*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ownership;
model aspirin_antiplatelet (event ='1')= ownership;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ownership+ aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 2: ownership and betablocker*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ownership;
model betablocker (event ='1')= ownership;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ownership+ betablocker';
options nofmterr;
run;
```

```
/*AIM 3: los and aspirin_antiplatelet (participant_los)*/
proc surveymeans data=nhamcs.nhamcs10ed_opdappend_end;
var los;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive los';
options nofmterr;
run;

proc surveyreg data=nhamcs.nhamcs10ed_opdappend_end;
model los = aspirin_antiplatelet / CLPARM;
domain participant_los;
cluster cpsum;
strata cstratm;
weight patwt;
title 'los+aspirin_antiplatelet';
options nofmterr;
run;

/*AIM 3: los and betablocker (participant_los)*/
proc surveyreg data=nhamcs.nhamcs10ed_opdappend_end;
model los = betablocker / CLPARM;
domain participant_los;
cluster cpsum;
strata cstratm;
weight patwt;
title 'los+betablocker';
options nofmterr;
run;

/*AIM 3: aspirin_antiplatelet and betablocker mortality*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*aspirin_antiplatelet*hdstat participant*betablocker*hdstat
/ chisq row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'hdstat*chisquare';
options nofmterr;
run;

/*AIM 4: descriptive ereminde*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_endingf;
tables participant*ereminde / row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive ereminde';
options nofmterr;
run;
```

```
/*AIM 4: antiplatelet and ereminde*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ereminde;
model aspirin_antiplatelet (event ='1')= ereminde;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'antiplatelet+ereminde ';
options nofmterr;
run;

/*AIM 4: betablocker and ereminde*/
proc surveylogistic data=nhamcs.nhamcs10ed_opdappend_end;
class ereminde;
model betablocker (event='1') = ereminde;
domain participant;
cluster cpsum;
strata cstratm;
weight patwt;
title 'ereminde+betablocker';
options nofmterr;
run;

/*Descriptive contraindication*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*contraindication / row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive contraindication';
options nofmterr;
run;

/*Descriptive betablockers*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*betablocker / row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive betablockers';
options nofmterr;
run;

/*chestpain and age*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*agecat*chestpain / chisq row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive chestpain';
options nofmterr;
run;
```

```
/*sex and age*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*agecat*sex / chisq row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'descriptive sex*age';
options nofmterr;
run;

/*hdstat and age*/
proc surveyfreq data=nhamcs.nhamcs10ed_opdappend_end;
tables participant*agecat*hdstat / chisq row CL CLWT;
cluster cpsum;
strata cstratm;
weight patwt;
title 'hdstat*age';
options nofmterr;
run;
```

APPENDIX B

IRB approval

VCU Memo
Virginia Commonwealth University

Office of Research Subjects Protection
BioTechnology Research Park
BioTech One, 800 E. Leigh Street, #114
P.O. Box 980568
Richmond, Virginia 23298-0568
(804) 828-0868
(804) 827-1448 (fax)

DATE: August 1, 2012

TO: Spencer Harpe, PhD, PharmD, MPh
Pharmacotherapy and Outcomes Science
Box 980533

FROM: Lloyd H. Byrd, MS 8/8/2012
Vice-Chairperson, VCU IRB Panel B
Box 980568

RE: **VCU IRB #: HM14455**
Title: Concordance of Acute Pharmacological Treatment Given in the Emergency Department with the ACC/AHA Performance Measures and its Effects on Short-Term Outcomes of Older Adults with Acute Myocardial Infarction

On July 17, 2012 the following research study ***qualified for exemption*** according to 45 CFR 46.101(b) Category 4. This determination includes the following items reviewed by this Panel:

RESEARCH APPLICATION/PROPOSAL: NONE

PROTOCOL: Concordance of Acute Pharmacological Treatment Given in the Emergency Department with the ACC/AHA Performance Measures and its Effects on Short-Term Outcomes of Older Adults with Acute Myocardial Infarction, version 5/21/12

ADDITIONAL DOCUMENTS:
- None

The Primary Reviewer assigned to your research study is Donna S. Gross, BA. If you have any questions, please contact Ms. Gross, IRB Coordinator, VCU Office of Research Subjects Protection, at dsgross@vcu.edu or 827-2261.

Attachment – Conditions of Approval (PLEASE NOTE RECENT CHANGES TO #3)

Conditions of Approval:

In order to comply with federal regulations, industry standards, and the terms of this approval, the investigator must *(as applicable)*:

1. Conduct the research as described in and required by the Protocol.

2. Provide non-English speaking patients with a translation of the approved Consent Form in the research participant's first language. The Panel must approve the translation.

3. The following changes to the protocol **must be** submitted to the IRB panel for review and approval before the changes are instituted. Changes that do not meet these criteria do not have to be submitted to the IRB. If there is a question about whether a change must be sent to the IRB please call the ORSP for clarification.

   THESE CHANGES MUST BE SUBMITTED:
   a) Change in principal investigator
   b) Any change that increases the risk to the participant
   c) Addition of children, wards of the state, or prisoner participants
   d) Changes in survey or interview questions (addition or deletion of questions or wording) that change the level of risk or adds questions related to sexual activity, abuse, past or present illicit drug use, illegal activities, questions reasonably expected to provoke psychological anxiety, or would make participants vulnerable, or subject them to financial, psychological or medical risk
   e) Changes that change the category of exemption or add additional exemption categories
   f) Changes that add procedures or activities not covered by the exempt category(ies) under which the study was originally determined to be exempt
   g) Changes requiring additional participant identifiers that could impact the exempt category or determination
   h) Change in inclusion dates for retrospective record reviews if the new date is after the original approval date for the exempt study. (ex: The approval date for the study is 9/24/10 and the original inclusion dates were 01/01/08-06/30/10. This could be changed to 01/01/06 to 09/24/10 but not to end on 09/25/10 or later.)
   i) Addition of a new recruitment strategy
   j) Increase in the planned compensation to participants

4. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.

5. Report Unanticipated Problems (UPs), following the VCU IRB requirements and timelines detailed in VCU IRB WPP VIII-7).

6. Promptly report and/or respond to all inquiries by the VCU IRB concerning the conduct of the approved research when so requested.

7. The VCU IRBs operate under the regulatory authorities as described within:
   a) U.S. Department of Health and Human Services Title 45 CFR 46, Subparts A, B, C, and D (for all research, regardless of source of funding) and related guidance documents.
   b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.
   c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

Vita

Maryam S. AlOwayesh

Phone: +(965) 66660525 - Email: alowayeshms@vcu.edu

EDUCATION

Virginia Commonwealth University-US, School of Pharmacy
PhD candidate, Pharmacotherapy and Health Outcomes Research, expected Graduation: *May 2013*

- Degree emphasis: Pharmacoepidemiology
- Supervisor: Dr. Spencer Harpe, PharmD, PhD, MPH

University of London-UK, School of Pharmacy
MSc, Clinical Pharmacy and International Practice and Policy, *October 2009*

- Thesis: The Initiation and Extent of Dose Titration of ACE-inhibitors and β-blockers Post-Acute Myocardial Infarction: a Prospective Audit.
- Supervisor: Pharmacist Paul Wright, MPharm, MSc

Kuwait University-Kuwait, School of Pharmacy
BSc of Pharmacy, *June 2006*

- Thesis: Targeting Adenosine Receptors as a Novel Treatment for Respiratory Diseases
- Supervisor: Dr. Ahmed Alhashim, MSc, PhD

AWARDS AND HONORS

- Member of the Golden Key International Honour Society "2012"
- Nominated for the Who's Who Among Students in American Universities and Colleges "2010"
- Kuwait University Scholarship (3 years PhD scholarship, competitive scholarship) "2009"
- Sheikh Salem Alali Education Fund Scholarship for sponsoring Masters studies "2008"
- Sultan Education Fund Scholarship for sponsoring Masters studies "2008"
- "Best Student Leadership Award" 2006 , awarded by the Dean for scholastic achievements in the Faculty of Pharmacy
- "Best Academic Performance Student Award" of 2005 awarded by the Vice Dean of Academics
- Annual Awards of Excellent Students Years 2001-2006

RESEARCH EXPERIENCE

Kuwait University-Kuwait, School of Pharmacy, Department of Pharmacy Practice
Research Assitant, *December 2009-June 2010*

- Supervisor: Prof. Karl Hannes Enlund, Chair of Pharmacy Practice Department
- Participated in a Literature Review (Anti-Parkinson Drug Use in the Elderly)

CLINICAL EXPERIENCE

Ministry of Health - Kuwait
Registered Pharmacist, *August 2006-August 2008*

- Pharmacy Dispensing in Specialized Primary Care Center (*Aug 2006- Jan 2007*).
- Mubarak Hospital (*Jan 2007- August 2008*).
  - Out-patient Pharmacy
  - In-patient Pharmacy
  - Member of the Coronary Care Unit Counseling Team
  - Member of the Scientific Committee

PUBLISHED WORK

- **Harpe SE, Phipps LB, Alowayesh MS. Effects of a learning-centered approach to assessment on students' attitudes towards and knowledge of statistics. Currents in Pharmacy Teaching and Learning. 2012; 4: 247–255.**

RESEARCH WORK IN PROGRESS

- Alowayesh MS. (in preperation). **Predicting Health Outcomes of Malnutrition in Older Adults using the Mini-Nutritional-Assessment Tool: a Systematic Review**. Target submission to *Age and Aging*.
- Alowayesh MS, and Wright P. (in preperation). **The Initiation and Extent of Dose Titration of ACE-inhibitors and β-blockers Post-Acute Myocardial Infarction: A prospective Audit**. Target Submission to *The Pharmaceutical Journal.*
- Alowayesh MS, and Holdford D. (in preparation). **Decision Analysis Model Evaluating the Cost-Effectiveness of Fidaxomicin and Vancomycin in the Treatment of Clostridium Difficile Infection (CDI) from a Hospital Perspective.** Target submission The Annals of Pharmacotherapy.

CONFERENCE PRESENTATIONS

Alowayesh MS, and Wright P. (May, 2011). **The Initiation and Extent of Dose Titration of ACE-inhibitors and β-blockers Post-Acute Myocardial Infarction**. Poster presentation in the ISPOR 16th Annual International Meeting. Baltimore, MD.

Alowayesh MS, and Holdford D. (October, 2011) **Decision Analysis Model Evaluating the Cost-Effectiveness of Fidaxomicin and Vancomycin in the Treatment of Clostridium Difficile Infection (CDI) from a Hospital Perspective.** Poster and Podium Presentation in the Annual Research and Career Day of VCU School Pharmacy. Richmond, VA.

Alowayesh MS, and Holdford D. (October, 2011) **Decision Analysis Model Evaluating the Cost-Effectiveness of Fidaxomicin and Vancomycin in the Treatment of Clostridium**

Difficile Infection (CDI) from a Hospital Perspective. Poster presentation in the Daniel T. Watts Research Symposium. School of Medicine – VCU. Richmond, VA.

STUDENT LEADERSHIP POSITIONS

- Joint President of Postgraduate Society in University of London, *2008 – 2009*
- Class Representative of MSc pharmacy students in University of London, *2008 – 2009*
- President of the Kuwait University Pharmacy Students Association, *2005 – 2006*
- Representative of the student body on the central accreditation committee (ACPE accreditation) of the school of pharmacy, assigned by the dean, *2004 – 2006*
- Head of the Educational Committee in the Pharmacy Student Association, *2002 – 2004*
- Class Representative of the 2001 pharmacy student in Kuwait University, *2001 – 2006*

PROFESSIONAL AFFILIATIONS

- Member of the International Society for Pharmacoeconomics and Outcomes Research
- Member of the American Association for the Advancement of Science
- Member of the International Pharmaceutical Federation
- Member of the Kuwaiti Pharmaceutical Association
- Member of London International Development Centre
- Member of the ISPOR VCU student chapter
- Member of the Golden Key International Honour Society

SOFTWARE/COMPUTER SKILLS

Research software/instruments: SPSS, JMP, SAS, and STATA .

PERSONAL DETAILS

Date of Birth: January 12, 1984

Nationality: Kuwaiti

Marital Status: Married

Languages: Arabic (Native), English (Fluent)