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Examining racial differences in coronary heart disease mortality and acute myocardial infarction recurrence: a community study

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An abstract of
A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Epidemiology
2021

ABSTRACT

Examining Racial Differences in Coronary Heart Disease Mortality and Acute Myocardial Infarction Recurrence: A Community Study

By **Duygu Islek Yaras, MD, MPH**

Despite considerable improvements in the prevention of coronary heart disease (CHD) over the past decade, significant racial disparities still exist in CHD mortality. The factors driving these inequalities are not well understood. In this dissertation, we examined racial disparities in CHD mortality by focusing on three keys but understudied aspects: hospitalization after presenting to the Emergency Department (ED) for an acute coronary syndrome (ACS), out-of-hospital mortality, and acute myocardial infarction (AMI) recurrence and mortality.

We used data from the Health Care Cost and Utilization Project (HCUP) and the cohort and surveillance components of the Atherosclerosis Risk in Communities (ARIC) Study. In the first study, we examined the ED records of three states, Florida, New York and Utah and found that racial disparities exist in rates of hospitalization among patients who visit the ED and receive a discharge code for ACS. We further report that health insurance does not explain these racial differences. In the second study, we report large differences in fatal incident CHD by race, in contrast to non-fatal incident CHD. Black individuals die from CHD at about twice the rate of White individuals, and the excess in mortality is seen irrespective of where these events occur in or out of the hospital. As a mediator, income explained 39% of racial disparities in out-of-hospital fatal CHD.

In the third study, in four US communities' part of the ARIC surveillance, Black individuals had higher recurrent and incident AMI rates than White individuals. The magnitude of the racial differences in recurrent AMI rates were more pronounced than incident AMI rates.

Our findings suggest an important area for quality improvement in healthcare. Our findings also provide insight on the importance of targeting lack of healthcare coverage and other potential barriers to access to care in order to decrease racial differences in CHD death and foster health equity. Timely access to emergency care, including secondary prevention treatments, and effective preventive interventions could decrease the racial disparities in fatal CHD events. Insights from this dissertation can assist stakeholders in identifying opportunities to improve prevention policies in order to decrease CHD mortality for all Americans.

Examining Racial Differences in Coronary Heart Disease

Mortality and Acute Myocardial Infarction Recurrence:

A Community Study

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ACKNOWLEDGEMENTS

I thank my advisor and dissertation committee chair, Dr. Viola Vaccarino, for her invaluable support from the first day of my Ph.D. It was a pleasure and honor working with her. I thank my dissertation committee members Dr. Alvaro Alonso, Dr. Mohammed K. Ali, and Dr. Amita Manatunga for their great contributions to this work and their mentorship throughout my Ph.D. Also, I would like to thank all faculty and colleagues at the Epidemiology Department at Emory Rollins School of Public Health for their support and friendship.

There are two other people without whom this Ph.D. would not be possible. First, I would like to acknowledge Dr. Benal Inceer, retired Professor of Clinical Psychology, whom I met in the first year of my Medical School when I was eighteen and who has been my life-long mentor (and my “second mother”) since then. Second, I would like to acknowledge Dr. Belgin Unal, Professor of Epidemiology and Public Health at Dokuz Eylul University, who has been my mentor and friend since I started my residency program back in Turkey.

The last one and a half years of my Ph.D. have been under isolation due to the COVID-19 pandemic, and I would not have been this happy and productive without my nuclear family and road mate, Yusuf Samet Yaras.

As a first-generation college graduate in my family, all my degrees have been supported by scholarships, awards, or grants until now. From now on, I would like to continue my career with the aspiration of “giving back.” I am sure there are tens and thousands of students waiting for equal education opportunities all around the globe. I commit this Ph.D. to them.

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CHAPTER 1: INTRODUCTION

1.1. Background and study motivation

Despite considerable improvements in the prevention of coronary heart disease (CHD) over the past decade, significant racial disparities still exist in CHD mortality and the case fatality of acute myocardial infarction (AMI), which is a common and recurrent presentation of CHD. Black individuals are more likely to die from CHD and after an AMI compared to White individuals[1-7.] The factors driving these inequalities, however, are not well understood. Here we propose three research questions to examine racial disparities in CHD mortality by focusing on three keys but understudied aspects: initial presentation, out-of-hospital mortality, and AMI recurrence and mortality.

First, there might be racial differences in the probability of being hospitalized among individuals presenting to the emergency department (ED) with acute coronary syndromes. Black people might be less likely to be hospitalized even if they present to the ED with the same presentation, such as chest pain as a symptom of AMI or unstable angina, as their White counterparts. Equitable delivery of secondary prevention of coronary heart diseases might be dependent on the receipt of health care at the initial clinical encounter for CHD which, in many cases, is the emergency department prior to hospitalization for an acute coronary syndrome. Additionally, people who were not hospitalized and sent home may present again to the ED with more severe disease and suffer higher mortality. Twenty years ago, an analysis of a clinical trial in the US suggested that a missed diagnosis of acute coronary syndromes is more common in Non-white than in White people and is associated with higher mortality[8]. This could contribute to racial disparities in CHD mortality (especially out-of-hospital mortality) and might have implications for timely initiation of health care delivery.

Second, among people who are not yet aware that they have CHD, Black individuals might be more likely to die out-of-hospital more than their White counterparts. Previous studies have reported that the Black-White disparity in CHD incidence is most pronounced for fatal CHD and case-fatality of CHD, rather than for non-fatal CHD events[5]. This raises the question of whether the total Black-White differences in the incidence of fatal CHD could be explained by a higher rate of out-of-hospital CHD deaths in Black individuals compared to Whites. This question has rarely been examined in the published literature. Previous investigations were mostly limited to hospitalized events among Medicare beneficiaries, which primarily include individuals aged ≥65 years. This age restriction may mask race-related disparities since Black individuals tend to develop AMI and die from it earlier in life than White individuals[5]. Examining racial differences in out-of-hospital CHD mortality, considering socioeconomic factors, namely, income and education, might have implications for equal prevention and health care delivery for CHD.

Third**,** acute myocardial infarction is naturally recurrent, and AMI survivors are at increased risk of recurrent infarctions, which occur at an annual rate that is six times higher than in people of the same age without CHD. Among people who survived the first AMI, Black individuals might be more likely to die from a second AMI compared to White counterparts. Examining racial differences in the rates and mortality of recurrent AMI could contribute to our understanding of racial differences in total CHD mortality.

1.2. Objective and Specific Aims

The objective of this dissertation is to investigate racial differences in the rates of initial hospitalization and readmission for acute coronary syndromes, namely, acute myocardial infarction (AMI) and unstable angina, to investigate racial differences in the rates of out-of-hospital fatal CHD, and the rates of recurrent AMI. We hypothesize that, compared with White counterparts, Black individuals, Hispanic individuals, Asian individuals and individuals of some racial minority groups are less likely to be hospitalized when they initially present to the emergency department (ED) with AMI or unstable angina and more likely to return to the ED. We also hypothesize that, compared with White counterparts, Black individuals are more likely to die out-of-hospital, and more likely to die from a recurrent AMI if they survived the first AMI.

We address the following aims/hypotheses:

Aim 1: Examine whether there are racial differences in the rates of being sent home in individuals who present to the emergency department and receive a discharge code for an acute myocardial infarction or unstable angina and role of health insurance as a mediator

Hypothesis 1: Black individuals, Hispanic individuals, Asian and Pacific Islander individuals are more likely to be sent home when they present for the first time to the ED and receive a discharge code of AMI or unstable angina compared with White individuals.

Aim 2: Among US adults free of coronary heart disease at baseline, examine racial differences in the rates of out-of-hospital and in-hospital incidence of fatal CHD, nonfatal CHD and total CHD. Also, investigate the mediating effect of socioeconomic status (income) and possible confounding by cardiovascular risk factors on these outcomes. The analysis is performed in a cohort of 15,792 participants aged 45-64 years sampled from 4 US communities between the years 1987-2019.

Hypothesis 2: Black individuals have a higher out-of-hospital CHD mortality rate than Whites. The higher total mortality of CHD in Black versus White individuals can be largely explained by differences in higher out-of-hospital mortality in Black vs. White individuals. Income, as a socioeconomic factor, mediates the association of race and incident CHD outcomes.

Aim 3: Among US adults who survived a previous AMI, examine racial differences in the rates of AMI recurrence (primary outcome) and 28- and 365- day case- fatality of recurrent AMIs (secondary outcome) and compare the recurrent AMI rates with incident AMIs in the same population. The analysis is performed in a surveillance population of 470,000 residents aged 35-84 years in 4 US communities between the years 2005-2014.

Hypothesis 3: Black individuals have higher rates of AMI recurrence and case-fatality rates after a recurrent AMI compared to White individuals.

1.3. Data Sources

We used data from The State Emergency Department Databases (SEDD)[9] and The State Inpatient Databases (SID)[10] of the Healthcare Cost and Utilization Project (HCUP)[11] and also data from The Atherosclerosis Risk in Communities (ARIC) Study[12].

HCUP is sponsored by the Agency for Healthcare Research and Quality (AHRQ) and includes a collection of health care databases, software tools, reports developed through a Federal State-Industry partnership. The State Inpatient Databases[10] and The State Emergency Department Databases[9] are a part of the collection of the HCUP[11]. The two datasets include state-wide longitudinal hospital care data (emergency care and inpatient hospitalization) in the United States, with all-payer information. The participating organizations in HCUP agreed to release their State-specific files through the HCUP Central Distributor under the auspices of AHRQ. The individual State databases are in the same HCUP uniform format and they represent the 100% of records processed by AHRQ. State-specific files include data from the community hospitals, which include all nonfederal, short-term, general and other specialty hospitals, excluding hospital units of institutions. We used patient-level information available for three states (FL, UT, NY) for years 2008, 2011, 2014, and 2017. After combination of the patient-level data from these states and years, the analysis included Emergency Department visits of 51,022,910 patients.

ARIC is an epidemiologic study for investigating risk factors and clinical outcomes of CHD and the variation in CHD risk and outcomes among population subgroups and over time[12]. ARIC data were collected for the period 1987-2019 among residents aged 45-84 years in four communities in the US, and include two parts: the Cohort Component and the Community Surveillance Component[13].

The Cohort Component began in 1987. Each ARIC field center (Washington County, MD; Forsyth County, NC; Jackson, MS; and selected Minneapolis suburbs, MN) randomly selected and recruited a cohort sample of approximately 4,000 individuals aged 45-64 from a defined population in their community. A total of 15,792 participants received an extensive in-person evaluation, where sociodemographic and cardiovascular data were collected.

As part of the Community Surveillance Component, the four entire communities (approximately 470,000 men and women aged 35-84 years) were systematically surveilled to determine the community-wide occurrence of hospitalized AMI and CHD deaths[14]. Hospitalized AMIs were identified from electronic discharge lists obtained from all hospitals serving the 4 communities. Trained ARIC staff members abstracted medical records for possible events, and collected data on age, residence in the community, discharge code, event characteristics and procedures performed during the hospitalization[15].

1.4. Public Health Importance

Improving the cardiovascular health of all Americans and addressing disparities in cardiovascular health and health care access to reduce cardiovascular mortality in patients with CHD have been an emerging public health concern[16-20]. This study is essential for understanding the effects of race on morbidity, mortality, and initial presentation of acute coronary syndromes, CHD and recurrent AMI rates, which could help maximize effective primary and secondary prevention strategies in the community. This study should help clarify race-related inequalities in CHD incidence and mortality. The results of our study can assist stakeholders in identifying opportunities to improve prevention policies in order to decrease cardiovascular disease morbidity and mortality for all Americans and minimize inequalities.

CHAPTER 2: BACKGROUND AND LITERATURE REVIEW

2.1. Definition and Epidemiology of Acute Coronary Syndromes

Cardiovascular disease is the number one cause of hospitalization, health care utilization, and mortality in the US[21-23]. Among all major cause of deaths in the US, cardiovascular disease deaths accounted for the highest number for both men and women in 2017[24]. This figure was the same for the number of cardiovascular disease deaths among all US race-ethnic groups, including White, Black, Hispanic and Asian or Pacific Islander individuals[24]. Cardiovascular diseases include coronary heart disease, strokes, heart failures and other subtypes of cardiovascular diseases. Coronary heart disease deaths account for the highest percentage among all cardiovascular disease deaths[24].

Atherosclerosis is the main cause for coronary heart disease. Atherosclerosis forms when

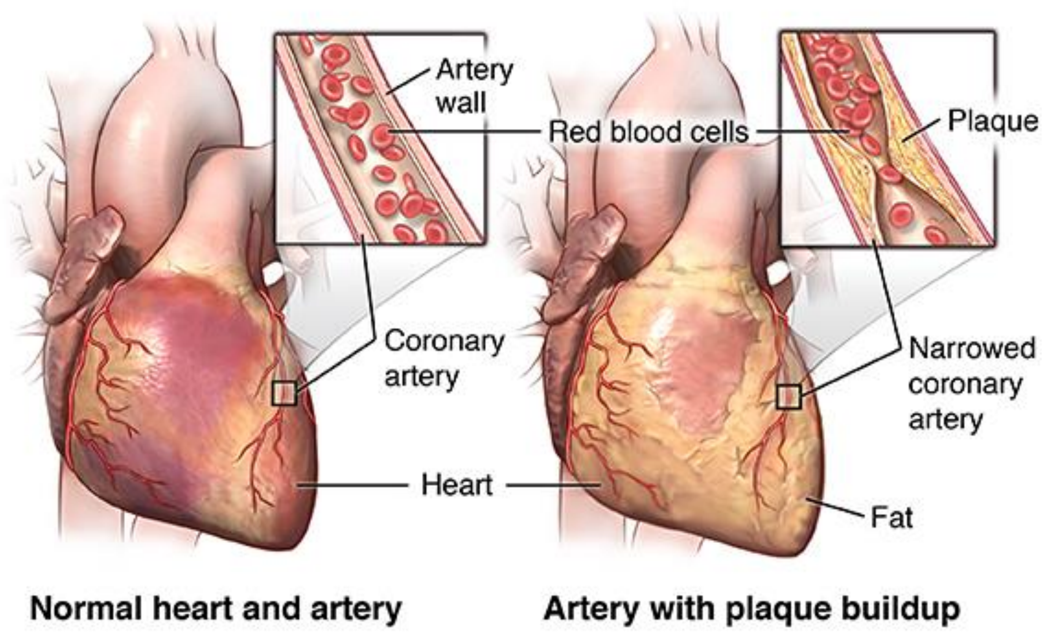

Figure 2-1 Illustration of plaque development inside the arteries in atherosclerosis[25].

fatty deposits called "plaque" accumulate inside the arteries. The "plaque" is made up of cholesterol, fatty substances, cellular waste products, calcium and fibrin, and causes thickening of the wall of the blood vessels and narrows the channel within the artery as seen in Figure 2-1. This affects the blood flow and even can partially or totally block blood flow through large- or medium-sized arteries in or leading to the heart resulting in "Coronary heart disease"[26]. Acute coronary syndromes account for a considerable proportion of cardiovascular diseases and include a range of thrombotic coronary heart diseases[27, 28]. Acute myocardial infarction (AMI) and unstable angina are subsets of acute coronary syndromes and coronary heart disease[29].

Acute coronary syndrome is a common health problem in the US population and it is likely to be the initial presentation of coronary artery disease in many patients. Approximately more than 800,000 individuals are expected to have acute coronary syndrome each year with 70% of them having non–ST-segment elevated subtype in the US[30]. The median age of patients presenting with acute coronary syndrome is 68 years (IQR:56 to 79) with a male-to-female ratio of approximately 3:2[31].

2.2. Symptoms and Initial Assessment of Acute Coronary Syndromes

Symptoms of acute coronary syndrome include chest pain, referred pain, nausea, vomiting, dyspnea and lightheadedness. Briefly, the initial assessment of chest pain or symptoms suggesting acute coronary syndrome are recommended to begin with an electrocardiogram (ECG) assessment within 10 minutes of presentation. If there is ST elevation in the ECG, the patient should be hospitalized. If there is no ST elevation, then assessment should continue with measurement of Troponin levels, physical examination and risk assessment. If cardiac troponin levels are positive, then the patient should be hospitalized. If not, then the assessment should still continue with repeated cardiac troponin measurement and serial ECGs three to six hours after symptom onset. If these are still not positive, then exercise treadmill testing, a stress myocardial perfusion study, or stress echocardiography are considered for further assessment[27, 32]. Accurate and timely hospitalization of people with acute coronary syndrome is an essential step in health care quality resulting in better health outcomes and lower mortality[27]. According to guideline recommendations, health care providers at the Emergency Department (ED) should risk-stratify patients with suspected acute coronary syndrome with risk scores based on the likelihood of acute coronary syndrome to decide on the need for hospitalization[33-35]. The diagram in Figure 2-2 summarizes the recommended algorithm for initial evaluation of patients who visit the Emergency Department with chest pain and suspected acute coronary syndrome.

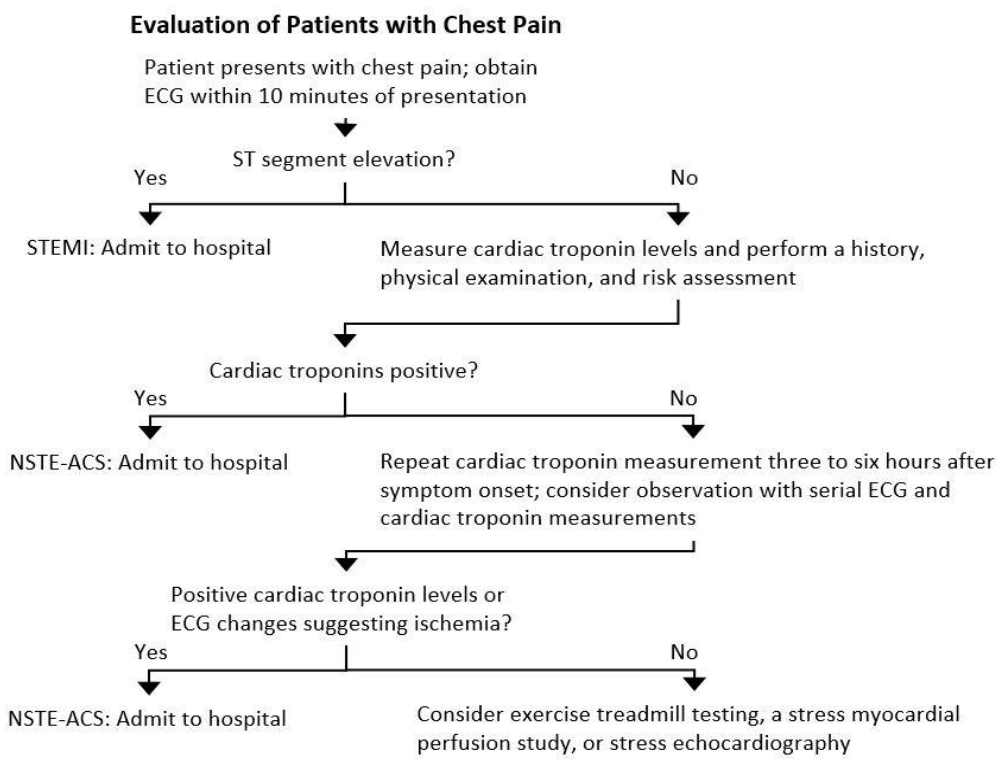

Figure 2-2 Algorithm for initial evaluation of patients with chest pain at the Emergency Department.

(Abbreviations: ECG: Electrocardiogram, STEMI: ST elevated myocardial infarction NSTE-ACS: Non-ST elevated acute coronary syndrome).

2.3. Acute Coronary Syndromes as a Diagnostic Challenge

Acute coronary syndrome diagnosis cannot always be made based on initial presentation even though the algorithm is appropriately followed[36, 37]. Some patients who have acute coronary syndromes might have atypical symptoms; and even may present without chest pain[27, 32, 38]. On the other hand, many patients who present with chest pain would not be diagnosed with an acute coronary syndrome. Non-cardiac causes of chest, back, or upper abdominal pain include pulmonary causes, such as pneumonia or gastrointestinal causes, such as gastroesophageal reflux[27]. Also, musculoskeletal causes, psychiatric disorders or other etiologies could be non-cardiac causes of chest pain[27]. Since not all patients with chest pain have acute coronary syndromes, differential diagnosis of acute coronary syndrome from noncardiac reasons can be a diagnostic challenge. On the other hand, having atypical symptoms of acute coronary syndrome may delay admission to hospital.

Previous studies have examined racial differences in symptom reporting and clinical presentation of acute coronary syndromes[27, 32, 38, 39]. In many of these studies, there were no meaningful differences by race for symptom presentation; Black and White patients reported a similar prevalence of chest pain, fatigue, or angina when they manifested both acute[40] and chronic coronary heart disease[41]. For example, Black and White patients were reported to express similar prevalence of chest pain and fatigue when they had coronary heart disease except that Black patients had more shortness of breath compared to Whites[41]. In parallel, another analysis reported no racial differences in the occurrence of acute myocardial infarction after adjustment for presenting signs and symptoms[40]. On the other hand, some studies suggested that Black patients could be more expressive about their symptoms compared to White patients even though they did not end up being diagnosed with acute coronary syndromes[39]. For example, a previous study suggested that even after adjusting for sociodemographic variables and other covariates, Black patients were about 60% as likely to have symptoms related to acute myocardial ischemia compared with White patients[39].

Overall, the previous literature suggests no evidence that Black patients have a lower likelihood of typical symptom presentation for acute coronary syndromes than White patients.

2.4. Racial differences in diagnosis and management of Acute Coronary Syndromes

There have been earlier studies of missed diagnoses of acute coronary syndromes in patients attending to the ED[8, 42]. One of these studies examined racial differences in missed diagnoses of acute coronary syndromes in the US in a large multicenter clinical trial twenty years ago[8]. The study reported that 5.8% of the Black patients were not hospitalized among patients meeting criteria for acute cardiac ischemia, as compared with 1.2% of the White patients, a rate that was more than four times as high among Non-white patients as among White counterparts[8]. The findings of this study suggest that there are racial differences in hospitalization rates in patients who admit to the ED with symptoms and signs suggesting acute coronary syndrome. However, the data of this study were collected twenty-seven years ago; thus, the findings may not reflect the current era. Also, since this study used data from a clinical trial that included patients from 10 hospitals in the US, the findings might not be generalizable to the whole US population.

Findings from other studies also suggest that missed diagnosis of acute coronary syndrome at the ED do occur. For example, in a study among Medicare beneficiaries, 10,093 Medicare beneficiaries were reported to die annually from atherosclerotic heart disease or myocardial infarction within seven days of discharge from the ED although their records did not indicate any life-threatening diagnosis[42].

Some previous studies investigated implicit racial biases which could impact the decisions of health care providers. For example, a systematic review summarized evidence of whether implicit racial bias exists among health care professionals and whether this is associated with health care outcomes. The results suggested that there is implicit racial bias among health care providers and this has a negative impact on patient–provider interactions, treatment decisions, treatment adherence, and patient health outcomes[43]. Another systematic review examined the same question in an ED setting, and reported that regardless of specialty, many physicians showed an implicit preference for White patients although this bias did not impact the physicians' clinical decision making[44]. Notably, these systematic reviews included a small number of studies, and might be inadequate to draw accurate conclusions on existing implicit racial biases among physicians.

Several other studies reported racial differences for "time to treatment" among patients who were hospitalized for myocardial infarction, where "time to treatment" was longer for Black patients compared to their White counterparts even after adjustment for clinical and sociodemographic variables[45-49]. However, the focus of these studies was racial differences 'after' hospitalization. None of these studies examined potential racial disparities at the time of the presentation to the ED.

Overall, the findings of these previous studies provide insights to raise the question whether there might be racial differences in hospitalization rates in patients who arrive to the ED with acute coronary syndromes. Black people might be less likely to be hospitalized even if they present to the ED with a similar presentation as their White counterparts. Timely hospitalization is a critical step in acute coronary syndrome treatment[27], therefore, examining racial differences in current hospitalization rates among those presenting to the ED using more extensive population data is crucial to explain CHD mortality differences between Black and White individuals. Examining the racial differences in hospitalization rates at the ED could contribute to our understanding of overall mortality differences in coronary heart disease by race.

2.5. Racial Differences in Out-of-Hospital Mortality of Coronary Heart Disease

Over the past decades, many studies reported significant disparities by race in CHD incidence and mortality, with Black individuals having worse outcome[1-7]. Previous papers examining trends in AMI hospitalization rates between 1999 and 2011 also reported lower declines in Black individuals than White individuals among Medicare fee-for-service beneficiaries[2, 23].

There have been efforts to explain these differences, but results have been inconsistent. Some studies suggested that traditional cardiovascular risk factors could explain race differences in CHD incidence[4]. For example, an analysis from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study suggested that race differences in CHD case fatality can be explained by CHD risk factors[50]. In another analysis that combined data from REGARDS, the Cardiovascular Health Study, and publicly available data from the ARIC cohort, race differences for fatal CHD disappeared after adjustment for CVD risk factors[5]. However, previous analyses from Medicare, REGARDS, and ARIC often used data collected more than 10 years ago, thus possibly missing recent trends in CHD rates.

Other studies reported lower rates of secondary prevention treatments, such as revascularization procedures in Black individuals compared to Whites counterparts[51-58]. However, these previous investigations were mostly limited to hospitalized events among Medicare beneficiaries, which primarily included individuals aged ≥65 years. This age restriction could mask race-related disparities since Black individuals tend to develop AMI and die from it earlier in life than White individuals[5].

A recent study reported no difference in total CHD incidence among Blacks vs. White individuals during an 11-year follow-up, up to 2007, with analysis from publicly available ARIC cohort data[5]. However, in the same study, Black men showed a higher incidence of fatal CHD than White men as well as higher case fatality rates[5]. These results could be explained by a higher rate of out-of-hospital CHD deaths in Black individuals, especially in Black men, if a larger proportion of fatal AMI events occur before reaching the hospital in Black compared with White people. Differences in healthcare-seeking behavior could play a role, specifically for young Black men who have lower access to health care than their White counterparts[7, 59-61]. However, up to now, race differences in out-of-hospital CHD deaths have rarely been examined in studies investigating differences in CHD incidence by race, including the ARIC study or any other prospective cohorts of CHD incidence. Examining racial differences in out-of-hospital CHD mortality, and considering possible mediating effects of socioeconomic factors which may drive access to healthcare, especially income, should inform efforts to deliver equitable prevention strategies for CHD to reduce disparities.

2.6. Racial Differences in the Rates of Recurrent Myocardial Infarction

Survivors of an AMI are at increased risk of recurrent infarctions, which occur at an annual rate that is six times higher than in people of the same age without CHD. Previous studies suggest that the 5-year mortality rate following an AMI is higher in Black patients than White patients[62]. Furthermore, between 2001 to 2003 and 2007 to 2009, age-adjusted mortality after AMI has decreased among White males, but no changes were reported for White females or Black males or females[30].

Part of the AMI outcome differences by race could reflect a higher reinfarction rate among Black than White patients. Among people who survived a first AMI, Black individuals may be more likely to experience a recurrent AMI and to die from it compared to White counterparts. Few studies have examined race-related differences in AMI recurrence. Most previous studies of race differences in AMI used administrative databases based on discharge diagnosis codes, which may be inaccurate and may have introduced bias[1, 4]. Examining racial differences in the incidence and mortality of recurrent AMI could contribute to our understanding of racial differences in total CHD mortality.

CHAPTER 3: METHODS

3.1. Study 1

3.1.1. Dataset - HCUP

To address Aim 1, we used the State Inpatient Databases (SID)[10] and State Emergency Department Databases (SEDD)[9] of the Healthcare Cost and Utilization Project (HCUP)[11]. HCUP includes a collection of health care databases, software tools, and reports developed through a Federal State-Industry partnership. The SID[10] and the SEDD[9] include state-wide hospital care data (emergency care and inpatient hospitalization) for three states, Florida, Utah and New York, in the United States, with all-payer information, including but not limited to Medicare, Medicaid, private insurance, self-pay, or those billed as 'no charge', for the years 2008, 2011, 2014, and 2016/2017.

The SEDD capture discharge information on all emergency department visits that do not result in an admission. Information on patients initially seen in the emergency department and then admitted to the hospital is included in the SID. The SID contain the universe of the inpatient discharge abstracts from participating States. To enumerate all emergency department visits, we combined the SEDD discharges with SID discharges that originate in the emergency department.

Data from community hospitals, which are defined as "all nonfederal, short-term, general and other specialty hospitals, excluding hospital units of institutions" are included in the datasets. Among community hospitals, data from academic medical centers and specialty hospitals such as obstetrics, gynecology, otolaryngology, short-term rehabilitation, orthopedic, and pediatric hospitals are also included to the HCUP. Noncommunity hospitals such as Federal hospitals (e.g., Veterans Affairs, Department of Defense, and Indian Health Service hospitals) are not included in the datasets. The individual State databases are in the same HCUP uniform format and represent 100% of records processed by AHRQ. However, the participating data organizations control the release of specific data elements. Therefore, some community hospitals may not be included in the SID or SEDD if their data were not provided by the data source. Data organizations participating in HCUP have agreed to release their SEDD and SID files through the HCUP Central Distributor under the auspices of AHRQ. Both the SEDD and SID data are translated into a uniform format by HCUP to facilitate multistate comparisons and analyses. Researchers and policymakers previously used the SEDD and SID to examine and identify State-specific trends in emergency department and inpatient health care utilization, access, charges, and outcomes associated with these health care utilizations. Uses are limited to research, analysis, and aggregate statistical reporting.

3.1.2. Definition of Variables

Exposure: The self -reported "race" variable is available at the patient level for the three states. We compared the outcomes of Black, Hispanic, Asian/Pacific Islander patients to the outcomes of White patients.

Outcome: The outcome variable is rates of being sent home among patients who visited the ED in the states of FL, UT, NY in years 2008, 2011, 2014, and 2016/2017, with a first clinical presentation of acute coronary syndrome. This is determined with ICD-9 and ICD-10 discharge codes for acute myocardial infarction and unstable angina. We were able to isolate the initial diagnosis by excluding those who have chronic CHD using the relevant ICD 9 or ICD 10 codes.

Covariates: Variables including age, sex, median household income quartile, urban/rural location, and health insurance status are included in the analysis. Age, sex and health insurance status was provided by HCUP at individual level. The median household income quartile and urban/rural location were defined and reported by HCUP based on the patient's ZIP code. The health insurance status is classified as Medicare, Medicaid, private insurance, self-pay, or other. The "median household income quartile" is defined based on a quartile classification of the estimated median household income for the state. The cut-offs for the quartile designation for each state is determined using ZIP code-demographic data. The assignment of median household income for a particular patient is, therefore, determined based on the median income of the patient's ZIP code. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. The "urban/rural location" are classified based on the patient's ZIP code. HCUP uses a classification scheme that distinguishes urban ZIP Codes by population size and characterizes rural ZIP Codes by their population and their association with larger urban areas. Based on this definition, we classified the patient's residency location as urban and rural. Cardiovascular risk factors include history of hypertension, diabetes, hypercholesterolemia, and obesity based on the ICD-9 and ICD-10 codes for diagnosis.

3.2. Study 2

3.2.1. Dataset - ARIC cohort

To address Aim 2, we used data from the cohort component of the Atherosclerosis Risk in Communities Study (ARIC). ARIC is a prospective epidemiologic study conducted in four US communities (Washington County, MD; Forsyth County, NC; Jackson, MS; and selected Minneapolis suburbs, MN)[28]. The Cohort Component began in 1987. Each ARIC field center randomly selected and recruited a cohort sample of approximately 4,000 individuals aged 45-64 from a defined population in their community. A total of 15,792 participants (27% Black and 73% White) received an extensive in-person evaluation, where sociodemographic and cardiovascular data were collected. Participants were reexamined in person every three years for the first nine years (1990-92, 1993-95, 1996-98), with additional exams in 2011-13, 2016-17, and 2017-18. Also, participants were contacted by phone yearly (biannually since 2012) to update contact information and assess their health status. At visit 1 (baseline, 1987–1989), trained interviewers administered a questionnaire to collect data on demographic characteristics, medical history, medication use, and smoking status. Information on years of education and household income was also collected. Since very few Non-White and Non-Black participants participated in ARIC (n=48), we excluded them from the analysis. After excluding individuals who had prevalent coronary heart disease at baseline (n=765), our analysis included 14,979 ARIC participants at baseline.

Follow-up is ongoing with adjudicated endpoint data through 12/31/2019 currently available. Procedures applied at all study centers were approved by all institutional review boards, and informed consent was obtained from all participants.

3.2.2. Definition of Variables

Exposure: Self-reported race at visit one is the exposure variable and was classified as "Blacks" and "Whites."

Outcomes: In-hospital and out-of-hospital mortality for CHD were the primary outcome variables. CHD events were ascertained by surveying discharge lists from local hospitals and death certificates from state vital statistics, as well as follow-up calls identifying hospitalizations and deaths during the previous year. Deaths at home or any other undefined place were defined as out-of-hospital deaths. Additional information was sought from the next of kin and other informants, certifying doctors and family physicians, and coroners or medical examiners for out-of-hospital deaths. A panel of physicians reviewed and adjudicated all events using established criteria[63, 64].

Covariates: Socioeconomic variables included income level and education. Level of education was categorized as “high school graduate or less” and “vocational school, college, and graduate school.” Income was categorized as annual income “less than 35,000” and “35,000 and over”. Cardiovascular risk factors include BMI, prevalent hypertension, prevalent diabetes, smoking status, and total cholesterol level which were measured at Visit 1. BMI was calculated as weight (in kilograms) divided by the square of height (in meters). Prevalent hypertension was defined as average systolic blood pressure of at least 140 mm Hg or average diastolic blood pressure of at least 90 mmHg (after 3 seated measurements of blood pressure taken by a certified technician using a random-zero sphygmomanometer after 5 minutes of rest) or self-reported diagnosis of hypertension by a physician, or use of hypertension medication. Prevalent diabetes was defined as a fasting glucose level of at least 126 mg/dL, or a casual blood glucose level of at least ≥200 mg/dL, or self-reported diagnosis of diabetes by a physician, or treatment for diabetes. At each visit, fasting glucose levels were measured by the modified hexokinase/glucose-6 phosphate dehydrogenase method. Fasting plasma total cholesterol concentration was assessed by enzymatic procedures and is included as continuous variables in the models. Smoking status is classified into three categories: never, former, or current smoker.

3.3. Study 3

3.3.1. Dataset - ARIC surveillance

To address Aim 3, we used data from the Community Surveillance component of the ARIC study. As part of the Community Surveillance component, four entire communities (approximately 470,000 men and women aged 35-84 years) have been systematically surveilled every year to determine the community-wide occurrence of hospitalized AMI and CHD deaths for years 2005-2014 [65]. ARIC Surveillance data includes 23% Blacks and 76% Whites.

Hospitalized AMIs were identified from electronic discharge lists obtained from all hospitals serving the four communities. Trained ARIC staff members abstracted medical records for possible events and collected data on age, race, sex, residence in the community, discharge codes, comorbidities, medications, event characteristics, procedures performed during the hospitalization, and mortality [15, 66].

3.3.2. Definition of Variables

Exposure: "Race" was the exposure variable. It was abstracted from medical records and was categorized as Black individuals vs. White individuals.

Outcomes: The rates of AMI recurrence are the primary outcome. Initial and recurrent AMI was defined as "definite or probable AMI" following standard ARIC definitions[12]. Information on chest pain, level of cardiac biomarkers (total creatinine phosphokinase, creatinine phosphokinase-myocardial band, lactate dehydrogenase, and troponin) and history of AMI and other cardiovascular comorbidities was abstracted from the medical records. Additionally, copies of up to three ECGs of the patients were sent to the University of Minnesota Electrocardiographic Reading Center for classification using the Minnesota code[67]. The AMI diagnosis was determined using a standardized computer algorithm based on chest pain, cardiac biomarkers, and electrocardiograms[64].

Covariates: The covariates available for this analysis included age and sex. We also used data on health insurance status, history of hypertension, history of diabetes, and smoking, abstracted from medical records to describe the initial characteristics of the population with a recurrent AMI.

3.3.3. Modeling Approach

For all aims, the initial models include only age and sex as covariates. **For Aim 1,** we used Generalized estimating equation models to compare racial differences in rates of being sent home among patients who visited the ED with a first clinical presentation of acute coronary syndrome. **For Aim 2,** we constructed Cox proportional hazard models to compare out-of-hospital mortality between Black and White participants, and logistic regression to compare in-hospital mortality. **For Aim 3,** we used Poisson regression to examine racial differences in AMI recurrence rates (primary outcome) and contrasted these rates with those of incident AMI. Models account for the stratified sampling design of the surveillance data and were weighted by the inverse of the sampling probability. Standard errors were computed taking into account the sampling[15].

3.3.4. Mediation Analysis

For aims 1 and 2, we applied mediation analysis to examine whether the socioeconomic factors partially or fully mediate racial differences in outcomes[68]. The mediation analysis methods allow considering the possible interactions between race and socioeconomic variables[68, 69]. **For Aim 1,** we considered mediating effects of health insurance status for hospitalization rates using inverse probability weighting. **For Aim 2,** we applied the mediation analysis using Marginal Cox Structural Models separately for the outcomes of out-of-hospital CHD mortality, in-hospital CHD mortality, and total CHD mortality. We used the inverse probability weighting method to examine the mediating effects of income for out-of-hospital, in-hospital, and total CHD mortality.

CHAPTER 4: RACIAL DIFFERENCES IN HOSPITALIZATION RATES OF PATIENTS WHO RECEIVE A DIAGNOSIS OF ACUTE CORONARY SYNDROME IN THE EMERGENCY DEPARTMENT

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4.1. Abstract

4.1.1. Background

Previous studies reported racial differences in missed diagnosis of acute coronary syndromes in patients visiting the Emergency Department (ED). We examined whether there are racial/ethnic differences in rates of being sent home in patients who visited the ED and received a diagnosis of acute myocardial infarction (AMI) or unstable angina, and whether having health insurance plays a role.

4.1.2. Methods

We examined 51,022,910 discharge records of ED visits in Florida, New York, and Utah in years 2008, 2011, 2014, 2016/7, using state-specific data from the Healthcare Cost and Utilization Project (HCUP). We identified ED admissions for AMI or unstable angina using the International Classification of Disease (ICD) ninth or tenth revision discharge codes. We excluded those with chronic coronary heart disease (CHD) to examine incident events only. We used generalized estimating equation models to compare rates of being sent home across race/ethnic groups including White, Black, Hispanic, and Asian/Pacific Islander patients. We used Poisson marginal structural models and inverse probability weighting to estimate the mediating role of health insurance status on the associations.

4.1.3. Results

Among 204,908 patients with a discharge code of AMI, comparing Black to White patients the incident rate ratio for being sent home was 1.42 (95 % CI, 1.22-1.65). The same figure was higher but not statistically significant for Hispanic patients compared with Whites. The rates of being sent home with a discharge code of AMI were similar in Asian or Pacific Islander patients compared to White patients (incidence rate ratio [IRR]= 1.06, 95 % CI, 0.69-1.64). In patients below 55 years of age, however, the corresponding figure was higher among all racial groups compared to White patients, but it was highest among Hispanic vs. White (IRR=1.99, 95 % CI, 1.72 - 2.29) and among Black vs. White patients (IRR=1.90, 95 % CI, 1.66 - 2.17). Health insurance status did not play any role as a mediator in these associations.

4.1.4. Conclusion

Racial disparities exist in rates of being sent home among patients who visit the ED and receive a discharge code for acute coronary syndrome. Health insurance does not explain these racial differences; other possible causes need to be investigated.

4.2. Introduction

In many patients, acute coronary syndrome (ACS) is the initial presentation of coronary artery disease. More than 800,000 individuals have acute coronary syndrome (ACS) each year in the US[24]. Immediate hospitalization of people with ACS is an essential step in the receipt of timely treatment, resulting in better health outcomes[27]. According to guideline recommendations, health care providers at the Emergency Department (ED) should risk-stratify patients based on the likelihood of ACS to decide on the need for hospitalization,[33-35] as timely hospitalization is a critical step in ACS treatment[27].

Previous studies reported missed diagnoses of acute myocardial infarction (AMI) in the ED[8, 42, 70-72], drawing attention to diagnostic errors in health care delivery[42, 73]. More than twenty years ago, one of these studies suggested that the risk of being sent home with an ACS was more than four times as high among Non-white patients as among White counterparts[8]. Failure to hospitalize patients with ACS could contribute to racial disparities in coronary heart disease (CHD) mortality, especially out-of-hospital mortality, and might have implications for timely initiation of health care delivery. However, although there is extensive literature on missed diagnoses in the ED[8, 42, 70-72], on avoidable admissions to hospitals and on overuse of the emergency care[74-76] , no previous study examined disparities in hospitalization rates among the patients who received a discharge code of ACS in the ED. The lack of investigation in this area may reflect the assumption that all patients with an ED discharge diagnosis of ACS would be hospitalized, and that if they are not, this would signify coding errors. On the other hand, if systematic differences are found by race, this would point to health equity issues. Examining racial differences at the population level in being hospitalized after presentation to the ED with ACS may illuminate disparities previously unknown in health care delivery.

In this study, we aimed to examine whether there are racial differences in the rates of being sent home among individuals who present to the ED and receive a discharge code of AMI or unstable angina. Also, since health insurance coverage can be an important determinant of access to health care[77], we examined the role of health insurance as a mediator in these associations. We hypothesized that Non-White patients are more likely to be sent home when they present for the first time to the ED and receive a diagnosis of AMI or unstable angina compared with White individuals. We further hypothesized that health insurance, as a mediator, drives racial disparities in these hospitalization rates.

4.3. Methods

4.3.1. Study population

We analyzed data from the State Inpatient Databases (SID)[10] and the State Emergency Department Databases (SEDD)[9] of the Healthcare Cost and Utilization Project (HCUP)[11]. HCUP includes a large collection of health care databases, software tools, and reports in the United States developed through a Federal State-Industry partnership[11]. Data organizations participating in HCUP have agreed to release their SEDD and SID files through the HCUP Central Distributor under the auspices of the Agency for Healthcare Research and Quality (AHRQ). The databases include all-payer, encounter-level information from community hospitals and have been widely used in previous studies[78-81]. The individual State databases are in the same HCUP uniform format and represent 100% of records processed by AHRQ. The participating data organizations control the release of specific data elements. Therefore, some community hospitals may not be included in the SID or SEDD if their data were not provided by the data source.

We examined data from Florida, New York, and Utah for the years 2011, 2014, 2016/2017 and additionally 2008 for Utah. We chose these states because they are populous, large, geographically distributed, and provided data at the patient level. To link emergency department visits with subsequent hospitalizations, we merged the SEDD (emergency department discharge files) with the SID (inpatient discharge files) using unique encrypted patient numbers at the patient level.

In total, we examined 51,022,910 patient-level ED discharge records. Among these records, there were 222,619 records with a discharge code of AMI and 55,830 records with a discharge code of unstable angina. We first identified and excluded duplicate records due to transfers from one hospital to another of the same patient, (n=14,738) to isolate the initial ED visits for each patient[82]. From the remaining 263,711 patient-level visits for an AMI or unstable angina, we excluded records of patients who left the ED against medical advice (n=2,500), who died (n=1,252), who had chronic CHD (n=3,150), who were under law enforcement (n=22), who were missing discharge status (n=50), or were missing the race variable (n= 2,742), who had duplicate records (n=4,464), or were of unspecified minority groups (n=12,570). We identified patients who had chronic CHD using the ICD 9 codes 412, 414.8, and 414.9, and the ICD 10 codes I25.2 and I25.9. After these exclusions, 192,938 patients were discharged from the ED with a discharge code of AMI and 42,998 patients were discharged with a code of unstable angina. Figure 4-1 summarizes the selection of the study population.

4.3.2. Definition of race and outcomes

The race variable used in this study was derived from the HCUP database and included four groups: White, Black, Hispanic, and Asian/Pacific Islander. Information on race and ethnicity was provided by the state-level databases and was combined by the HCUP into a single race variable, giving ethnicity precedence over race. For example, if a patient was of Black racial group and Hispanic ethnicity, then he/she was classified as a member of the "Hispanic" racial group. This classification was used in previous analyses using HCUP data[79].

The outcome variable was the rates of being sent home among patients who visited the ED and had a primary discharge code for AMI and unstable angina. To identify patients who had a discharge diagnosis of AMI, we used the ICD-9 codes of 410.0 through 410.9 as the primary discharge code for years 2008, 2011, and 2014, and ICD-10 codes of I21.0-I21.02, I21, I21.1-I21.4, I21.11, I21.21, I21.29, I24.8, I21A, I21.A1, and I21.A9 for years 2016 and 2017. For identification of unstable angina, we used the primary ICD-9 discharge codes of 411.1, 411.8 and 411.89 for years 2008, 2011, and 2014 and ICD-10 discharge codes of I25.110, I12.00, and I12.0 for years 2016 and 2017.

4.3.3. Definition of covariates

We included "health insurance status" as a mediator to the models. In mediation analysis, we considered those who had Medicare, Medicaid, private and other insurance as "insured" and those who self-paid as "uninsured". Other covariates included age, sex, median household income quartile, and urban/rural location. The median household income quartile and urban/rural location were defined and reported by HCUP based on the patient's ZIP code. We also examined the ICD-9 and ICD-10 codes for obesity, metabolic syndrome, hypertension, diabetes, and hypercholesterolemia among patients with acute coronary syndromes. However, the prevalence of these comorbidities in the study population was much lower than expected. Therefore, we did not include these factors in the models to avoid introducing bias to our estimates.

4.3.4. Statistical Analysis

First, we tabulated the distributions of baseline sociodemographic factors of patients sent home and those hospitalized with a diagnosis of AMI or unstable angina at their ED visit, overall and by race. Next, we computed rates and 95% confidence intervals (CI) of being sent home with a discharge code of AMI and unstable angina by race.

In an initial model (Model 1) we used generalized estimating equations (GEE) which accounted for clustering of patients within hospitals, using a Poisson distribution, to compare the rates of being sent home (without being hospitalized) with a diagnosis of AMI or unstable angina between White and Non-White patients. Model 1 provided incident rate ratios, adjusted for age, sex, and state and "diagnosis" (either AMI or unstable angina). Next, we did a mediation analysis, where we hypothesized that health insurance is a mediating factor on the pathway between race and being sent home after the ED visit**.** We used inverse probability weighting to avoid violation of a major mediation analysis assumption,[69] which requires that there should not be any mediator-outcome confounders affected by the exposure[69]. Therefore, we constructed a Poisson marginal structural model (Model 2) which allowed to use inverse probability weighting[83, 84] to examine the mediating role of health insurance. As seen in Figure 4-2**,** since race, as the exposure, is an upstream variable, there could be a path (path 1) from race to income, urban/rural residence, and state, which could be confounders of the association between health insurance and outcome of being sent home (through paths 2 and 5). Therefore, simply adjusting for all covariates in the models could result in biased results for mediation analysis. The use of methods such as inverse probability weighting, which allows separating the effect of health insurance from the effect of other covariates, is recommended to get more accurate estimates[83, 85]. We additionally created a Poisson model (Model 3) that adjusts for all covariates except health insurance to compare our results with Model 2. Furthermore, we examined the results by age group, by stratifying the data to 'below 55 years of age' and '55 years and over' using the same modelling approach. Finally, to investigate possible consequences of an improper ED discharge, we examined the rates of readmission within 30 days among those sent home after their initial discharge from the ED with a diagnosis of AMI or unstable angina.

In a sensitivity analysis, we repeated the mediation analysis by reclassifying those who had "Medicaid" as "uninsured" since patients with Medicaid tend to be a socioeconomically disadvantaged group. Also, to address a possible misclassification of patients with chronic CHD as being mistakenly assigned a discharge code of AMI or unstable angina in the ED, we examined racial differences among those excluded due to having a code of chronic CHD.

A previous clinical trial reported sex differences in the rate of missed diagnoses of AMI in the ED among patients below 55 years of age[8]. Therefore, in a secondary analysis, we stratified by age (below 55 years of age and 55 years and older).

In this study, we used administrative data with synthetic person identifiers. No human subjects were involved and no IRB approval was required. All data cleaning and analysis methods used were consistent with the Health Insurance Portability and Accountability Act (HIPAA) privacy rules. All analysis was performed with SAS 9.4 (Cary, NC).

4.4. Results

4.4.1. Characteristics of the study population

Of the 192,938 patients who received a discharge code of AMI in the ED, 4,117 (2.1 %) were sent home. Of the 42,998 patients who received a discharge code of angina, 12,513 (29.1 %) were sent home. The patients who were sent home with a discharge code of AMI or unstable angina were less likely to be White, were younger, and had less health insurance coverage than those who were hospitalized. Income distribution and location of residence, however, were similar (Table 4-1). Results were fairly consistent when examined within race (Table 4-4 and Table 4-5).

4.4.2. Racial differences in rates of being sent home after receiving a discharge code of ACS

Among the total of 235,936 patients who visited the ED and received a discharge code of ACS (either AMI or unstable angina), the proportion being sent home was 11.6 % among Black patients, which was the highest proportion of all racial groups. The corresponding figures were 5.9 % among White patients, 8.9 % among Hispanic patients, and 8.6 % among Asian or Pacific islander patients (Table 4-2). In age and sex-adjusted GEE models the incidence rate ratio (IRR) for being sent home was 1.26 (95% CI, 1.18 - 1.34) in Black patients, and 1.23 (95 % CI, 1.15 - 1.32) in Hispanic patients compared with White patients (Model 1, Table 4-2). Differences were smaller and nonsignificant among Asian or Pacific Islander patients. When AMI and unstable angina were examined separately, a larger proportion of patients in all race groups were sent home after a diagnosis of unstable angina than after a diagnosis of AMI, but differences for Black patients as compared with White patients were larger for AMI than for unstable angina (Table 4-2). Health insurance status did not play any role as a mediator in the association of race with being sent home in the entire sample and among AMI and unstable angina subgroups (Model 2, Table 4-2), and results remained consistent after health insurance was removed from the model (Model 3, Table 4-2).

In patients below 55 years of age, the rate of being sent home with an AMI was higher among all racial groups compared to White patients (Figure 4-3). The magnitude of incident rate ratios was especially high among Hispanic vs. White patients (IRR=1.99, 95 % CI, 1.72 - 2.29) and among Black vs. White patients (IRR=1.90, 95 % CI, 1.66 - 2.17). In contrast, among patients 55 years and older, there were no racial differences in rates of being sent home after an ED diagnosis of AMI. For unstable angina, however, results were similar by age (Figure 4-3). Again, in mediation analysis, health insurance did not play any role as a mediator in these associations.

In sensitivity analyses, after we reclassified those who had “Medicaid” as “uninsured” health insurance continued to have no role in mediating the association of race with being sent home after the ED visit. There were no racial differences in hospitalization rates among 3099 patients who visited the ED and were excluded from our analysis due to having a diagnosis of chronic CHD. In secondary analyses examining sex differences, the rate of being sent home was 1.57 (95% CI: 1.35, 1.82) times higher in women vs. men below 55 years of age in patients with a discharge code of AMI. Sex differences were attenuated but were still significant among patients who received a discharge code of unstable angina. There were no sex differences above 55 years of age (Table 4-6).

Among the patients sent home with a discharge code of ACS in their initial visit to the ED, 412 patients (2.5 %) retuned to the ED within 30 days and received again a discharge code of ACS. This proportion was higher in Black patients (3.2 %) than other groups (2.6 % for

Hispanic patients, 2.4 % for Asian/ Pacific Islander and 2.1 % for White patients). Among Black patients, 61.1 % of those returning to the ED and receiving a discharge diagnosis of ACS were ultimately hospitalized, whereas the corresponding hospitalization rates were lower in the other groups, especially among White patients (Table 4-3).

4.5. Discussion

In this study, Black and Hispanic patients were more likely to be sent home with a discharge code of AMI or unstable angina after their visit to the ED compared to White patients. In contrast, differences were small in Asian patients vs. White patients. However, among patients below 55 years of age, all racial groups were more likely to be sent home after receiving an ED diagnosis of ACS than their White counterparts. Health insurance had no role as a mediator in explaining these associations.

Our results support and expand those of previous clinical trials, which reported that approximately 2% of patients with AMI were sent home from the emergency department (ED)[8, 72]. Our findings also agree with previous data suggesting that patients with AMI were more likely not to be hospitalized if they were Non-White[8]. However, in these previous studies, patients were sent home due to a missed diagnosis. A new finding of our study is that this race-based disparity extends to patients who received a discharge code of an ACS, suggesting that the diagnosis was not missed. Our results illuminate a potential inequity in health care delivery that was not described before, which has clinical and public health significance. While absolute differences in hospitalization rates by race in our study may seem small, since more than 800,000 individuals are estimated to have an ACS each year in the US[24], an absolute difference of 5.7 % between Black and White patients (Table 4-2) would translate, on a population level, to approximately 45,000 more Black patients being sent home with an ACS, compared to White patients each year.

One might argue that variability in health care and coding patterns across hospitals, rather than patients' race, may be the driving factors in the differences in missed hospitalizations we describe[86]. Previous studies suggested that the proportion of missed diagnoses in patients with AMI varied across the hospital's academic status[87], and the patient distribution by race is known to vary by hospital[88, 89]. While we did not have information on hospital characteristics, we accounted for the clustering of patients within hospitals in our models. Therefore, it is unlikely that differences in hospital academic status explain our findings.

Another possible explanation may rely on errors in coding of AMI in ED discharge records, as the tendency of overusing a code of AMI has been reported already many decades ago[90]. However, the validity of an AMI code as a principal diagnosis has been shown to be high in administrative databases in more contemporary studies[91-93], which suggests that our findings cannot be entirely explained by coding errors of AMI. Furthermore, if miscoding were an issue, it would likely not be differential by race, and thus it would result in attenuation, rather than overestimation, of the race differences we found. Our finding that Black patients had the highest rate of returning to the ED within 30 days with a repeat discharge code of ACS (while White patients had the lowest rate) argues against coding errors. More Black patients also were ultimately hospitalized at their second ED visit. This suggests that more hospitalizations for ACS were truly overlooked for Black patients than other groups at their first ED encounter.

A third explanation could be related to implicit racial biases in the clinical decision-making of health care providers[43, 44, 94]. A systematic review of studies of implicit racial bias among ED health care professionals reported that, regardless of specialty, physicians tended to show an implicit preference for White patients, although this bias did not impact the physicians' clinical decision making[44]. We did not have data on physician characteristics, such as racial/ethnic background, age, or years of practice. Therefore, it is not possible to draw conclusions on physician implicit bias from our findings. Prior studies have also suggested that low-income patients are more likely to refuse care even when offered, resulting in lower admission rates to hospitals with ACS[95]. It was inferred that this could be due to poor financial capability or different expectations from the medical system. However, since we excluded the patients who left the ED against medical advice, and also adjusted for income quartiles in some of our models, these factors are unlikely to explain our results.

It is also unlikely that differences by race in clinical presentation of ACS play a role in our findings. First, most previous investigations of racial differences in symptom reporting and clinical presentation of ACS have found no meaningful differences by race[40, 41]. Second, in our study the patients were sent home *despite the fact* that their discharge was coded as an ACS by the ED physician.

Given that availability of health insurance is closely associated with health care access[77, 96], we had hypothesized that health insurance coverage would explain at least partially the association between race and being sent home with a discharge code of ACS. Surprisingly, we found that this was not the case. Further investigations should examine other factors associated with racial differences in access to hospitalization among patients presenting with ACS in the ED.

Our study has several strengths. We used the HCUP datafiles, which capture all ED visits for AMI and unstable angina in non-federal facilities for the selected states and years. Therefore, we were able to avoid possible selection bias related to patients selecting certain health care facilities versus others based on their insurance status[97]. Also, we included Asian patients and patients from all age groups in our analysis, which allowed us to improve on findings of previous studies which were based on smaller populations with more limited race distribution[8] or Medicare populations only, which primarily include patients of age 65 or older[87, 98].

Our study also has some limitations. HCUP datafiles are administrative datasets that do not provide information on clinical findings during the ED visit. We used the primary ICD 9 or ICD 10 discharge codes to identify ED visits for AMI and unstable angina and could not verify the diagnosis with ECG findings or blood test results. To minimize misclassification, we excluded patients with chronic CHD using ICD 9 or 10 codes. However, this information was also subject to physician's coding behavior and we might have missed some patients with chronic CHD if the physician chose not to record this information. Moreover, we were not able to capture patients who had AMI or unstable angina but received a different diagnosis in the ED. Furthermore, we used income data from the HCUP datafiles which was ecologically defined based on the patient's ZIP code. Although this is a good proxy for "individual income," it can be subject to misclassification. Race information was not self-reported as recommended by recent guidelines for disparities research[99, 100]. Instead, it was provided by the individual states (the data sources of HCUP), which could have been subject to misclassification[101]. Finally, patients with cardiovascular risk factors, such as obesity, metabolic syndrome, or hypertension, may be more likely to be hospitalized than patients without these conditions. Since reliable data on these factors were not available, we were not able to include them in our models.

In conclusion, based on our findings, racial disparities exist in hospitalization of ACS at the ED, which are especially marked among younger patients. Our data suggest an important area for quality improvement in healthcare. Equal delivery of health care in the initial diagnosis and timely hospitalization of ACS is crucial to reduce mortality and eliminate racial disparities in health outcomes. Hospital quality improvement programs that aim to enhance hospital adherence to clinical care guidelines could reduce or even eliminate racial differences in guideline-recommended care for ACS[102-104]. Such programs should be prioritized by policymakers to minimize racial inequalities in hospitalization rates for ACS.

Table 4-1 Characteristics of patients who visited the Emergency Department with an acute coronary syndrome in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

	AMI (N= 192938)		Unstable Angina (N= 42998)	
	Sent home (N= 4117) (2.1 %)	Hospitalized (N= 188821) (97.9 %)	Sent home (N=12513) (29.1 %)	Hospitalized (N=30485) (70.9 %)
Age, mean (SD)	60.7 (19.9)	68.7 (14.3)	61.8 (14.2)	64.3 (13.6)
Sex (% men)	2446 (59.4)	114325 (60.6)	7218 (57.7)	18313 (60.1)
Race, n (%)				
White	2824 (68.6)	141196 (74.8)	7212 (57.6)	19704 (64.6)
Black	629 (15.2)	20967 (11.1)	2875 (23.0)	5659 (18.6)
Hispanic	599 (14.6)	23547 (12.5)	2123 (17.0)	4329 (14.2)
Asian or Pacific Islander	65 (1.6)	3111 (1.7)	303 (2.4)	793 (2.6)
Income quartile, n (%)				
1st quartile (lowest)	1253 (30.4)	55997 (30.3)	4403 (35.7)	9682 (32.5)
2nd quartile	1281 (31.1)	55014 (29.8)	3344 (27.1)	8382 (28.2)
3rd quartile	914 (22.2)	41600 (22.5)	2455 (19.9)	6165 (20.7)
4th quartile (highest)	594 (14.4)	32074 (17.4)	2115 (17.2)	5521 (18.6)
Insurance type, n (%)				
Medicare	1880 (46.4)	116753 (62.6)	6595 (53.1)	17180 (56.8)
Medicaid	486 (12.0)	14494 (7.8)	1742 (14.0)	3889 (12.9)
Private insurance	1185 (29.3)	40919 (21.9)	3074 (24.7)	7020 (23.2)
Self-pay	369 (9.1)	9787 (5.2)	666 (5.4)	1319 (4.4)
Other	130 (3.2)	4526 (2.4)	350 (2.8)	826 (2.7)
Location of residence, n (%)				
Urban	2408 (58.5)	113510 (60.3)	8349 (66.9)	19462 (64.0)
Rural	1702 (41.3)	74686 (39.7)	4127 (33.1)	10925 (36.0)
Geographic state, n (%)				
Florida	2414 (58.7)	113057 (59.8)	6921 (55.3)	14909 (48.9)
New York	1397 (34.0)	68044 (36.0)	5255 (42.0)	14625 (48.0)
Utah	306 (7.3)	7720 (4.2)	337 (2.7)	951 (3.1)

Abbreviations: AMI: Acute myocardial infarction

Table 4-2 Association of race with being sent home with an acute coronary syndrome after the emergency department visit in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

	Total (N=235936)			
	White patients	**Black patients**	**Hispanic patients**	**Asian or Pacific Islander patients**
Total patients (n)	170936	30130	30598	4272
Patients sent home (n)	10036	3504	2722	368
Proportion %	5.9	11.6	8.9	8.6
Model 1, IRR (95 % CI)	**REF**	1.26 (1.18 - 1.34)	1.23 (1.15 - 1.32)	1.11 (0.93 - 1.31)
Model 2, IRR (95 % CI)	**REF**	1.26 (0.71 - 2.24)	1.23 (0.86 - 1.74)	1.11 (0.47 - 2.63)
Model 3, IRR (95 % CI)	**REF**	1.24 (1.15 - 1.35)	1.24 (1.13 - 1.36)	1.09 (0.91 - 1.29)
	Patients with AMI (N=192938)			
	White patients	**Black patients**	**Hispanic patients**	**Asian or Pacific Islander patients**
Total patients (n)	144020	21596	24146	3176
Patients sent home (n)	2824	629	599	65
Proportion %	2.0	2.9	2.5	2.0
Model 1, IRR (95 % CI)	**REF**	1.42 (1.22 - 1.65)	1.27 (1.08 - 1.48)	1.06 (0.69 - 1.64)
Model 2, IRR (95 % CI)	**REF**	1.29 (1.04 - 1.59)	1.22 (1.01 - 1.47)	1.03 (0.69 - 1.52)
Model 3, IRR (95 % CI)	**REF**	1.39 (1.18 - 1.65)	1.35 (1.10 - 1.64)	1.11 (0.75 - 1.64)
	Patients with Unstable angina (N=42998)			
	White patients	**Black patients**	**Hispanic patients**	**Asian or Pacific Islander patients**
Total patients (n)	26916	8534	6452	1096
Patients sent home (n)	7212	2875	2123	303
Proportion %	26.8	33.7	32.9	27.6
Model 1, IRR (95 % CI)	**REF**	1.23 (1.16 - 1.30)	1.23 (1.15 - 1.31)	1.13 (0.97 - 1.32)
Model 2, IRR (95 % CI)	**REF**	1.23 (1.15 - 1.33)	1.23 (1.13 - 1.33)	1.18 (0.99 - 1.41)
Model 3, IRR (95 % CI)	**REF**	1.22 (1.15 - 1.29)	1.22 (1.14 - 1.30)	1.09 (0.96 - 1.24)

Abbreviations: IRR: Incident rate ratio AMI: Acute myocardial infarction
*Model 1 is a GEE model, with a Poisson distribution, accounting for clustering of patients in hospitals with an independent correlation matrix structure, and adjusted for age, sex, state, and diagnosis (only for total patients)
*Model 2 is a Poisson marginal structural model adjusted for age, sex, state, income quartile, urban/rural location of residence and diagnosis (only for total events). Health insurance is included as a mediator to the model. Inverse probability weighting method is applied.
*Model 3 is a Poisson model adjusted for age, sex, state, income quartile, urban/rural location of residence and diagnosis (only for total events).

Table 4-3 Readmissions within 30 days among those sent home with an AMI or unstable angina in their initial visit to the ED visit in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7

	White patients	**Black patients**	**Hispanic patients**	**Asian or Pacific Islander patients**
Patient sent home in the initial ED visit (n)	10036	3504	2722	368
Patients returned to the ED within 30 days (n)	209	113	71	9
Proportion %	2.1	3.2	2.6	2.4
Patients hospitalized in the second ED visit (n, %)	67 (32.1)	69 (61.1)	35 (49.3)	5 (55.6)

Table 4-4 Characteristics of patients who visited the Emergency Department with an acute myocardial infarction by race in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

	White individuals (N=144020)		Black Individuals (N=21596)		Hispanic Individuals (N=24146)		Asian individuals (N=3176)	
	Sent home (N=2824) (2.0 %)	Hospitalized (N=141179) (98.0 %)	Sent home (N=629) (2.9 %)	Hospitalized (N=20965) (97.1 %)	Sent home (N=599) (2.5 %)	Hospitalized (N=23546) (97.5 %)	Sent home (N=65) (2.0%)	Hospitalized (N=3111) (98 %)
Age, mean (SD)	65.1 (16.5)	69.7 (14.1)	49.4 (21.6)	63.8 (49.4)	52.9 (24.2)	67.3 (14.4)	52.3 (24.5)	65.4 (13.9)
Sex (% men)	1742 (61.7)	86627 (61.4)	321 (51.0)	11103 (32.1)	339 (56.6)	14427 (61.3)	44 (67.7)	2156 (69.3)
Income quartile, n (%)								
1st quartile, lowest	706 (25.0)	35244 (25.0)	305 (48.5)	10609 (50.6)	231 (38.6)	9585 (40.7)	11 (16.9)	557 (17.9)
2nd quartile	924 (32.7)	43389 (30.7)	171 (27.2)	4563 (21.7)	174 (29.1)	6162 (26.2)	12 (18.5)	896 (28.8)
3rd quartile	670 (23.7)	33063 (23.4)	99 (15.7)	3127 (14.9)	122 (20.4)	4582 (19.5)	23 (35.4)	818 (26.3)
4th quartile, highest	465 (16.5)	26810 (19.0)	43 (6.8)	1944 (9.2)	67 (11.2)	2662 (11.3)	19 (29.2)	654 (21.0)
Insurance type, n (%)								
Medicare	1472 (52.1)	90655 (64.2)	178 (28.3)	11200 (53.4)	209 (34.9)	13552 (57.6)	21 (32.3)	1328 (42.7)
Medicaid	174 (6.2)	7020 (5.0)	157 (25.0)	3427 (16.3)	145 (24.2)	3238 (13.8)	10 (15.4)	808 (26.0)
Private insurance	829 (29.4)	31976 (22.7)	169 (26.9)	3963 (18.9)	163 (27.2)	4282 (18.2)	24 (36.9)	697 (22.4)
Self-pay	212 (7.5)	6580 (4.7)	92 (14.6)	1441 (6.9)	57 (9.5)	1550 (6.6)	8 (12.3)	216 (6.9)
Other	101 (3.6)	3523 (2.5)	19 (3.0)	623 (3.0)	8 (1.3)	347 (1.5)	0 (0.0)	33 (1.1)
Location of residence, n (%)								
Urban	1339 (47.4)	74426 (52.7)	502 (79.8)	15940 (76.3)	516 (86.1)	20400 (86.6)	51 (78.5)	2728 (87.7)
Rural	1479 (52.6)	66337 (47.3)	127 (20.2)	4945 (23.7)	82 (13.9)	3033 (13.4)	14 (21.5)	367 (12.3)
Geographic state								
FL	1652 (58.5)	83821 (59.4)	382 (60.7)	12152 (58.0)	361 (60.3)	16235 (69.0)	19 (29.2)	849 (27.3)
NY	900 (31.9)	50450 (35.7)	246 (39.1)	8758 (41.8)	211 (35.2)	6678 (28.4)	40 (61.5)	2138 (68.7)
UT	272 (9.6)	6908 (4.9)	1 (0.2)	55 (0.3)	27 (4.5)	633 (2.7)	6 (9.2)	124 (4.0)

Table 4-5 Characteristics of patients who visited the Emergency Department with an unstable angina by race in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

	White individuals (N=26916)		Black individuals (N=8534)		Hispanic individuals (N=6452)		Asian individuals (N=1096)	
	Sent home (N=7212) (26.8 %)	Hospitalized (N=19701) (73.2 %)	Sent home (N=2875) (33.7 %)	Hospitalized (N=5659) (66.3 %)	Sent home (N=2123) (32.9 %)	Hospitalized (N=4329) (67.1 %)	Sent home (N=303) (27.7 %)	Hospitalized (N=793) (72.4 %)
Age mean (SD) y	64.4 (13.6)	66.1 (13.0)	56.9 (14.2)	59.8 (14.1)	59.6 (14.2)	62.4 (13.8)	62.0 (14.6)	62.8 (12.9)
Sex (% men)	4392 (60.9)	12326 (62.6)	1467 (51.0)	2918 (51.6)	1186 (55.9)	2553 (59.0)	173 (57.1)	514 (64.8)
Income quartile, n (%)								
1st quartile, lowest	1845 (25.6)	5014 (25.5)	1570 (54.6)	2793 (49.4)	935 (44.0)	1764 (40.8)	53 (17.5)	111 (14.0)
2nd quartile	2107 (29.2)	6012 (30.5)	623 (21.7)	1133 (20.0)	541 (25.5)	1013 (23.4)	73 (24.1)	224 (28.3)
3rd quartile	1569 (21.8)	4257 (21.6)	406 (14.1)	876 (15.5)	406 (19.1)	807 (18.6)	74 (24.4)	223 (28.1)
4th quartile, highest	1557 (21.6)	4040 (20.5)	240 (8.4)	646 (11.4)	220 (10.4)	627 (14.5)	98 (32.3)	207 (26.1)
Insurance type, n (%)								
Medicare	4003 (55.5)	11703 (59.4)	1490 (51.8)	2925 (51.7)	984 (46.4)	2253 (52.0)	118 (38.9)	298 (37.6)
Medicaid	537 (7.5)	1369 (7.0)	632 (22.0)	1321 (23.3)	496 (23.4)	924 (21.3)	77 (25.4)	275 (34.7)
Private insurance	2054 (28.5)	5045 (25.6)	490 (17.0)	998 (17.6)	445 (21.0)	814 (18.8)	85 (28.1)	161 (20.3)
Self-pay	324 (4.5)	825 (4.2)	182 (6.3)	244 (4.3)	141 (6.6)	209 (4.8)	19 (6.3)	41 (5.2)
Other	254 (3.5)	613 (3.1)	59 (2.1)	127 (2.2)	34 (1.6)	76 (1.8)	3 (1.0)	10 (1.3)
Location of residence								
Urban	3949 (54.8)	10355 (52.6)	2309 (80.3)	4580 (80.9)	1813 (85.4)	3792 (87.6)	278 (91.8)	734 (92.6)
Rural	3248 (45.2)	9295 (47.4)	553 (19.7)	1059 (19.1)	304 (14.6)	513 (12.4)	22 (8.2)	56 (7.4)
Geographic state								
FL	4305 (59.7)	10132 (51.4)	1413 (49.2)	2464 (43.5)	1133 (53.4)	2184 (50.5)	70 (23.1)	129 (16.3)
NY	2641 (36.6)	8706 (44.2)	1456 (50.6)	3186 (56.3)	936 (44.1)	2097 (48.4)	222 (73.3)	633 (79.8)
UT	266 (3.7)	863 (4.4)	6 (0.2)	9 (0.2)	54 (2.5)	48 (1.1)	11 (3.6)	31 (3.9)

Table 4-6 Association of sex with being sent home with an acute coronary syndrome after the emergency department visit, stratified by age in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

Total				
Below 55 years old(N=49,376)			55 years and over (N=201,908)	
	Men	Women	Men	Women
Total patients (n)	34847	14529	117462	84446
Patients sent home (n)	3397	2129	6981	5374
Proportion %	9.7	14.7	5.9	6.4
Model 1, IRR (95 % CI)	ref	1.19 (1.11 - 1.28)	ref	1.06 (1.01 - 1.12)
Model 2, IRR (95 % CI)	ref	1.24 (1.00 - 1.53)	ref	1.08 (0.85 - 1.36)
Patients with AMI				
Below 55 years old (N= 37,253)			55 years and over (N= 167,655)	
	Men	Women	Men	Women
Total patients (n)	27153	10100	97,568	70087
Patients sent home (n)	860	516	1753	1265
Proportion %	3.2	5.1	1.8	1.8
Model 1, IRR (95 % CI)	ref	1.57 (1.35 - 1.82)	ref	1.02 (0.91 - 1.15)
Model 2, IRR (95 % CI)	ref	1.67 (1.44 - 1.92)	ref	1.03 (0.93 - 1.13)
Patients with Unstable angina				
Below 55 years old (N=12,123)			55 years and over (N=34,253)	
	Men	Women	Men	Women
Total patients (n)	7694	4429	19,894	14359
Patients sent home (n)	2537	1613	5,228	4109
Proportion %	33.0	36.4	26.3	28.6
Model 1, IRR (95 % CI)	ref	1.09 (1.02 - 1.17)	ref	1.07 (1.02 - 1.13)
Model 2, IRR (95 % CI)	ref	1.11 (1.03 - 1.19)	ref	1.09 (1.03 - 1.16)

Abbreviations: AMI: Acute myocardial infarction
*Model 1 is a GEE model, accounting for clustering of patients in hospitals with an independent correlation matrix structure, and adjusted for age, race, diagnosis (only for total patients), and state
*Model 2 is a Poisson marginal structural model adjusted for age, race, state, income quartile, urban/rural location of residence and diagnosis (only for total events). Health insurance is included as a mediator to the model. Inverse probability weighting method is applied.

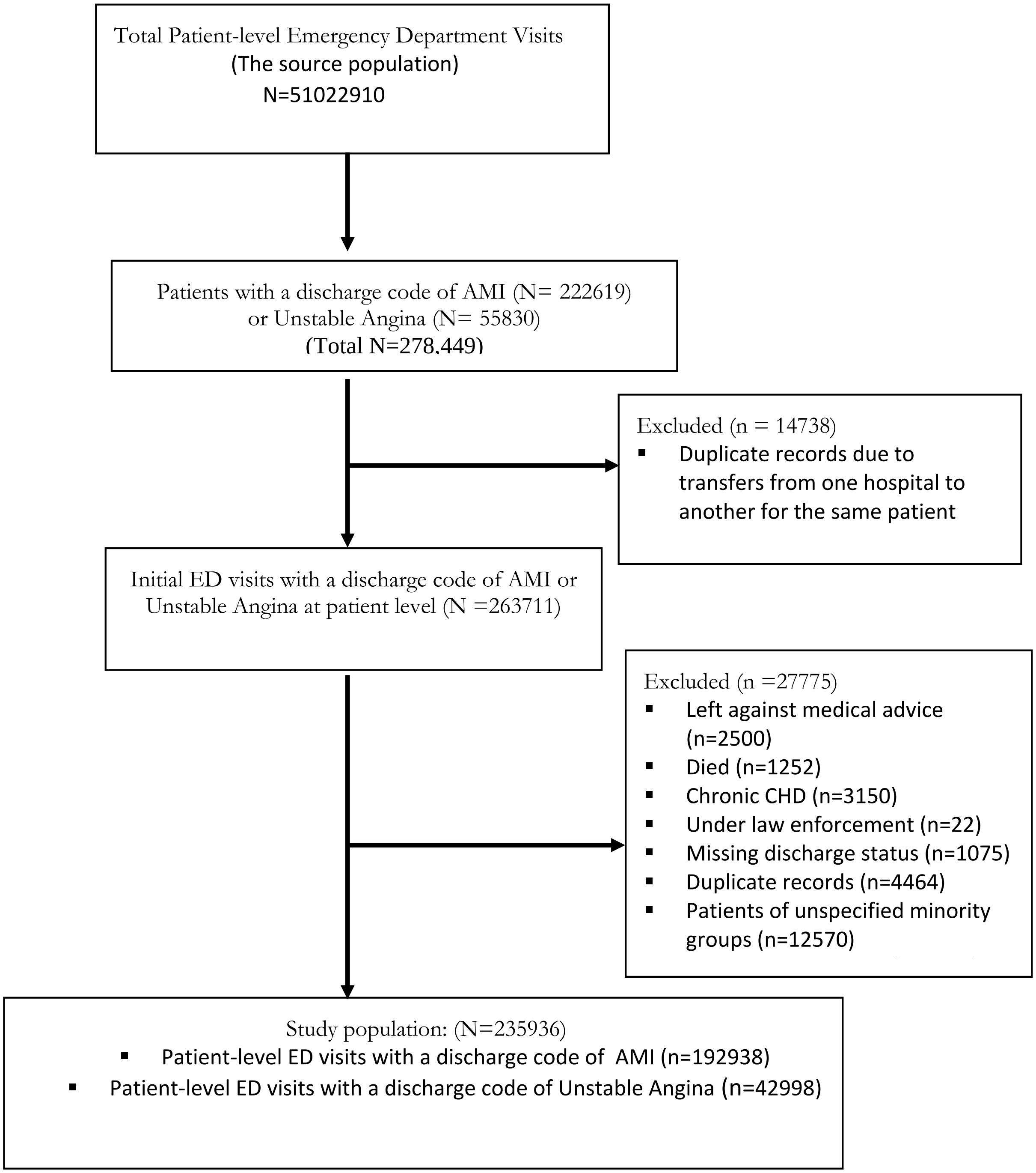

Figure 4-1 Profile of the study population obtained from the H-CUP State Databases of Florida, New York and Utah in years 2008, 2011, 2014, 2016/7.

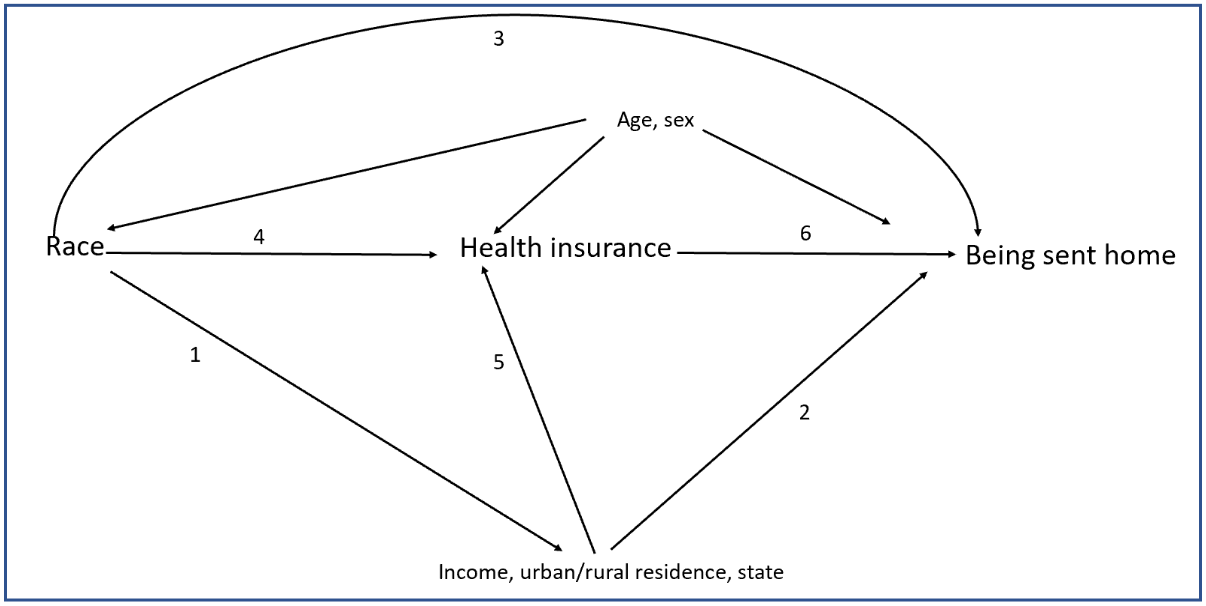

Figure 4-2 Direct acyclic graph as a conceptual model demonstrating the associations between race, being sent home from the emergency department as an outcome, health insurance (as the mediator) and other covariates.

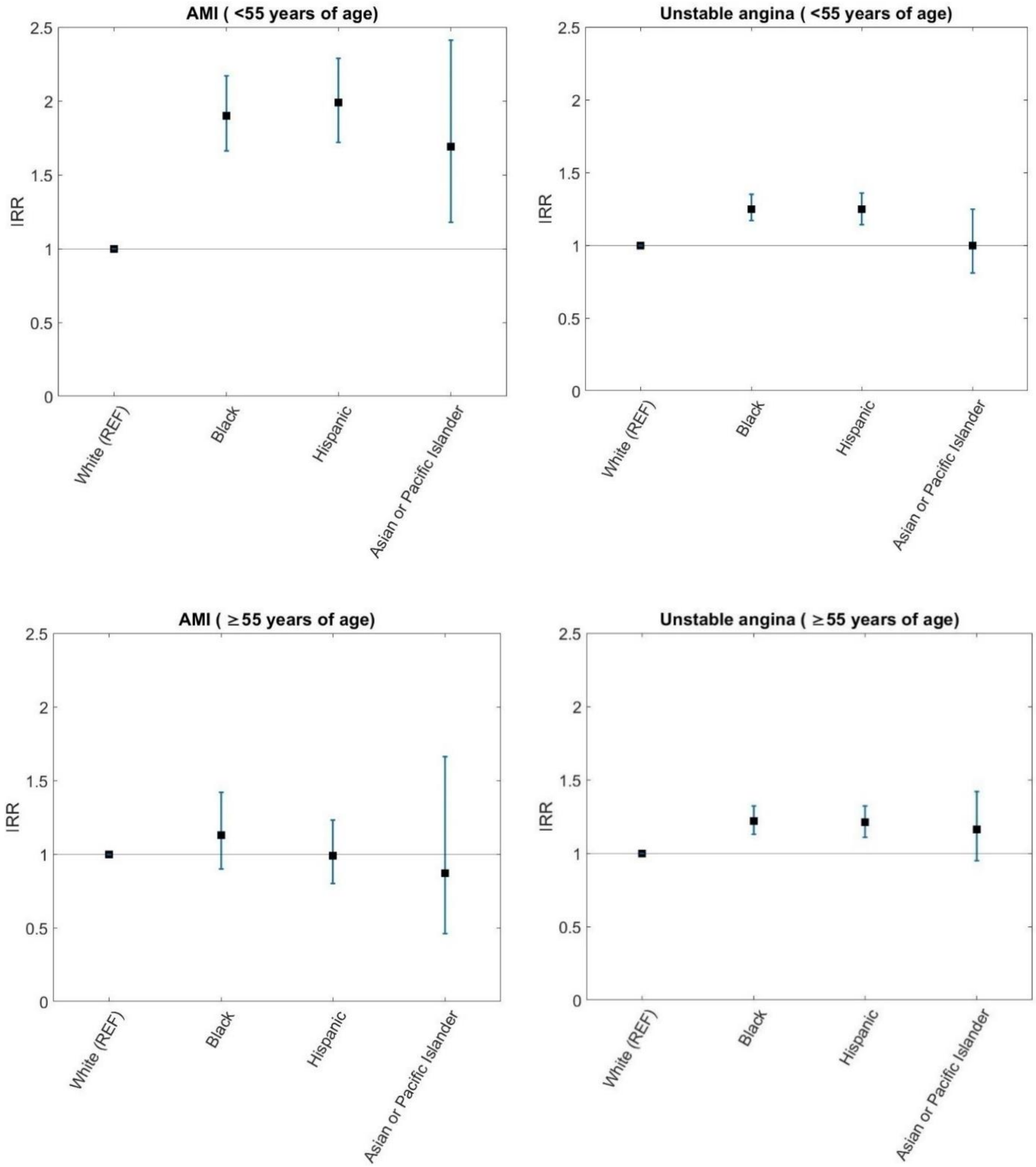

Figure 4-3 Association of race with being sent home with an acute coronary syndrome after the emergency department visit, stratified by age, in FL, NY and UT, in years 2008, 2011, 2014 and 2016/7.

CHAPTER 5:RACIAL DIFFERENCES IN FATAL OUT-OF-HOSPITAL CORONARY HEART DISEASE AND THE ROLE OF INCOME: FINDINGS FROM THE ARIC COHORT STUDY (1987-2019)

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5.1. Abstract

5.1.1. Background

Black individuals have higher incident fatal coronary heart disease (CHD) than White counterparts, however, these disparities do not exist in incident nonfatal CHD. Racial differences in out-of-hospital fatal CHD could explain the excess risk in fatal CHD among Black individuals. We examined racial disparities in incident in- and out-of-hospital fatal CHD, and whether socioeconomic status might play a role in this association.

5.1.2. Methods

We used data from the Atherosclerosis Risk in Communities (ARIC) study, including 4,095 Black and 10,884 White participants, followed between 1987-89 until 2019. Race was self-reported. We excluded 765 individuals with prevalent CHD at baseline. We calculated the incidence rates of in- and out-of-hospital fatal, nonfatal, and total CHD. First, we examined racial differences in sex- and age-adjusted proportional hazard models. Second, we created Cox marginal structural models to examine the mediating role of income after adjusting for covariates, including education and cardiovascular risk factors.

5.1.3. Results

The mean age (S.D.) was 53.4 (5.8) in Black participants and 54.2 (5.7) years in White participants. The incidence rate of in- and out-of-hospital fatal CHD was 2.3 and 1.2 in Black participants, and 1.4 and 0.8 in White participants per 1,000 person-years, respectively. The sex- and age-adjusted hazard ratios comparing out-of-hospital and in-hospital incident fatal CHD in Black versus White participants were 1.81 (95% CI, 1.42-2.30) and 2.02 (95% CI, 1.70-2.40),

respectively. In mediation analysis, the income-controlled direct effects of race in Black participants vs. Whites attenuated to 1.44 (95% CI, 1.06-1.94) for out-of-hospital incident fatal CHD and to 1.77 (95% CI, 1.41-2.21) for in-hospital incident fatal CHD.

5.1.4. Conclusions

Higher rates of in-hospital fatal CHD in Black participants vs. White counterparts likely drive the differences in fatal CHD. As a mediator, income explained 39% of racial disparities in out-of-hospital and 19% of in-hospital fatal CHD.

5.2. Introduction

While the incidence and mortality of coronary heart disease (CHD) have been declining over the past several decades in the United States[15, 24, 105], larger declines are observed in White individuals than Black counterparts.[15] Black individuals continue to have higher prevalence of CHD, and higher hospitalization rates mortality from CHD than White individuals[1-7]. However, these disparities do not seem to persist when considering non-fatal CHD events[5, 50]. Studies from large population studies have reported no difference in total CHD incidence among Blacks vs. White individuals[5, 50]. However, in the same populations, Black men showed a higher incidence of fatal CHD and case-fatality than White men, which was not completely explained by social determinants of health[5, 50]. These findings could be driven by a higher rate of out-of-hospital CHD deaths in Black individuals, perhaps because of a lower access to healthcare, if a larger proportion of fatal CHD events occur before reaching the hospital in Black individuals compared with White counterparts. However, no previous studies have examined race-based differences in out-of-hospital deaths due to CHD and whether socioeconomic status, as a proxy for healthcare access, could be a mediating factor of such differences.

In 2018, 78% of CHD deaths were reported to occur out of the hospital in the US[24]. Despite this, existing studies of CHD mortality differences by race have rarely considered racial differences in out-of-hospital fatal CHD. Furthermore, most previous studies were conducted among Medicare beneficiaries ≥65 years of age, which could mask race-related disparities since Black individuals tend to develop CHD and die from it earlier in life than White individuals[5, 51-58]. Previous studies also tended to overlook potential methodological biases that could arise from the complex nature of the associations between race and other factors. Examining racial differences in out-of-hospital incident fatal CHD and considering the role of socioeconomic status and other factors, should inform efforts to deliver equitable prevention strategies and healthcare delivery for CHD to reduce disparities.

In the Atherosclerosis Risk in Communities (ARIC) study, we examined racial differences in the rates of out-of-hospital and in-hospital (post-admission) incidence of fatal CHD among US adults free of CHD at baseline. To consider a full range of outcomes, we also examined non-fatal incident CHD and case fatality among those who were hospitalized. We further investigated the mediating effect of socioeconomic status (income) and possible confounding by education and cardiovascular risk factors on these outcomes. We hypothesized that Black individuals have a higher incidence of CHD than White individuals, and that the higher CHD incidence among Black individuals reflects a higher out-of-hospital CHD mortality rate in Black vs. White people. We further hypothesized that income, as a socioeconomic mediator, drives the racial disparities in incident CHD outcomes.

We summarized our hypothesis regarding race differences in incident CHD and the role of other factors in a conceptual direct acyclic graph (Figure 5-1). Since race is an upstream variable, education and cardiovascular risk factors could be mediators in the path between race and incident CHD (paths 1 and 2). However, education and cardiovascular risk factors could also be confounders of the association between income and incident CHD (paths 5 and 2). As a result, education and cardiovascular risk factors could be both mediators and confounders in the association of race with incident CHD. We used inverse probability weighting methodology to avoid potential biases arising from these complex relationships between race, other factors, and incident CHD.

5.3. Methods

5.3.1. Study Population

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to the ARIC publications committee. The ARIC study is a prospective epidemiologic study conducted in four US communities (Washington County, MD; Forsyth County, NC; Jackson, MS; and selected Minneapolis suburbs, MN)[28]. Each ARIC field center randomly selected and recruited a cohort of approximately 4,000 individuals aged 45-64 years from a defined community. Since very few Non-White and Non-Black participants participated in ARIC (n=48), we excluded them from the analysis. After excluding individuals who had prevalent coronary heart disease at baseline (n=765), our analysis included 14,979 ARIC participants at baseline.

Participants received an extensive in-person evaluation, where sociodemographic and cardiovascular data were collected. Participants were reexamined in person every three years for the first nine years (1990-92, 1993-95, 1996-98), with additional exams in 2011-13, 2016-17, and 2017-18. Also, participants were contacted by phone yearly (biannually since 2012) to update contact information and assess their health status. At visit 1 (baseline, 1987–1989), trained interviewers administered a questionnaire to collect data on demographic characteristics, medical history, and cardiovascular risk factors. Information on household income and years of education was also collected. Follow-up is ongoing with adjudicated endpoint data through 12/31/2019 currently available. Procedures applied at all study centers were approved by each institutional review board, and informed consent was obtained from all participants.

Definition of Exposure: Self-reported race at visit one was the exposure variable, which was classified as "Blacks" and "Whites."

Definition of in- and out-of-hospital incident CHD: In ARIC, CHD events were ascertained by surveying discharge lists from local hospitals and death certificates from state vital statistics and follow-up calls identifying hospitalizations and deaths during the previous year. Out-of-hospital incident fatal CHD included deaths of participants who died at home or in other undefined places, or "deaths on arrival" to the hospital. In-hospital fatal CHD included deaths that occurred in hospitals and in nursing homes. Additional information was sought from the next of kin and other informants, certifying doctors and family physicians, and coroners or medical examiners for out-of-hospital deaths. A panel of physicians reviewed and adjudicated all events using established criteria[63, 64].

Definition of Covariates: Socioeconomic variables included level of income and education. We categorized education as "high school graduate or less" and "vocational school, college, and graduate school." Income was categorized as annual income "less than 35,000" and "35,000 and over". Cardiovascular risk factors included body mass index (BMI), prevalent hypertension, prevalent diabetes, smoking status, and total cholesterol levels measured at Visit 1. BMI was calculated as weight (in kilograms) divided by the square of height (meters) and was classified as “below 30.0” and “30.0 and above”. Prevalent hypertension was defined as a systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mmHg, or self-reported diagnosis of hypertension by a physician, or use of hypertension medication. Blood pressure was measured by a certified technician using a random-zero sphygmomanometer after 5 minutes of rest and the average of three seated measurements was used. Prevalent diabetes was defined as a fasting glucose level of at least 126 mg/dL, or a casual blood glucose level of at least ≥200 mg/dL, or a self-reported diagnosis of diabetes by a physician, or use of antidiabetic medications. Fasting glucose levels were measured by the modified hexokinase/glucose-6 phosphate dehydrogenase method. Fasting plasma total cholesterol concentration was assessed by enzymatic procedures and was classified as “below 200 mg/dl” or “200 mg/dl and above”. Smoking status was classified as “current”, “former” and “never” smoker.

5.3.2. Statistical Analysis

First, we tabulated the distributions of baseline sociodemographic factors and cardiovascular risk factors by race. Next, we computed incidence rates per 1,000 person-years and 95% confidence intervals (CI) for fatal, nonfatal and total CHD by race. For fatal CHD, we also examined separately out-of-hospital and in-hospital CHD death.

We constructed age- and sex-adjusted Cox proportional hazard models (Model 1) to compare in and out-of-hospital fatal CHD, nonfatal CHD, and total incident CHD between Black and White participants. We used logistic regression to compare racial differences in in-hospital CHD mortality among those hospitalized. In these models, we tested race and sex interactions.

We then constructed Cox marginal structural models to examine the mediating role of income using inverse probability weighting[83, 84] (Model 2). In our mediation analysis, we hypothesized that income is a mediating factor on the pathway between race and the incident CHD outcomes**.** Inverse probability weighting allowed us to avoid violation of a major mediation analysis assumption,[69] which requires that there should not be any mediator-outcome confounders affected by the exposure[69]. As seen in Figure 5-1**,** since race, as the exposure, is an upstream variable, there could be a path (path 1) from race to education and cardiovascular risk factors, which could also be confounders of the association between income and incident CHD (through paths 2 and 5). Therefore, simply adjusting for all covariates in the models could result in biased results for mediation analysis. The use of methods such as inverse probability weighting, which allows separating the effect of income from the effect of other covariates, is recommended to get more accurate estimates[83, 85]. We then calculated the % mediated by income, using the formula: (ln (HR_1)- ln (HR_2)) *100 / ln (HR_1), where ln (HR_1) is the natural logarithm of the hazard ratio calculated from Model 1, and ln(HR_2) is the natural logarithm of the hazard ratio calculated from Model 2. For Model 2, we also tested potential race and income interactions.

In a sensitivity analysis, we repeated the mediation analysis without including education as a covariate since education and income could be highly correlated with each other. Also, we reclassified those who were "dead on arrival" to the hospital as in-hospital fatal CHD rather than out-of-hospital fatal CHD, and re-ran the models. Also, since race and study center are correlated in ARIC, we created a combined "race-center" variable and compared the CHD outcomes among them, as previously applied in other ARIC studies[106].

As a secondary analysis, we examined race differences for the exact place of death (i.e., at home, or in undefined place) for out-of-hospital incident CHD.

An institutional review board at each site approved the ARIC study, and study participants provided written informed consent at all study centers. We also obtained approval from the Emory University Institutional Review Board (IRB00111905).

5.4. Results

5.4.1. Characteristics of participants at baseline

The characteristics of the study population by race described in Table 5-1. Among participants, 43 % were men, and 27 % were Black. Black participants were slightly younger; the mean (SD) age was 53.4 (5.8) for Black participants and 54.2(5.7) for White participants. There were large differences in education and income by race. Among Black participants, 19.7 % had no formal education or only went to grade school, and 21.6 % graduated from high school. Among White participants, corresponding percentages were 5.3 and 36.6. Among Black participants, 52.4 % had an annual income of less than 16,000 US$; that figure was 12.2 % among the White participants. Smoking status and prevalence of hypercholesterolemia were similar by race, but Black individuals had a higher BMI and a higher prevalence of hypertension and diabetes.

5.4.2. Racial differences in fatal and nonfatal incident CHD

Table 5-2 shows the association of race with incident fatal, nonfatal, and total CHD events in the ARIC Cohort. The fatal CHD incidence rate was higher in Black participants (3.5 per 1,000 person years, (95 % CI, 3.1-3.9) than in White participants (2.2, 95 % CI, 2.0-2.4). Comparing Black to White participants, the hazard ratio of fatal incident CHD was 1.92 (95 % CI, 1.67-2.21) in age and sex-adjusted models and 1.63 (95 % CI, 1.36-1.95) in Cox marginal structural models. Income mediated 25 % of the association of race with fatal CHD. In contrast, the nonfatal CHD incidence per 1,000 person-years was similar by race; the age and sex-adjusted hazard ratio comparing Black to White participants was 1.06 (95 % CI, 0.94-1.20). Income did not play any role as a mediator in the association of race and non-fatal CHD. Overall, the total incident CHD rate was higher in Black versus White participants and in sex- and age- adjusted models, the hazard ratios was 1.35 (95 % CI, 1.23-1.47) in Black versus White participants. Income mediated 34 % of this association.

5.4.3. Racial differences in out-of-hospital and in-hospital fatal incident CHD

The hazard ratio for out-of-hospital fatal incident CHD was higher in Black than White participants in sex and age- adjusted models (HR, 1.81, 95 % CI, 1.42-2.30) (Table 5-3). Income, as a mediator, explained 39 % of this association. The magnitude of the race difference was roughly similar for out-of-hospital fatal CHD and in-hospital fatal CHD (HR, 2.02, 95% CI, 1.70-2.40). However, income as mediator played more of a role for out-of-hospital than in-hospital CHD death (proportion mediated, 39 % vs. 19 %).

Among those hospitalized, the case-fatality of incident CHD was also elevated in Black patients compared with White patients (HR, 1.69, 95 % CI, 1.33-2.15) (Table 5-4). In all the analyses above, there were no significant interactions between race and sex (Table 5-6, Table 5-7 and Table 5-8). However, after stratification by sex, among men the racial difference was especially elevated for out-of-hospital death, while among women the estimates for out-of-hospital and in-hospital mortality were similar (Figure 5-2). There were also no interactions between race and income.

In sensitivity analyses, the role of income in mediating the association of race with incident CHD remained similar after we excluded education from the Cox marginal structural models (Table 5-5**).** Among Black participants, eight individuals were dead on arrival to the hospital, and among White participants twelve were dead on arrival. After we reclassified out-of-hospital and in-hospital fatal incident CHDs by considering those who were "dead on arrival" as "in-hospital deaths," the hazard ratios comparing Black versus White participants remained similar to the primary analysis (HR=1.77, 95 % CI: 1.38-2.27) (Table 5-9). Also, our conclusions remained the same when we compared the CHD outcomes between 'race-center' groups (Table 5-10 and Table 5-11)

In secondary analyses of out-of-hospital deaths, most Black and White participants died in their homes, but Black individuals were more likely to die than White individuals both at home (HR=1.69, 95 % CI: 1.26-2.26) and in an undefined place (HR= 2.06, 95 % CI: 1.28-3.30) (Table 5-12).

5.5. Discussion

In this community-based cohort study, both out-of-hospital and in-hospital incident fatal CHD was approximately doubled in Black versus White individuals, whereas there was no difference by race in incident non-fatal CHD. In mediation analysis, income played a much larger role in the association of race with out-of-hospital death than for in-hospital CHD death. Our results suggest that CHD is more fatal in Black than in White individuals irrespective of where the event occurs. The higher rates of fatal incident CHD in our study parallel previous reports that the first clinical presentation of CHD is more fatal among Black individuals compared with Whites[15, 50, 105]. Our results are also in agreement with data from the REGARDS study which also showed higher in- and out-of-hospital fatal incident CHD in Black participants than White participants[5].

One reason for the higher rate of fatal CHD in Black than in White individuals could be a higher rate of sudden cardiac death among Black people. Sudden cardiac death was indeed almost twice as high in Black than in White participants in previous analyses of the ARIC[107] and the REGARDS studies[108]. However, we found an excess of mortality among Black individuals for both out-of-hospital and in-hospital death, therefore it is unlikely that the higher rate of fatal CHD in Black persons is simply a reflection of a higher rate of sudden cardiac death.

A second explanation for racial differences in incident fatal CHD could be due to differences in the time between symptom onset and arrival to the hospital,[109] since significant delays in seeking medical care could increase the possibility of death from CHD. Based on previous studies, Black individuals tend to have longer prehospital delays[110, 111] and are more likely to be unaware of the symptoms of an incipient CHD event[112] compared with White individuals.

A third possible explanation is that Black individuals have a higher prevalence of major CHD risk factors and lower rates of access to interventions aimed at controlling these risk factors compared to White counterparts[113-115]. Previous literature reported higher in-hospital mortality and lower secondary prevention uptake, such as revascularization procedures in Black individuals compared to Whites individuals[51-58]. Furthermore, Black patients are reported to have longer waiting times to treatment after hospitalization than White patients[116], resulting in delays for the receipt of secondary prevention interventions which could contribute to higher mortality[117]. The higher rates of in-hospital incident fatal CHD and of case-fatality in Black vs. White individuals in our analysis are consistent with previous studies[5, 118, 119]. However, in our study, the race-related disparities in both out-of-hospital and in-hospital fatal CHD did not completely disappear after adjusting for cardiovascular risk factors, suggesting that racial differences in cardiovascular risk factors cannot completely explain outcome differences.

We show that the lower income of Black individuals plays an important role in explaining race differences in CHD death, and that this effect is especially pronounced for out-of-hospital fatal CHD, as it explains 39 % of the racial differences in this outcome. In agreement with our results, income previously was reported to be the main drivers of racial differences in sudden cardiac arrest in ARIC[107] and other investigations[120]. Furthermore, lower income and education have been associated with lower awareness of CHD, including the alarming symptoms of an acute myocardial infarction[112]. Our findings extend this literature to out-of-hospital death as a whole, and suggest a potential role for access to care, as a lower access to health care due to limited income could cause delays in seeking care or even discourage care altogether[121]. Our study has several strengths, including the large sample size, the long duration of follow-up in a community-based setting, and the rigorous methods we used for mediation analysis. Using inverse probability weighting with marginal structural models helped avoid the potential biases associated with mediation analysis which might have been present in previous studies. Another strength was the use of self-reported race, as suggested by the recent guidelines for disparities research,[99, 100] rather than inferring race from other sources. Furthermore, the ARIC study has active surveillance of events through hospital records and adjudication by an expert committee, minimizing event misclassification. For the adjudication of out-of-hospital incident CHD deaths, the ARIC study incorporated multiple sources of information, including interviews with the next of kin and physicians. However, a limitation is that all participants in the Jackson site were Black, and participants in the Minnesota and Maryland sites were predominantly White; therefore, we were not able to fully separate differences by race from differences by study site. However, our conclusions remained the same after we compared outcomes across "race-center" groups in a sensitivity analysis. Also, we recognize that we could only consider socioeconomic and cardiovascular risk factors in our analysis. It is likely that other environmental, social, cultural and policy factors could play a role in the excess CHD death among Black persons.

In conclusion, we report large differences in fatal incident CHD by race, in contrast to non-fatal incident CHD. Black individuals die from CHD at about twice the rate of White individuals, and the excess in mortality is seen irrespective of where these events occur in or out of the hospital. These findings highlight the need for better primary prevention interventions among Black people to prevent CHD death. Socioeconomic factors are important in explaining this disparity for out-of-hospital deaths, suggesting a key role of healthcare access. Our results suggest the importance of targeting lack of healthcare coverage and other potential barriers to access to care in order to decrease racial differences in CHD death and foster health equity. Timely access to emergency care and effective preventive interventions could decrease the racial disparities in fatal CHD events.

5.6. Acknowledgments

The authors thank the staff and participants of the ARIC study for their important contributions.

5.7. Sources of Funding

The Atherosclerosis Risk in Communities study has been funded in whole or in part with Federal funds from the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services, under Contract nos. (HHSN2682017000001I, HHSN268201700002I, HHSN268201700003I, HHSN268201700005I, HHSN268201700004I). Dr Duygu Islek is funded by the American Heart Association pre-doctoral fellowship (Award number: 19PRE34380062).

Table 5-1 Characteristics of ARIC cohort participants at baseline (1987-89) by race (n=14979).

	Black participants (n=4095)	**White participants (n=10884)**
Age, mean (SD), y	53.4 (5.8)	54.2 (5.7)
Education, No (%)		
Grade school or less	805 (19.7)	580 (5.3)
High school, but no degree	884 (21.7)	1212 (11.1)
High school graduate	881 (21.6)	3975 (36.6)
Vocational school	278 (6.8)	980 (9.0)
College	708 (17.3)	3135 (28.8)
Graduate school or Professional school	527 (12.9)	989 (9.1)
Income (US$), No (%)		
<16 000	1931 (52.4)	1272 (12.2)
16 000 to <25 000	666 (18.1)	1457 (14.0)
25 000 to <35 000	466 (12.6)	2034 (19.5)
35 000 to <50 000	360 (9.8)	2393 (23.0)
≥50 000	262 (7.1)	3259 (31.3)
Smoking status No. (%)		
Current	1212 (29.7)	2688 (24.7)
Former	951 (23.3)	3733 (34.3)
Never	1924 (47.1)	4455 (41.0)
BMI, No. (%)		
< 30.0	2423 (59.4)	8434 (77.6)
≥ 30.0	1653 (40.6)	2439 (22.4)
Hypertension, No. (%)	2252 (55.3)	2844 (26.2)
Diabetes, No. (%)	753 (18.9)	922 (8.5)
Total Cholesterol, No. (%)		
< 200 mg/dl	1559 (40.2)	4025 (37.1)
≥ 200 mg/dl	2322 (59.8)	6830 (62.9)

Table 5-2 Association of race with incident non-fatal, fatal and total coronary heart disease in the ARIC Cohort (1987-2019) (n=14979).

	Black participants (n=4095)	**White participants (n=10884)**	**Proportion mediated by income**
Incident Fatal CHD			
Events	307	570	
Person-years	87630	258590	
Incidence Rate (95 % CI) per 1,000 person-years	3.50 (3.13-3.91)	2.20 (2.02-2.39)	
Model 1*, HR (95% CI)	1.92 (1.67-2.21)	**ref**	
Model 2†, HR (95% CI)	1.63 (1.36-1.95)	**ref**	25 %
Incident Non-fatal CHD			
Events	347	1125	
Person-years	87630	258590	
Incidence Rate (95 % CI) per 1,000 person-years	3.96 (3.56-44.0)	4.35 (4.10-4.61)	
Model 1*, HR (95% CI)	1.06 (0.94-1.20)	**ref**	
Model 2†, HR (95% CI)	1.00 (0.85-1.16)	**ref**	0 %
Total Incident CHD			
Events	654	1695	
Person-years	87630	258590	
Incidence Rate (95 % CI) per 1,000 person-years	7.46 (6.91-8.05)	6.55 (6.24-6.87)	
Model 1*, HR (95% CI)	1.35 (1.23-1.47)	**ref**	
Model 2†, HR (95% CI)	1.21 ((1.08-1.36)	**ref**	34 %

* Model 1 is Cox proportional hazard model, adjusted for age and sex.

† Model 2 is Cox marginal structural model, adjusted for age, sex, education and cardiovascular risk factors (smoking, BMI, hypertension, diabetes, total cholesterol). Income is included as a mediator to the model. Inverse probability weighting method is applied.

Table 5-3 Association of race with out-of-hospital and in-hospital fatal incident coronary heart disease in the ARIC Cohort (1987-2019) (n=14979).

	Black participants (n=4095)	**White participants (n=10884)**	**Proportion mediated by income**
Out-of-hospital Fatal Incident CHD*			
Events	103	210	
Person years	87630	258590	
Incidence Rate (95 % CI) per 1,000 person-years	1.18 (0.96-1.42)	0.81 (0.71-0.93)	
Model 1†, HR (95% CI)	1.81 (1.42-2.30)	**ref**	
Model 2‡, HR (95% CI)	1.44 (1.06-1.94)	**ref**	39 %
In hospital Fatal Incident CHD§			
Events	204	354	
Person years	87630	258590	
Incidence Rate (95 % CI) per 1,000 person-years	2.33 (2.02-2.66)	1.37 (1.23-1.52)	
Model 1†, HR (95% CI)	2.02 (1.70-2.40)	**ref**	
Model 2‡, HR (95% CI)	1.77 (1.41-2.21)	**ref**	19 %

* Out-of-hospital fatal coronary heart disease include deaths of participants who died at home, other undefined place or who were dead on arrival to hospital

† Model 1 is Cox proportional hazard model, adjusted for age and sex.

‡ Model 2 is Cox marginal structural model, adjusted for age, sex, education and cardiovascular risk factors (smoking, BMI, hypertension, diabetes, total cholesterol). Income is included as a mediator to the model. Inverse probability weighting method is applied.

§ In-hospital fatal coronary heart disease include deaths which occurred in hospital and in nursing homes

Table 5-4 Association of race with case-fatality of coronary heart disease among those hospitalized in the ARIC cohort 1987-2019 (n=14979).

	Black participants (n=4095)	**White participants (n=10884)**
Hospitalized CHD cases (n=1900)	487	1413
In-hospital CHD deaths (n=428)	140	288
Case-fatality of CHD (%) (95 %CI)	28.7 (24.9-32.9)	20.4 (18.4-22.6)
Model 1*, OR (95% CI)	1.69 (1.33-2.15)	**ref**

*Model 1 is a logistic regression model, adjusted for sex and age.

Table 5-5 Role of income as a mediator in the association of race with incident CHD outcomes after education is excluded from models: Results from sensitivity analysis in ARIC Cohort (1987-2019) (n=14979).

	Black participants (n=4095)	**White participants (n=10884)**	**Proportion mediated by income**
Incident Fatal CHD			
Model*, HR (95% CI)	1.65 (1.39-1.95)	ref	24 %
Incident Non-Fatal CHD			
Model*, HR (95% CI)	0.98 (0.85-1.13)	ref	0.0 %
Total incident CHD			
Model*, HR (95% CI)	1.21 (1.08-1.34)	ref	37 %
Out-of-hospital Fatal incident CHD†			
Model*, HR (95% CI)	1.55 (1.16-2.08)	ref	25 %
In hospital Fatal incident CHD‡			
Model*, HR (95% CI)	1.72 (1.40-2.11)	ref	24 %

* Cox marginal structural model where education is excluded from the model for sensitivity analysis. Income included as a mediator to the model. Inverse probability weighting method is applied. Other covariates include age, sex, and cardiovascular risk factors (smoking, BMI, hypertension, diabetes, total cholesterol).

† Out-of-hospital fatal coronary heart disease include deaths of participants who died at home, other undefined place or who were dead on arrival to hospital

‡ In-hospital fatal coronary heart disease include deaths which occurred in hospital and in nursing homes.

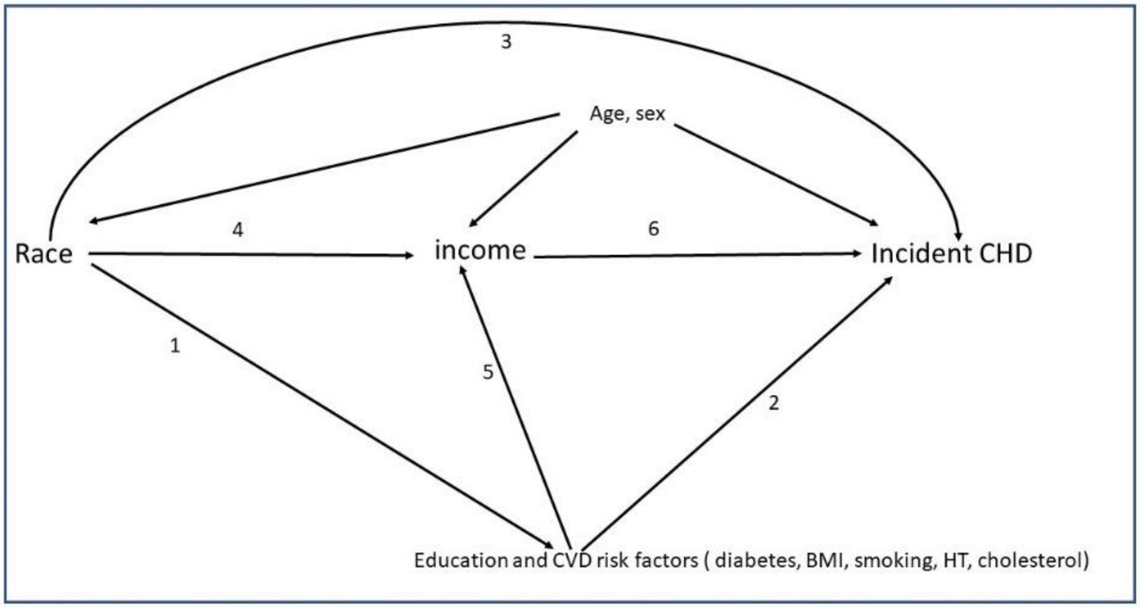

Figure 5-1 Direct acyclic graph as a conceptual model demonstrating the race and incident coronary heart disease associations through income (as the mediator) and other covariates.

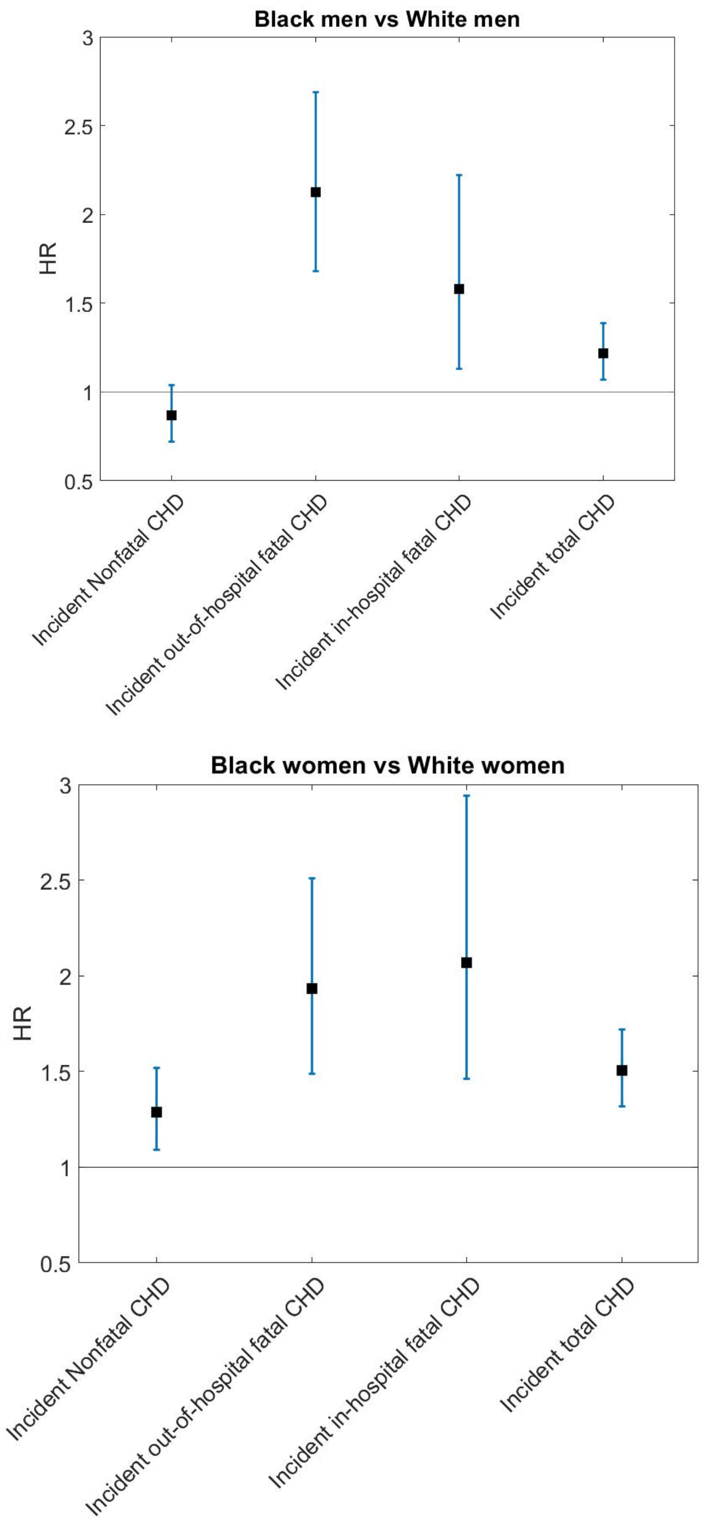

Figure 5-2 Hazard ratios comparing racial differences in incident CHD outcomes among men and women.

Table 5-6 Race and sex interactions for incident fatal, non-fatal and total coronary heart disease in ARIC cohort (1987-2019) (n=14979).

	Black participants		White participants	
	Men (N=1536)	Women (N=2559)	Men (N=4947)	Women (N=5937)
Incident Fatal CHD				
Cases	157	150	345	225
Person-years	30271	57359	110437	148153
Incidence Rate (95 % CI) per 1,000 person-years	5.19 (4.42-6.05)	2.62 (2.22-3.06)	3.12 (2.86-3.41)	1.52 (1.36-1.69)
Model 1*, HR (95% CI)	3.88(3.16-4.77)	1.94 (1.58-2.39)	2.04 (1.73-2.42)	ref
Incident Non-fatal CHD				
Cases	142	205	650	475
Person-years	30271	57359	110437	148153
Incidence Rate (95 % CI) per 1,000 person-years	4.69 (3.97-5.51)	3.57 (3.11-4.09)	5.89 (5.51-6.27)	3.21 (2.97-3.46)
Model 1*, HR (95% CI)	1.66 (1.37-2.00)	1.24(1.05-1.46)	1.86 (1.65-2.09)	ref
Total Incident CHD				
Cases	299	355	995	700
Person-years	30271	57359	110437	148153
Incidence Rate (95 % CI) per 1,000 person-years	9.88 (8.81-11.05)	6.19 (5.57-6.86)	9.01 (8.54-9.480	4.72 (4.44-5.02)
Model 1*, HR (95% CI)	2.38 (2.07-2.72)	1.46 (1.29-1.66)	1.92 (1.74-2.11)	ref

* Model 1 is Cox proportional hazard model, adjusted for age and includes the interaction term ‘sex*race’.

Table 5-7 Race and sex interactions for in-hospital and out-of-hospital incident fatal CHD in ARIC cohort (1987-2019) (n=14,979).

	Black participants		White participants	
	Men (N=1536)	Women (N=2559)	Men (N=1509)	Women (N=2533)
Out of hospital incident fatal CHD				
Cases	48	55	131	79
Person-years	30271	57359	110437	148153
Incidence Rate (95 % CI) per 1,000 person-years	1.59 (1.18-2.08)	0.96 (0.73-1.24)	1.19 (1.03-1.36)	0.53 (0.44-0.64)
Model 1*, HR (95% CI)	3.55 (2.47-5.09)	2.11 (1.49-2.98)	2.25 (1.70-2.97)	ref
In hospital incident fatal CHD				
Cases	109	95	210	144
Person-years	30271	57359	110437	148153
Incidence Rate (95 % CI) per 1,000 person-years	3.60 (2.97-4.33)	1.66 (1.35-2.02)	1.90 (1.69-2.12)	0.97 (0.84-1.11)
Model 1*, HR (95% CI)	4.11 (3.20-5.27)	1.88(1.45-2.44)	1.93 (1.56-2.38)	ref

* Model 1 is Cox proportional hazard model, adjusted for age and includes the interaction term sex*race.

Table 5-8 Race and sex interactions for case-fatality among those who were hospitalized in ARIC cohort 1987-2019 (N=14979).

	Black participants		White participants	
	Men (N=1536)	Women (N=2559)	Men (N=1509)	Women (N=2533)
Hospitalized CHD cases (n=1900)	209	278	816	597
In-hospital CHD deaths (n=428)	67	73	166	122
Case-fatality of CHD (%) (95 %CI)	32.1 (26.1-38.7)	26.3 (22.2-30.8)	20.3 (18.1-22.7)	20.4 (17.8-23.2)
Model 1*, OR (95% CI)	1.95 (1.37-2.79)	1.44 (1.03-2.01)	0.98 (0.75-1.27)	**ref**

*Model 1 is a logistic regression model adjusted for age and includes the interaction term sex*race

Table 5-9 Association of race with out-of-hospital and in-hospital fatal incident coronary heart disease after recategorization of deaths for sensitivity analysis in ARIC Cohort (1987-2019) (n=14,979).

	Black participants (n=4095)	White participants (n=10884)	Proportion Mediated by income
Out-of-hospital Fatal CHD*			
Events	95	198	
Person years	86449	258590	
Incidence Rate (95 % CI) per 1,000 person-years	1.10 (0.89-1.33)	0.77 (0.66-0.88)	
Model 1[†], HR (95% CI)	1.77(1.38-2.27)	ref	
Model 2[‡], HR (95% CI)	1.41 (1.03-1.92)	ref	40 %
In-hospital Fatal CHD[§]			
Events	212	366	
Person years	86449	258590	
Incidence Rate (95 % CI) per 1,000 person-years	2.45 (2.14-2.80)	1.42 (1.28-1.57)	
Model 1[†], HR (95% CI)	2.03 (1.71-2.41)	ref	
Model 2[‡], HR (95% CI)	1.77 (1.42-2.21)	ref	19 %

* For the sensitivity analysis; out-of-hospital fatal coronary heart disease include deaths of participants who died at home and any other undefined place. Those who were dead on arrival are considered as “in-hospital deaths”.
† Model 1 is Cox proportional hazard model, adjusted for age and sex.
‡ Model 2 is Cox marginal structural model, adjusted for age, sex, education and cardiovascular risk factors (smoking, BMI, hypertension, diabetes, total cholesterol). Income is included as a mediator to the model. Inverse probability weighting method is applied.
§ For the sensitivity analysis, in-hospital fatal coronary heart disease includes deaths which occurred in hospital and in nursing homes. Also, those who were dead on arrival are considered as “in-hospital deaths”.

Table 5-10 Association of 'race-center' groups with incident coronary heart disease outcomes in ARIC Cohort (1987-2019) (n=14,979).

	White, Minnesota N=3790	**White, Washington N=3720**	**White, Forsyth, North Carolina N=3374**	**Black, Forsyth, North Carolina N=457**	**Black, Jackson, Mississippi N=3585**
Incident Fatal CHD					
Events	160	253	157	25	279
Person-years	91523	88601	78466	9081	77368
Incidence Rate (95 % CI) per 1,000 person-years	1.75 (1.50-2.04)	2.86 (2.52-3.22)	2.00 (1.71-2.33)	2.75 (1.83-4.00)	3.61 (3.20-4.05)
Model 1*, HR (95% CI)	**ref**	1.55 (1.27-1.89)	1.11 (0.89-1.38)	1.68 (1.10-2.57)	2.46 (2.02-3.00)
Incident Non-fatal CHD					
Events	351	414	360	35	309
Person-years	91523	88601	78466	9081	77368
Incidence Rate (95 % CI) per 1,000 person-years	3.84 (3.45-4.25)	4.67 (4.24-5.14)	4.59 (4.13-5.08)	3.85 (2.73-5.30)	3.99 (3.57-4.46)
Model 1*, HR (95% CI)	**ref**	1.19 (1.04-1.38)	1.19 (1.03-1.38)	1.09 (0.77-1.55)	1.21 (1.04-1.42)
Total Incident CHD					
Events	511	667	517	60	588
Person-years	91523	88601	78466	9081	77368
Incidence Rate (95 % CI) per 1,000 person-years	5.58 (5.11-6.08)	7.53 (6.97-8.12)	6.59 (6.04-7.18)	6.61 (5.09-8.44)	7.60 (7.00-8.23)
Model 1*, HR (95% CI)	**ref**	1.31 (1.16-1.47)	1.17 (1.03-1.32)	1.28 (0.98-1.67)	1.60 (1.42-1.81)

* Model 1 is Cox proportional hazard model, adjusted for age and sex.

Table 5-11 Association of 'race-center' groups with incident in- and out-of-hospital fatal coronary heart disease in ARIC Cohort (1987-2019) (n=14,979).

	White, Minnesota N=3790	**White, Washington N=3720**	**White, Forsyth, North Carolina N=3374**	**Black, Forsyth, North Carolina N=457**	**Black, Jackson, Mississippi N=3585**
Out-of-hospital Fatal Incident CHD					
Events	71	85	42	13	80
Person-years	91523	88601	78466	9081	77368
Incidence Rate (95 % CI) per 1,000 person-years	0.78 (0.61-0.97)	0.96 (0.77-1.18)	0.54 (0.39-0.72)	1.43 (0.80-2.38)	1.03 (0.83-1.28)
Model 1*, HR (95% CI)	**ref**	1.18 (0.86-1.61)	0.68 (0.46-0.99)	2.02 (1.12-3.66)	1.65 (1.20-2.29)
In-hospital Fatal Incident CHD					
Events	87	166	113	12	199
Person-years	91523	88601	78466	9081	77368
Incidence Rate (95 % CI) per 1,000 person-years	0.95 (0.77-1.17)	1.87 (1.60-2.18)	1.44 (1.19-1.72)	1.32 (0.72-2.24)	2.57 (2.23-2.95)
Model 1*, HR (95% CI)	**ref**	1.87 (1.44-2.43)	1.46 (1.11-1.93)	1.46 (0.80-2.67)	3.16 (2.45-4.08)

* Model 1 is Cox proportional hazard model, adjusted for age and sex.

Table 5-12 Hazard Ratios for incident out-of-hospital fatal CHDs and for the exact place of death in ARIC Cohort (1987-2019) (N=14,979).

	Black participants (n=4095)	White participants (n=10884)
Dead on arrival to hospital		
Events	8	12
Person-years	86449	258590
Incidence Rate (95 % CI) per 1,000 person-years	0.09 (0.04-0.17)	0.05
Model 1*, HR (95% CI)	2.38 (0.97-5.85)	ref
Died in other undefined place		
Events	28	50
Person-years	86449	258590
Incidence Rate (95 % CI) per 1,000 person-years	0.32 (0.22-0.46)	0.19
Model 1*, HR (95% CI)	2.06 (1.28-3.30)	ref
Died in residency		
Events	67	148
Person-years	86449	258590
Incidence Rate (95 % CI) per 1,000 person-years	0.78 (0.61-0.98)	0.57
Model 1*, HR (95% CI)	1.69 (1.26-2.26)	ref

*Model 1 only adjusted for sex and age.

CHAPTER 6:RACIAL DIFFERENCES IN RECURRENT ACUTE MYOCARDIAL INFARCTION IN THE COMMUNITY: FINDINGS FROM THE ARIC COMMUNITY SURVEILLANCE STUDY FROM 2005 TO 2014

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6.1. Abstract

6.1.1. Background

Racial differences in recurrent acute myocardial infarction (AMI) were previously reported primarily among elderly populations over 65 years old. This might mask racial disparities since Black individuals tend to have fatal AMI earlier in life than White individuals. We examined racial differences in the rates of recurrent AMI, along with incident AMI, in a community population aged 35 and over, overall and by sex and age

6.1.2. Methods

The Atherosclerosis Risk in Communities (ARIC) Study sampled hospitalizations for recurrent and incident AMI in a surveillance population of 470,000 residents aged 35-84 years in 4 U.S. communities between the years 2005-2014 using ICD-9-CM codes. AMI hospitalizations were validated by standardized review procedures. After accounting for sampling design, we used Poisson regression models to estimate racial differences in recurrent and incident AMI rates.

6.1.3. Results

Recurrent and incident AMI rates per 1000 population were 8.8 (95% CI, 8.3-9.2) and 20.7 (95 % CI, 20.0-21.4) in Black men, 6.8 (95% CI, 6.5-7.0) and 14.1 (95 % CI, 13.8-14.5) in White men, 5.3 (95% CI, 5.0-5.7) and 16.2 (95 % CI, 15.6-16.8) in Black women, and 3.1 (95% CI, 3.0-3.3) and 8.8 (95 % CI, 8.6-9.0) in White women, respectively. The age-adjusted incident rate ratios (IRR) of recurrent AMI were higher in Black women vs. White women (IRR, 2.09 95 % CI, 1.64-2.66) and Black men vs. White men (IRR, 1.58 95 % CI, 1.30-1.92)). The corresponding IRRs were slightly lower for incident AMI: Black women vs. White women, IRR,

1.65 (95 % CI, 1.42-1.92) and Black men vs. White men, IRR, 1.49 (95 % CI, 1.30-1.71). There were no significant sex and race interactions.

6.1.4. Conclusions

In four U.S. communities, Black individuals had higher recurrent and incident AMI rates than White individuals. The magnitude of the racial differences in recurrent AMI rates were more pronounced than incident AMI rates particularly among women.

6.2. Introduction

Survivors of an acute myocardial infarction (AMI) are at risk of recurrent infarctions, which occur at an annual rate that is six times higher than the incidence of AMI in people of the same age without coronary heart disease (CHD)[24]. Previous studies suggest that Black patients have worse 30-day and 5-year mortality following an AMI than White patients[62, 122]. Part of the differences in the outcome of AMI by race could reflect a higher reinfarction rate in Black patients compared with White patients. However, few studies have examined race-related differences in AMI recurrence. Furthermore, most previous studies of race differences in the outcome of AMI examined Medicare beneficiary patients 65 years of age or older[1, 4, 122-124]. Examining older patients could mask race-related differences since Black individuals tend to develop AMI and die from it earlier in life than White individuals[5]. Also, most studies did not differentiate between incident and recurrent AMI events[123] or only examined composite cardiovascular disease events after the incident AMI[125]. Finally, most studies relied on administrative databases without adjudication of AMI events[1, 4, 124] which could result in event misclassification.

Clarification of racial differences in recurrent AMI would improve understanding of race-related disparities in total CHD. In the community surveillance component of the Atherosclerosis Risk in Communities (ARIC) study, we examined racial differences in the rates of recurrent AMI, overall and by sex and age, and contrasted the results with the rates of incident AMI. We hypothesized that Black individuals have a higher rate of AMI recurrence in addition to a higher rate of MI incidence compared to White individuals.

6.3. Methods

6.3.1. Study population

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to the Atherosclerosis Risk in Communities (ARIC) publications committee.

We used data from the community surveillance component of the ARIC study. Four entire communities were systematically surveilled to describe the community-wide occurrence of hospitalized AMI and CHD deaths for years 2005-2014. The surveilled communities included Forsyth County, North Carolina; the city of Jackson, Mississippi; eight northern suburbs of Minneapolis, Minnesota; and Washington County, Maryland, for a total of approximately 470,000 men and women aged 35-84 years[65]. We excluded 1779 Non-White and Non-Black participants as suggested by the ARIC surveillance community analysis guidelines, since Non-White and Non-Black participants were not technically part of population sampled[126].

6.3.2. Definition of exposure

We used the “race” abstracted from the hospital medical records as the exposure variable and categorized it as "Black individuals" vs. "White individuals."

6.3.3. Identification of recurrent and incident AMI events

Both recurrent and incident hospitalized AMI were identified from the electronic discharge lists of the 31 hospitals serving the four ARIC communities. Trained ARIC staff members abstracted medical records for sampled events and collected information on age, residence in the community, and discharge codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 402, 410–414, 427, 428, and 518.4). The events were randomly selected within each discharge code, but the sampling fraction varied by sex, race, and center[127]. Information on chest pain, level of cardiac biomarkers (total creatinine phosphokinase, creatinine phosphokinase-myocardial band, lactate dehydrogenase, and troponin) and history of AMI and other cardiovascular comorbidities was abstracted from the medical records. Additionally, copies of up to three ECGs of the patients were sent to the University of Minnesota Electrocardiographic Reading Center for classification using the Minnesota code[67]. The AMI diagnosis was determined using a standardized computer algorithm based on chest pain, cardiac biomarkers, and electrocardiograms[64]. A recurrent AMI was defined as any 'definite or probable AMI' for which the medical record stated a history of AMI following standard ARIC definitions[128]. An incident AMI was defined as an AMI event in a person for whom the medical record either stated that there was no history of AMI or did not contain any reference to a history of AMI.

A panel of physicians reviewed the cases to make the final diagnosis decision if the discharge diagnosis codes and the computer diagnosis did not align. Events occurring outside the study area were not included. In case of patients transferred from a surveillance hospital, the transferring surveillance hospital's diagnostic information was used for the events' validation.

As a secondary analysis, we examined racial differences in 28-day and 365-day case-fatality of recurrent and incident AMI. In ARIC, hospitalized AMI events were linked to death certificate data provided by the state health departments or the National Death Index[129] to determine the 28-day and 365-day case-fatality of validated AMI events. The data for deaths was reviewed and assigned a diagnosis by the ARIC Mortality and Morbidity Classification Committee using standardized criteria[64]. Further details are provided in the ARIC Study Surveillance Manual[129].

6.3.4. Statistical Analysis

First, we tabulated the distributions of information on recurrent and incident AMI events by race and sex. Next, we computed incidence rates per 1,000 persons and 95% confidence intervals (CI) for both recurrent and incident AMI by race and sex. We constructed age-adjusted Poisson regression models (Model 1) to compare incident and recurrent AMI rates in Black men vs. White men and in Black women vs. White women and tested race and sex interactions. We also examined racial differences by age group in men and women separately. Among men, we used 5-year age groups, ranging from 40-44 years to 80-84 years. Among women, to allow a sufficient number of cases, we used 3 age groups: 35-59, 60-74, and 75-84.

To obtain a complete description of racial differences in outcome of AMI, as a secondary analysis we also calculated the 28-day and 365-day case-fatality rate of both recurrent and incident hospitalized AMI events. We used logistic regression to compare the case-fatality of both recurrent AMI and incident AMI in Black men vs. White men and in Black women vs. White women.

We used established procedures for surveillance data while creating the models. In ARIC, sampling probabilities were reviewed periodically and modified over the surveillance period for efficiency. The methods for the sampling procedure are described in detail elsewhere[127]. We weighted all statistical models and computed standard errors by stratified random sample methodology to reflect the sampling scheme. All analyses were conducted in SAS version 9.4. An institutional review board at each site approved the ARIC study. We also obtained approval from the Emory University Institutional Review Board (IRB00111905).

6.4. Results

6.4.1. Characteristics of the study population

Between 2005 and 2014, after applying population weights 13,101 incident and 5,368 recurrent AMI events occurred in the ARIC surveillance communities aged 35-84. Of the recurrent events, 957 occurred in Black men, 2444 in White men, 636 in Black women, and 1330 in White women. The basic characteristics of patients hospitalized for a recurrent AMI are described in Table 6-1. Corresponding data for incident AMI are reported in Table 6-4. The mean age (S.D.) for recurrent AMI was 58.8 (0.6) in Black men, 67.7 (0.6) in White men, 61.1 (0.5) in Black women, and 69.9 (0.7) in White women. While the mean age for recurrent AMI was similar to that for incident AMI in Black men and women, it was older among White men and women. Among both recurrent and incident AMI events, there were large racial differences by health insurance status. The percentage of patients who had no health insurance among Black individuals was about twice of those among White individuals. Current smoking frequency, history of hypertension and diabetes were higher among Black patients than among White patients, either men or women and for both recurrent and incident AMI events.

6.4.2. Racial differences in rates of recurrent and incident AMI

Table 6-2 shows the association of race with recurrent AMI and incident AMI events. The recurrent AMI rate per 1000 population was higher in Black men (8.8, 95 % CI, 8.3-9.2)) than White men (6.8, 95% CI, 6.5-7.0), and in Black women (5.3, 95% CI, 5.0-5.7) than White women (3.1, 95% CI, 3.0-3.3). Comparing Black men with White men, the age-adjusted incident rate ratio (IRR) for recurrent AMI was 1.58 (95 % CI, 1.30-1.92). The same figure was 2.09 (95 % CI, 1.64-2.66) comparing Black women with White women.

The magnitude of racial differences in incident AMI rates was slightly less than racial differences in recurrent AMI rates, especially for women. Comparing Black men with White men, the IRR for incident AMI was 1.49 (95% CI, 1.30-1.71) and comparing Black women with White women, it was 1.65 (95% CI, 1.42-1.92). There were no significant interactions for recurrent or incident AMI in age-adjusted Poisson models.

6.4.3. Racial differences in rates of recurrent AMI among age groups

Figure 6-1 illustrates racial differences in recurrent AMI rates among different age groups by sex. The age-adjusted IRR of recurrent AMI in Black vs. White individuals was higher in magnitude among the younger age groups and declined among older age groups among both men and women. There was a significant interaction between race and age ($p < 0.001$).

6.4.4. Racial differences in the 28- and the 365-day case-fatality ratio of recurrent AMI

Table 6-3 compares 28-day and 365-day mortality for recurrent and incident AMI between Black and White individuals. Among the recurrent AMI, 28- and 365-day case-fatality were slightly lower in Black men vs. White men (respectively, OR, 0.88, 95% CI, 0.48-1.61 and

OR, 0.79, 95% CI, 0.52-1.22). In contrast, among the incident AMI, the 28-day and 365-day age-adjusted case-fatalities were higher in Black men vs. White men (respectively, OR, 1.29, 95% CI, 1.18-1.40 and OR, 1.93, 95% CI, 1,43-2.60). Among both recurrent and incident AMI, the 28- and 365-day case-fatality were higher in Black women vs. White women (Table 6-3**).**

6.5. Discussion

In this community-based surveillance study, the rates of recurrent AMI were higher in Black than in White community individuals who had survived an AMI, both among men and among women. Age-adjusted racial differences in recurrent AMI were higher in magnitude among younger age groups and disappeared among those aged 70 years and over. Also, both 28- and 365-day case-fatality of recurrent AMI were higher in Black women vs. White women, although the estimated differences were not significant. The corresponding case fatality was slightly lower in Black men vs. White men. Our analysis suggests that the magnitude of the racial differences in recurrent AMI rates was higher than the racial differences in incident AMI, particularly among women.

Earlier studies have reported declining trends in recurrent AMI[4, 15, 123]. However, previous analyses in Medicare populations indicate that these declines were less in Black individuals compared to White counterparts[1, 2, 130]. Our findings parallel these previous analyses but also extend them to the population aged 35-84 years, as the first study of race differences in reinfarction in the broad community. Our analysis additionally suggests that racial differences in recurrent AMI are more pronounced among women and younger age groups.

Several factors could explain racial disparities in recurrent AMI. First, patient-level risk factors and existing pre-AMI health status could play a role. Reports from large clinical databases have suggested that racial differences in mortality and readmission after the index AMI could be attributable to patient-related factors, such as cardiovascular risk factors and comorbidities[122, 131, 132]. A recent analysis of the REGARDS cohort study also suggested that racial disparities in cardiovascular events, as a composite outcome, after an incident AMI are largely dependent on differences in pre-admission health history and clinical characteristics of the AMI[125]. Black individuals have a higher prevalence of cardiovascular risk factors such as hypertension, diabetes, obesity than White individuals in the community[113]; therefore, racial disparities in incident AMI could be explained by these patient-level differences[133]. However, our study shows that racial differences continue to exist for recurrent AMI among those who have experienced an incident AMI, and the disparity is actually magnified. These results implicate differences by race in access to secondary prevention opportunities after the first AMI. Indeed, some studies have suggested that racial disparities in AMI outcomes could be explained by differences in use of secondary prevention therapies[124, 134]. A recent data analysis from 400 US hospitals suggests that Black patients are less likely to receive several types of preventive approaches than Whites, such as smoking cessation counseling, and therapies such as clopidogrel[58]. Also, previous literature suggests that Black patients with acute AMI are less likely than White patients to receive invasive coronary interventions[57, 135]. Early revascularization is associated with a reduction in long-term mortality of AMI[135]. Also, time from the onset of AMI to the use of these interventions could play a role in racial disparities in recurrent AMI rates and case-fatality. Shorter time to interventions, such as percutaneous coronary intervention, is associated with lower mortality after AMI[136]. Several studies reported that among patients hospitalized for AMI, "time to treatment" was longer for Black patients than White patients even after adjustments for clinical and sociodemographic variables[49, 137]. Thus, differences in time to treatment could contribute to racial disparities in the case-fatality of recurrent AMI.

Other factors could explain racial differences in rates of recurrent AMI. Physician bias, attitudes, and patients' perceptions of their own health could contribute to differences in follow-up care[138, 139]. Also, participation in cardiac rehabilitation, which is associated with lower mortality after an AMI[140], could play a role since Black people are less likely to participate in and get a referral to cardiac rehabilitation after an AMI compared to White counterparts[141, 142]. Furthermore, Black individuals are reported to be less aware of the symptoms of an AMI and less likely to call emergency services in the setting of an AMI than White individuals[112].

Our findings extend the literature of racial disparities in recurrent AMI from predominantly elderly populations (e.g., Medicare populations) to younger age groups. In our study, the racial difference in recurrent AMI was only seen among younger patients, and became similar in Black and White individuals around age 70 years, and even lower among Blacks than Whites after age 75 years. A previous study reported that racial differences in hospital death after AMI are larger among younger as opposed to older patients[143]. Since Black individuals tend to develop CHD at younger age and die from it earlier in life than Whites[5], this "race-crossover effect" could mask a survivorship bias, such that Black persons developing CHD at older age may represent a more resilient group [144].

Our study has several strengths, including the large sample size, the inclusion of younger age groups (beginning at age 35 years), the event adjudication by an expert committee which minimizes misclassification, and the utilization of a decade-long surveillance system in a community-based setting. Our study also has some limitations. We could not separate race effects from regional effects since the ARIC study design only provides sufficient numbers of

Black individuals appropriate for analysis in 2 communities (Jackson, Mississippi, and Forsyth County, North Carolina). Also, since this was a community surveillance design, and ARIC did not follow up all community residents, there was no data on patient-level socioeconomic and cardiovascular risk factors, except for information abstracted from the medical records for the AMI hospitalization (smoking and history of hypertension and diabetes). Also, we were not able to adjust for risk factors abstracted from the medical records in the models, since the events were sampled for surveillance based only on sex, race and age group and sampling probabilities were not available for other factors. For these same reasons, incident events could not be linked to recurrent events on an individual basis. Finally, the ARIC surveillance study did not provide data on post-discharge factors that might influence the recurrence and the case fatality of AMI, such as receipt of preventive treatments or physician follow-up after discharge, which will need to be considered in future patient-level cohort studies.

In conclusion, we found large disparities for recurrent AMI rates by race in the community. The magnitude of these racial disparities is stronger for recurrent events than incident events, and racial disparities are seen among younger people only. While future study is needed to explain the reason for such disparities, differential use of secondary prevention interventions after the first AMI may be implicated. Equal access to health care services, including secondary prevention treatments, timely revascularization and enrollment in cardiac rehabilitation, could help decrease disparities for recurrent events after the first AMI. These interventions should specifically target younger populations to narrow the racial gap in the outcome of AMI.

6.6. Acknowledgments

The authors thank the staff and participants of the ARIC study for their important contributions.

6.7. Sources of Funding

The Atherosclerosis Risk in Communities study has been funded in whole or in part with Federal funds from the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services, under Contract nos. (HHSN2682017000001I, HHSN2682017000002I, HHSN268201700003I, HHSN268201700005I, HHSN268201700004I). Dr Duygu Islek is funded by the American Heart Association pre-doctoral fellowship (Award number: 19PRE34380062).

Table 6-1 Basic characteristics of the patients who were hospitalized for a recurrent AMI event between years 2005-2014 by race and sex in the ARIC Surveillance Community Study.

	Black Men (N=957)	**White Men (N=2444)**	**Black Women (N=636)**	**White Women (N=1330)**
Age, mean (SE)	58.8 (0.6)	67.7 (0.6)	61.1 (0.5)	69.9 (0.7)
Health insurance status No (%)				
No insurance	139 (16 %)	136 (7 %)	55 (9 %)	39 (4 %)
Medicare	91 (11 %)	173 (8 %)	47 (8 %)	83 (8 %)
Medicaid	306 (36 %)	233 (11 %)	309 (53 %)	220 (21 %)
Prepaid insurance or health plan	178 (21 %)	1307 (64 %)	132 (22 %)	627 (60 %)
Other	136 (16 %)	193 (9 %)	44 (7 %)	80 (8 %)
Smoking history No (%)				
Current	415 (44 %)	853 (36 %)	185 (29 %)	302 (23 %)
Never	273 (29 %)	545 (23 %)	321 (51 %)	547 (42 %)
Past smoker	248 (27 %)	991 (41 %)	124 (20 %)	462 (35 %)
Comorbidities No (%)				
History of hypertension	884 (92 %)	2100 (86 %)	602 (95 %)	1156 (87 %)
History of diabetes	483 (50 %)	376 (15 %)	385 (60 %)	294 (22 %)

Table 6-2 Association of race with recurrent and incident myocardial infarction events in the ARIC Community Surveillance Study between years 2005-2014.

	Black Men	**White Men**	**Black Women**	**White women**
Recurrent AMI				
Cases	957	2444	636	1330
The community population at risk	109301	362019	119730	429977
Incident Rate (95 % CI) per 1,000	8.8 (8.3-9.2)	6.8 (6.5-7.0)	5.3 (5.0-5.7)	3.1 (3.0-3.3)
Model 1[1], IRR (95% CI)	1.58 (1.30-1.92)	**ref**	2.09 (1.64-2.66)	**ref**
Incident AMI				
Cases	2259	5119	1939	3784
The community population at risk	109301	362019	119730	429977
Incident Rate (95 % CI) per 1,000	20.7 (20.0-21.4)	14.1 (13.8-14.5)	16.2 (15.6-16.8)	8.8 (8.6-9.0)
Model 1[1], IRR (95% CI)	1.49 (1.30-1.71)	**ref**	1.65 (1.42-1.92)	**ref**

IRR: Incident rate ratio

[1] Model 1 is a Poisson regression model adjusted for age

Table 6-3 Racial differences in 28-and 365-day mortality of recurrent and incident acute myocardial infarction in the ARIC Surveillance Community Study between years 2005-2014.

	Black Men	**White Men**	**Black Women**	**White Women**
		Recurrent AMI		
28-day case-fatality				
Fatal events (n)	53	199	54	131
Total recurrent AMI cases	957	2444	636	1330
Case-fatality %	5.54 (4.44-6.88)	8.14 (7.28-9.09)	8.49 (6.84-10.49)	9.85 (8.59-11.28)
Model 1[1], OR (95% CI)	0.88 (0.48-1.61)	ref	1.44 (0.74-2.83)	ref
365-day case-fatality				
Fatal events (n)	126	497	117	263
Total recurrent AMI cases	957	2444	636	1330
Case-fatality %	13.16 (11.47-15.07)	20.35 (19.03-21.71)	18.40 (16.01-21.06)	19.77 (18.04-21.63)
Model 1[1], OR (95% CI)	0.79 (0.52-1.22)	ref	1.40 (0.85-2.30)	ref
		Incident AMI		
28-day case-fatality				
Fatal events (n)	165	344	160	357
Total recurrent AMI cases	2259	5119	1939	3784
Case-fatality %	7.29 (6.45-8.26)	6.72 (6.17-7.32)	8.25 (7.28-9.34)	9.43 (8.68-10.25)
Model 1[1], OR (95% CI)	1.29 (1.18-1.40)	ref	1.25 (0.82-1.92)	ref
365-day case-fatality				
Fatal events (n)	358	584	316	619
Total recurrent AMI cases	2259	5119	1939	3784
Case-fatality %	15.85 (14.62-17.15)	11.41 (10.70-12.16)	16.30 (14.96-17.72)	16.36 (15.39-17.37)
Model 1[1], OR (95% CI)	1.93 (1.43-2.60)	ref	1.46 (1.05-2.02)	ref

[1]Model 1 is the age-adjusted logistic regression model. Survey logistic procedure was used to calculate the odds ratios.

Table 6-4 Basic characteristics of the patients who were hospitalized for an incident AMI between years 2005-2014 by race and sex in the ARIC Surveillance Community Study.

	Black Men (N=2259)	**White Men (N=5119)**	**Black Women (N=1939)**	**White women (N=3784)**
Age, mean (SE)	58.7 (0.4)	63.9 (0.5)	60.7 (0.8)	68.3 (0.4)
Health insurance status No (%)				
No insurance	375 (20 %)	445 (11 %)	199 (11 %)	195 (6 %)
Medicare	189 (10 %)	338 (8 %)	109 (6 %)	204 (6 %)
Medicaid	553 (30 %)	323 (8 %)	763 (44 %)	435 (14 %)
prepaid insurance or health plan	561 (30 %)	2706 (65 %)	578 (33 %)	2083 (66 %)
other	185 (10 %)	355 (9 %)	82 (5 %)	225 (7 %)
Smoking history No (%)				
Current	964 (44 %)	1570 (32 %)	511 (27 %)	894 (24 %)
Never	714 (33 %)	1728 (35 %)	1010 (53 %)	1738 (47 %)
Past smoker	518 (24 %)	1658 (33 %)	374 (20 %)	1034 (28 %)
Comorbidities No (%)				
History of hypertension	1900 (84 %)	3319 (65 %)	1716 (88 %)	2845 (75 %)
History of diabetes	1047 (46 %)	1605 (31 %)	1009 (52 %)	1419 (38 %)

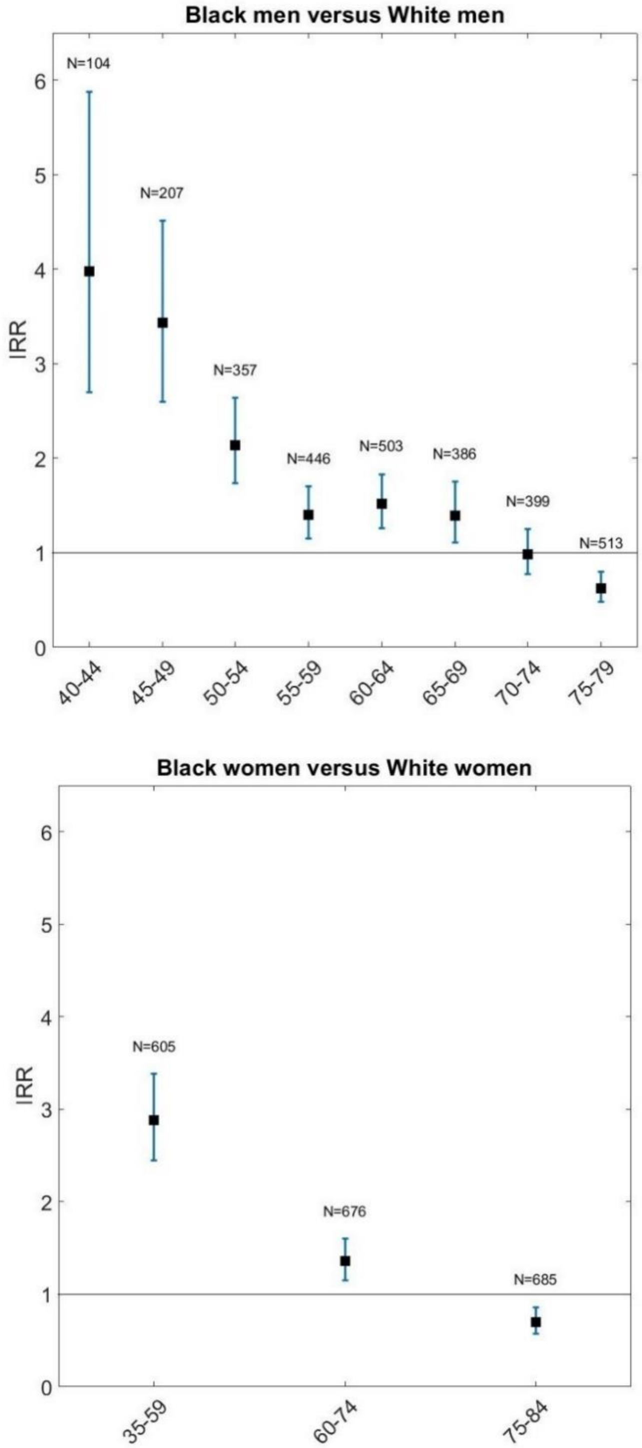

Figure 6-1 Racial differences in recurrent AMI rates among different age groups by sex in the ARIC Surveillance (2005-2014).

(IRR: incident rate ratios. Among women, age brackets were collapsed to allow for a sufficient number of events

The N reported above the IRR reflects the total number of observations in each specified age group.)

CHAPTER 7: SUMMARY AND FUTURE DIRECTIONS

7.1. Summary

In the United States, an American will have an acute myocardial infarction (AMI) approximately every 40 seconds[30]. Over the past decades, despite considerable improvements in the prevention of coronary heart disease (CHD), significant racial disparities in the trends of CHD incidence and mortality have been highlighted [1-7]. The factors driving these inequalities, however, are not well understood. The overarching goal of this dissertation was to take a broad approach to this issue and investigate racial differences in the rates of initial hospitalization for acute coronary syndromes, in the rates of out-of-hospital fatal CHD, and in the rates of recurrent AMI. These areas have been relatively neglected in previous research, but could help illuminate important aspects of race disparities in CHD incidence and outcome and inform prevention strategies. We hypothesized that, compared with White counterparts, Non-White individuals are less likely to be hospitalized when they initially present to the emergency department (ED), more likely to die out-of-hospital, and more likely to die from a recurrent AMI if they survived the first AMI.

In the first study, we used data from the State Inpatient Databases[145] and the State Emergency Department Databases[146] of the Healthcare Cost and Utilization Project (HCUP)[147] to examine whether there are racial differences in the rates of being sent home in individuals who present to the ED and receive a discharge code of AMI or unstable angina. Also, we examined the role of health insurance as a mediator in these associations. Our results suggest that Black and Hispanic patients were more likely to be sent home with a discharge code of AMI or unstable angina after their visit to the ED compared to White patients. In contrast, differences were small in Asian patients vs. White patients. However, among patients below 55 years of age, disparities were magnified and all racial groups were more likely to be sent home after receiving an ED diagnosis of ACS than their White counterparts. Health insurance had no role as a mediator in explaining these associations. These findings suggest that important racial disparities exist in hospitalization of ACS at the ED, which are especially marked among younger patients. Our results suggest an important area for quality improvement in healthcare.

In the second study, we used data from the cohort component of the Atherosclerosis Risk in Communities (ARIC) study to examine racial differences in the rates of out-of-hospital and in-hospital incidence of fatal CHD among US adults free of CHD at baseline. To consider a full range of outcomes, we also examined non-fatal incident CHD and case fatality among those who were hospitalized. We further investigated the mediating effect of income on these outcomes. Our results suggest that both out-of-hospital and in-hospital incident fatal CHD was approximately doubled in Black versus White individuals, whereas there was no difference by race in incident non-fatal CHD. These findings highlight that CHD is more fatal in Black than in White individuals irrespective of where the event occurs. Income, as a mediator, played a much larger role in the association of race with out-of-hospital death than for in-hospital CHD death, suggesting a key role of healthcare access.

In the third study, we used data from the surveillance component of the Atherosclerosis Risk in Communities (ARIC) study, to examine racial differences in the rates of recurrent AMI at the community level, overall and by sex and age, and contrasted the results with the rates of incident AMI. Our findings suggest that the rates of recurrent AMI were approximately twice as high in Black than in White individuals who had survived an AMI, both among men and among women. The magnitude of these racial disparities was stronger for recurrent events than incident events, and, again, racial disparities were seen predominantly among younger people. Equal access to health care services, including secondary prevention treatments, could help decrease disparities for recurrent events after the first AMI. Our results suggest that a focus on younger populations should help reduce inequalities in CHD.

7.2. Strengths

This dissertation project had several strengths. In the first study, we used the HCUP datafiles, which capture all ED visits for AMI and unstable angina in non-federal facilities for the selected states and years. This allowed us to avoid selection bias related by insurance status or physician reporting, and likely increased the precision of our results[97]. Also, we included Asian patients and patients from all age groups in our analysis, which allowed us to improve on findings of previous studies which reported hospitalization rates among smaller populations, samples less diversity in race distribuion[8] or in Medicare populations only, which primarily include patients over the age 65[87, 98]. In both the first and the second study, we used rigorous methods, namely inverse probability weighting, which helped avoid the potential biases associated with mediation analysis which might have been present in previous studies.

In the second study, we analyzed data from a large cohort with a long duration of follow-up in a community-based setting. For mediation analysis. Another strength, specific to this project, was the use of self-reported race, as suggested by the recent guidelines for disparities research,[99, 100] rather than inferring race from other sources.

In the third study, we analyzed data from a decade-long surveillance system in a community-based setting which provided us a large sample size with the inclusion of younger age groups. For both the second and the third project, using data from the ARIC study allowed us to minimize event misclassification since all events in ARIC are adjudicated by an expert committee.

7.3. Limitations

This dissertation project had some limitations. In the first study, we used the primary ICD 9 or ICD 10 discharge codes to identify ED discharges with AMI and unstable angina and could not verify the diagnosis with ECG findings or blood test results since HCUP datafiles are administrative datasets that do not provide information on clinical findings. In the same analysis, we excluded patients with chronic CHD using ICD 9 or 10 codes to minimize misclassification, however, this information was subject to physician's coding behavior and we might have missed some patients with chronic CHD if the physician chose not to record this information. Furthermore, we used an income classification variable from the HCUP datafiles that was constructed as an ecologic measure based on the patient's ZIP code. Although this was a good proxy for "individual income," it could be subject to misclassification. Finally, information on race was not self-reported as recommended by recent guidelines for disparity research[99, 100]. Instead, it was provided by the individual states (the data sources) that participated in HCUP, which could be another source of misclassification[101].

In the second and third study, as a limitation in ARIC study, all participants in the Jackson site were Black, and participants in the Minnesota and Maryland sites were predominantly White; therefore, we were not able to fully separate differences by race from differences by study site. Also, specific to the third study which was based on ARIC community surveillance, there was no data available on patient-level socioeconomic and cardiovascular risk factors, except for information abstracted from the medical records for the AMI hospitalization (smoking and history of hypertension and diabetes). Furthermore, we were not able to adjust for risk factors abstracted from the medical records in the models, since the events were sampled for surveillance based only on sex, race and age group and sampling probabilities were not available for other factors. For these same reasons, there was no follow up of community residents and incident events could not be linked to recurrent events on an individual basis.

7.4. Public Health Impact and Future Directions

Improving the cardiovascular health of all Americans and addressing disparities in health and health care access to reduce cardiovascular mortality has long been a national priority[16-20]. In this dissertation project, we aimed to understand racial differences in specific understudied outcomes, namely, hospitalization after presenting to the ED for an ACS, out-of-hospital CHD mortality, and AMI recurrence and mortality to clarify the origins of these disparities at the community level.

The results of this dissertation can assist stakeholders in identifying opportunities to improve prevention policies and reduce inequalities in care in order to decrease cardiovascular disease morbidity and mortality for all Americans.

Our first study suggests an important area for quality improvement in healthcare. Our findings, suggesting racial differences in hospitalization rates at the ED, imply that hospital quality improvement programs should be prioritized by policymakers to reduce racial disparities in hospitalization rates of ACS. Hospital quality improvement programs, which aim to enhance hospital adherence to care guidelines, can reduce or even eliminate racial differences in guideline-recommended care for ACS[102-104].

The findings of our second study highlight an emerging need to target potential barriers, such as health insurance coverage, to access health care in order to prevent the excess of CHD death in Black individuals. Our findings suggest that timely access to emergency care and effective preventive interventions could decrease racial disparities in fatal CHD events and foster health equity.

The findings of our third study suggest that public health interventions to prevent disparities in recurrent AMI events should target younger people since the disparities were observed in young age groups in the community. Equal access to health care services, including secondary prevention treatments, timely revascularization and enrollment in cardiac rehabilitation, could help decrease differences by race in the rates of recurrent events after the first AMI.

This dissertation project sheds light on research areas to be investigated in future studies. Surprisingly, health insurance coverage did not have any role in explaining the associations between race and being sent home with a discharge code of ACS in our first study.
These findings warrant further investigation to examine other possible factors associated with racial differences in hospitalization rates in patients who receive a discharge code of ACS at the ED. Furthermore, post-discharge factors after AMI hospitalization might influence the recurrence and the case fatality of AMI. Receipt of preventive treatments or physician follow-up after discharge can have roles in explaining disparities in recurrent AMI. The role of these factors will need to be considered in future studies. Finally, we recognize that we could only consider socioeconomic and cardiovascular risk factors in this dissertation project. It is likely that other environmental, social, cultural and policy factors play a role in the excess CHD death among Non-White individuals. The role of these factors should be investigated in future studies.

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