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## Original Research

# Racial disparity in atherosclerotic cardiovascular disease in hospitalized patients with diabetes 2005–2015: Potential warning signs for future U.S. public health

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## ABSTRACT

**Introduction:** The pattern of atherosclerotic cardiovascular disease (ASCVD) and diabetes driven hospitalizations in the United States (U.S.) is unclear. We attempted to identify the disparate outcome in race related ASCVD hospitalizations with comorbid diabetes.

**Methods:** Adults aged  $\geq 40$  years old with ASCVD (acute coronary syndrome (ACS), coronary artery disease (CAD), stroke, or peripheral arterial disease (PAD)) as the first-listed diagnosis with comorbid diabetes as a secondary diagnosis were determined using the U.S. 2005–2015 National (Nationwide) Inpatient Sample (NIS) data. The incidence of other modifiable cardiovascular risk factors (hypertension, dyslipidemia, smoking/substance abuse, obesity, and renal failure), in hospital procedures and outcomes was estimated. Complex samples multivariate regression was used to determine the odds ratio (OR) with 95% confidence Interval (CI) of risk associations and to determine patient comorbidity adjusted ASCVD related in-hospital mortality rate.

**Results:** The rate of total ASCVD hospitalizations with comorbid diabetes adjusted to the U.S. census population increased by 5.7% for black men compared to 4% for black women. There was a higher odd of an ASCVD hospitalization if there was comorbid hypertension (Odds Ratio (OR) 1.29; 95% CI 1.28–1.31), dyslipidemia (OR 2.03; 95% CI 2.01–2.05), renal failure (OR 1.84; 95% CI 1.82–1.86), and smoking/substance use disorder (OR 1.31; 95% CI 1.29–1.33). White Women had the highest risk-adjusted incidence of ASCVD related in-hospital mortality (4.2%) relative to black women (3.9%), compared to white men (3.6%) and black men (3.5%) respectively.

**Conclusions:** Despite improving treatment options for ASCVD in the diabetic population, blacks with diabetes continue to have a higher hospitalization burden with a concomitant disparity in comorbid presentation and outcome. Further evaluation is the need to understand these associations.

## 1. Introduction

U.S. blacks have a relatively high incidence of atherosclerotic cardiovascular disease (ASCVD) [1]. ASCVD related adverse events are more frequent in U.S. blacks with ASCVD when compared to whites [2]. Furthermore, there is considerable variation in traditional metabolic parameters like subclinical inflammation, underlying lipoprotein profile, adipokine levels in blacks [3]. The presence of concomitant diabetes predictably accelerates the pathogenic process precipitating acute ASCVD events requiring hospitalization [4]. Hospitalizations for ischemic heart disease, stroke, and not uncommonly PAD result in a substantial burden on the healthcare system [5]. It gets compounded by

regional, socio-economic, racial, and sex disparities in health care delivery. Unfortunately, racial minorities, specifically blacks, despite representing thirteen percent of the U.S [6], a significant minority in the American population, are underrepresented in multiple CV outcome trial populations and guideline documents [7]. Given the above concerns, it becomes imperative to understand the incidence of ASCVD, and its outcome in U.S. blacks with diabetes.

To understand this shortcoming, we evaluated and compared racial and sex-specific national trends in ASCVD related hospital hospitalizations with comorbid diabetes among adult patients aged 40 years and older. We also evaluated the role of comorbid factors in patients with diabetes leading to a hospitalization with a principal diagnosis ASCVD.

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Further, we attempt to estimate ASCVD related in-hospital procedural selection and in-hospital mortality. The principal diagnosis of ASCVD is defined as one of four specific diagnoses: coronary artery disease (CAD), peripheral artery disease (PAD), acute myocardial infarction (AMI), and ischemic stroke (referred to from now on as stroke).

## 2. Methods

### 2.1. Data source

Data were obtained from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) databases of years 2005–2015 [8]. The NIS is a nationwide administrative

database reporting discharge-level data collected from a 20% stratified sample of hospitals in the USA [9,10]. Each record in the NIS includes data on demographics, hospital characteristics, expected payment source, primary and secondary diagnoses and procedures, severity and comorbidity measures, total charges, length of stay, and discharge status. Discharge weights (trend weights for data before 2012) are provided for each record and can be used to obtain national estimates. The NIS data files are publicly available to other researchers to reproduce our analyses. This study was considered exempt from the Institutional Review Board approval because patients were not involved in any part of developing the research question, study outcome measures, study design, or conduct of the study. There are no plans to disseminate the results of the research to study participants.

### 2.2. Study population

For this report, the study population of adult hospitalizations (defined by administrative per in-hospital stay discharge data) aged 40 years and older were selected. Hospitalizations with ASCVD was defined using the following Clinical Classification Software (CCS) principal diagnosis categories- 100: acute myocardial infarction (AMI); 101: coronary artery disease (CAD); 109: acute cerebrovascular disease (i.e., stroke); 114: Peripheral and visceral atherosclerosis (PAD); 116: Aortic and peripheral arterial embolism or thrombosis. CCS categorizes the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis, and procedure codes into a manageable number of clinically meaningful categories. This clinical grouper makes it easier to understand patterns of diagnoses and procedures use quickly. Furthermore, the principal diagnosis is that condition established after study to be chiefly responsible for the patient's admission and discharge from the hospital. Secondary diagnoses are concomitant conditions that coexist at the time of admission or develop during the stay. All-listed diagnoses in the database include the principal diagnosis plus additional secondary conditions. Major cardiovascular risk factors are identified using elixhauser comorbidity conditions (Hypertension, Obesity, Diabetes, renal failure) provided in the dataset, as well as CCS secondary diagnosis codes (Table 1). Procedure CCS codes were used to identify hospitalizations undergoing major limb amputation.

### 2.3. Baseline characteristics and outcome measures

The primary variable evaluated was patient race. The race is directly coded in the NIS and contains the following categories: Non-Hispanic

Whites, Non-Hispanic Blacks (representing A.A and referred as blacks), Asian, Native American, and others. The current study analyzed disparity between blacks and whites further dividing it into men and women. The unit of analysis was the hospital discharge (henceforth labeled; hospitalizations), not a person or patient. A person admitted to the hospital multiple times in 1 year could have been counted each time as a separate discharge from the hospital. Time in years was used as a continuous variable.

We used the following as comorbid baseline characteristics: demographics (age, sex, primary insurance payer, a weekend admission, median household income for patient's ZIP code), hospital-level characteristics (bed size, teaching status), and Elixhauser comorbid conditions (heart failure, alcohol abuse, anemia, rheumatoid arthritis/collagen vascular diseases, chronic pulmonary disease, coagulopathy, depression, hypertension, hypothyroidism, liver disease, cancer, fluid and electrolyte disorders, neurological disorders, obesity, peripheral vascular disease, chronic renal failure). Our primary objective was to elucidate racial difference in a principal ASCVD related hospitalization with comorbid diabetes. Secondary objectives were 1: Identify the pattern of comorbid modifiable risk factor profiles of ASCVD hospitalizations with diabetes over time. We chose the following as Modifiable risk factors based on their association with diabetes and ASCVD in the literature: Hypertension, Dyslipidemia, Obesity, renal failure, and smoking/substance abuse); 2: determine the presence of concomitant vascular bed involvement. 3: racial disparity for inpatient procedures related to ASVD hospitalizations comparing the incidence of major limb amputations. Finally, we review the disparity in ASCVD hospitalizations related in-hospital mortality.

### 2.4. Statistical analysis

Weighted data were used for all statistical analyses. Baseline characteristics were compared using the Pearson  $\chi^2$  test for categorical variables and Student t-test for continuous variables. Cumulative incidence rate was estimated for ASCVD hospital admissions with diabetes over time. Analyses of proportions over time were performed using the Cochran-Armitage test for trend. Complex samples multivariable logistic regression models accounting for clustering and stratification of data were used to compare the risk predictors of odds of admission with ASCVD, odds of in-hospital procedure. The regression coefficient of comorbid value was used to calculate risk adjusted in-hospital mortality between black men, black women, white men, and white women. Variables used in the regression models were age, primary expected insurance payer, weekend admission, median household income for the patient's ZIP code, hospital-level characteristics, and all comorbidities listed above. Analyses were done using SPSS software, version 26 (SPSS, Chicago).

## 3. Results

### 3.1. Study population

From 2005 to 2015, there were a nationally estimated 407,546,802 hospitalizations in the United States after the application of sampling weights. The following data were excluded: (1) Hospitalizations without comorbid diabetes in the secondary diagnosis field and (2) Non-white or non-black race. It resulted in leftover estimated 50,102,513 hospitalizations, which we classified as white men/women or black men/women with diabetes as a comorbidity in the secondary diagnosis field.

### 3.2. All-cause hospitalizations with comorbid diabetes: patient characteristics

Characteristics of the black and white hospitalizations with diabetes as comorbidity are listed in Table 2. There was a relatively unchanged annual change in hospitalization rate for white men and white women.

**Table 1**  
Clinical Classification software (CCS) Codes used in current study.

Coronary Artery Bypass Graft	CCS 44
Percutaneous Coronary Intervention	CCS 45
Major Limb Amputation	CCS 157
Smoking/Substance Abuse	CCS 663
Dyslipidemia	CCS 53

Abbreviations – CCS, Clinical Classification Software.

Table 2

Racial and Sex differences: Baseline Demographics, Other-Comorbidities and Hospital Characteristics of in-hospital hospitalizations with comorbid diabetes.

	Total	White Men	Black Men	White Women	Black Women
	50,101,647	19,992,826	4,186,193	20,075,039	5,847,589
Age					
Age 40-65	41.8%	40.4%	59.9%	36.3%	52.1%
Age >65	58.2%	59.6%	40.1%	63.7%	47.9%
Weekend admission	20.0%	19.4%	21.2%	20.0%	21.2%
Elective Admission	19.5%	21.2%	13.7%	20.5%	14.6%
Primary Payer					
Medicare	67.8%	67.1%	57.3%	72.1%	62.6%
Medicaid	7.7%	5.2%	14.5%	6.6%	15.2%
Private	19.5%	22.3%	19.4%	17.6%	16.6%
Self Pay	2.5%	2.4%	4.8%	1.9%	3.3%
No Charge	0.3%	0.3%	0.6%	0.2%	0.5%
Other	2.2%	2.8%	3.4%	1.6%	1.8%
Median household income					
0 to 25th Percentile (poorest)	31.8%	25.7%	50.8%	28.0%	52.7%
26th to 50th Percentile	26.6%	27.5%	21.5%	28.3%	21.4%
51st to 75th Percentile	23.0%	25.1%	16.5%	24.3%	15.7%
76th to 100th Percentile (richest)	18.6%	21.8%	11.2%	19.4%	10.1%
APRDRG Severity of illness Class					
1	11.9%	12.5%	10.6%	11.8%	11.1%
2	41.2%	40.1%	38.5%	42.8%	41.6%
3	37.1%	37.1%	39.7%	36.4%	37.7%
4	9.8%	10.3%	11.2%	8.9%	9.7%
Comorbidities					
Modifiable Risk Factors (Dyslipidemia, Chronic Kidney Disease, Obesity, Hypertension, and smoking/substance abuse)					
No risk Factor	12.6%	13.4%	11.7%	13.0%	9.5%
One Risk Factor	32.0%	30.7%	32.2%	33.2%	32.2%
Two Risk Factors	37.7%	38.0%	38.2%	37.0%	38.5%
> Three Risk Factors	17.7%	17.9%	17.9%	16.8%	19.7%
Elixhauser Comorbidities and others					
Dyslipidemia	46.1%	49.3%	45.6%	40.1%	40.8%
Substance Use Disorder	22.9%	27.1%	27%	19.1%	18.6%
HIV	0.2%	0.1%	0.8%	0.0%	0.4%
Alcohol Abuse	2.8%	4.0%	6.4%	1.1%	1.7%
Deficiency Anemia	22.7%	19.9%	27.7%	22.5%	29.3%
Collagen Vascular Disease	2.8%	1.6%	1.0%	4.0%	3.7%
Chronic Blood loss anemia	1.4%	1.3%	1.3%	1.5%	1.5%
CHF	16.0%	15.3%	15.4%	16.6%	16.8%
Chronic Pulmonary Disease	24.8%	24.2%	18.7%	27.0%	23.3%
Coagulopathy	4.8%	5.9%	5.0%	4.1%	3.6%
Depression	12.2%	9.9%	6.1%	16.5%	9.6%
Diabetes, Uncomplicated	81.3%	80.8%	77.2%	83.0%	79.7%
Diabetes, with complications	18.7%	19.2%	22.8%	17.0%	20.3%
Drug Abuse	2.2%	1.9%	6.7%	1.4%	3.0%
Hypertension	74.3%	72.9%	77.7%	73.5%	79.7%
Hypothyroidism	14.5%	9.5%	4.0%	23.0%	10.1%
Liver Disease	3.5%	3.8%	4.5%	3.1%	2.6%
Lymphoma	0.8%	1.0%	0.9%	0.7%	0.7%
Fluid and electrolyte disorders	27.7%	26.0%	28.8%	28.8%	29.0%
Metastatic Cancer	2.1%	2.3%	2.1%	1.9%	1.9%
Other neurological disorders	8.3%	7.5%	8.1%	9.1%	8.5%
Obesity	19.6%	17.5%	13.9%	21.7%	23.7%
Paralysis	3.1%	2.9%	5.2%	2.5%	4.4%
Peripheral vascular disorders	10.8%	12.8%	11.6%	9.0%	9.2%
Psychoses	4.7%	3.9%	4.7%	5.3%	5.1%
Pulmonary Circulation Disorders	2.8%	2.4%	2.4%	3.2%	3.4%
Renal failure	22.5%	22.9%	32.8%	18.7%	27.0%
Tumor	2.3%	2.8%	2.7%	1.9%	1.7%
Peptic Ulcer Disease	0.0%	0.0%	0.0%	0.0%	0.0%
Valvular Disease	4.7%	4.7%	2.8%	5.4%	3.5%
Weight loss	4.3%	4.2%	5.1%	4.0%	4.5%
Hospitalizations Per Hospital Bedsize					
Small (<200)	14.2%	14.2%	11.3%	15.6%	11.5%
Medium	26.3%	25.9%	26.5%	26.5%	27.0%
Large	59.5%	59.9%	62.3%	57.9%	61.6%
Teaching Status					
Rural	12.9%	13.2%	6.4%	15.5%	7.2%
urban non-teaching	40.7%	42.3%	31.8%	43.3%	32.3%
urban teaching	46.5%	44.5%	61.7%	41.2%	60.5%

Comparatively, among black men and black women there was an increased trend from 2005 to 2010, with decreasing hospitalization rates of ASCVD with diabetes from 2011 to 2014. There was a higher relative trend of black women hospitalizations compared to white women. Compared to white, black hospitalizations included significantly younger patients (mean age:  $69 \pm 0.1$  vs.  $64.1 \pm 0.1$  years,  $p < 0.001$ ), more likely to be women (50.1% vs. 58.3%,  $p < 0.01$ ), had a higher likelihood to be on Medicaid (5.9% vs 14.9%,  $P < 0.001$ ) and resided in the poorest household median income quartile zip code (26.8% vs 51.9%,  $p < 0.001$ ).

Incidence of other modifiable risk factors (Hypertension, Dyslipidemia, Obesity, Renal failure, and smoking/other substance use disorders) listed in the secondary diagnosis were evaluated in the diabetic hospitalizations over time. For hospitalizations with comorbid diabetes, there was an overall uniform increase in cumulative modifiable risk factor profile from 2005 to 2015 (Fig. 1).

There was considerable racial disparity in the incidence of other modifiable risk factors. Compared to white, all black hospitalizations with diabetes had a lower incidence of dyslipidemia (47.5% vs. 40.5%;  $P < 0.001$ ). Obesity was equally present in both ethnicities (19.6% vs. 19.6%;  $P < 0.4$ ). Compared to white, black hospitalizations had a higher incidence of comorbid hypertension (73.2% vs. 78.9%;  $P < 0.001$ ) and renal failure (20.8% vs. 29.4%;  $P < 0.001$ ).

### 3.3. Hospitalizations among adults with a principal diagnosis of ASCVD

Overall, there were 5,409,501 inpatient white and black hospitalizations with ASCVD from 2005 to 2015. From 2005 to 2014, the rate of total cumulative ASCVD hospitalizations adjusted to the U.S. census population amongst white adults was relatively unchanged. The rate of total ASCVD hospitalizations adjusted to the U.S. census population amongst black men increased by 5.7% compared to 4% for black women cumulatively (Fig. 2). The time trend of ASCVD hospitalizations was avoided for the year 2015, given the change of ICD-9 to ICD-10 coding. The increase in ASCVD hospitalizations in blacks was primarily driven by a higher admission for stroke (29.9% of inpatient ASCVD hospitalization

in 2005 compared to 41.7% of inpatient ASCVD hospitalization in 2014,  $p$  trend  $< 0.001$ ).

### 3.4. Association of modifiable risk factors with the incidence of ASCVD admission

Complex samples multiple logistic regression analysis was performed to allow for the determination of the independent contribution of each additional modifiable risk factor on the odds of an ASCVD hospitalizations compared to a non-ASCVD hospitalization. There was a higher odd of an ASCVD hospitalization if there was comorbid hypertension (Odds Ratio (OR) 1.29; 95% Confidence Interval (CI) 95% 1.28–1.31), Dyslipidemia (OR 2.03; 95% CI 2.01–2.05), renal failure (OR 1.84; 95% CI 1.82–1.86), and smoking/substance use disorder (OR 1.31; 95% CI 1.29–1.33). Obesity was associated with a lower odd of ASCVD related hospitalizations (OR 0.83; 95% CI 0.82–0.84) with comorbid diabetes. The pattern was uniform across race and sex. Nevertheless, comorbid hypertension resulted in a comparatively greater odd of an ASCVD related hospitalizations in blacks (Fig. 3).

### 3.5. ASCVD hospitalizations: racial variation in comorbid cardiovascular disease, procedural variation

There were 5,409,501 inpatient white and black hospitalizations with a principal diagnosis of ASCVD, accounting for 10.8% of total hospitalizations with comorbid diabetes as a secondary diagnosis.

There was significant variation in the burden of concomitant cardiovascular bed involvement (comorbid CAD, PAD, and prior stroke) amongst ASCVD hospitalizations (Fig. 4). White men had a higher burden of comorbid cardiovascular bed involvement compared to white women, black men, and black women ( $p$  trend  $< 0.001$ ). A significant discrepancy existed regarding the utilization of procedures for ASCVD hospitalizations (Fig. 5). When compared to white men, white women (OR 0.83; 95% CI 0.82–0.84) had a lower odds of undergoing major limb amputation, whereas black men (OR 0.83; 95% CI 0.82–0.84) and black women (OR 0.83; 95% CI 0.82–0.84) had a high odd of undergoing a

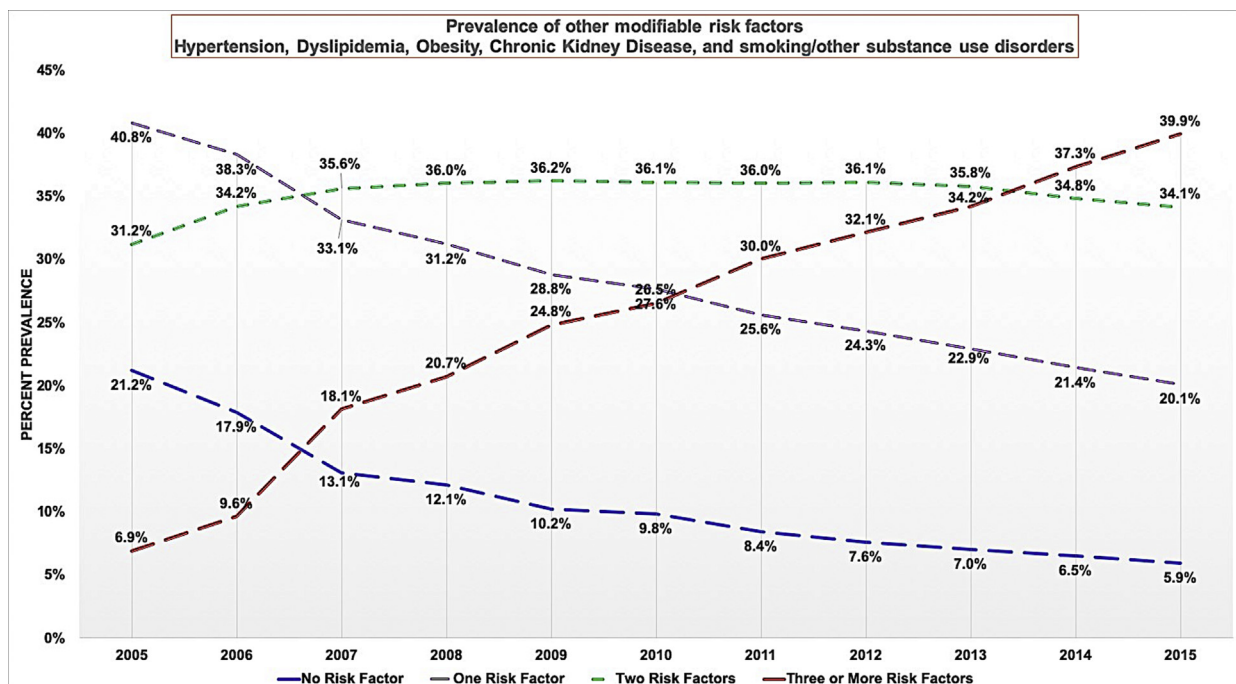


Fig. 1. All cause inpatient hospitalizations with comorbid diabetes, modifiable risk factor incidence.

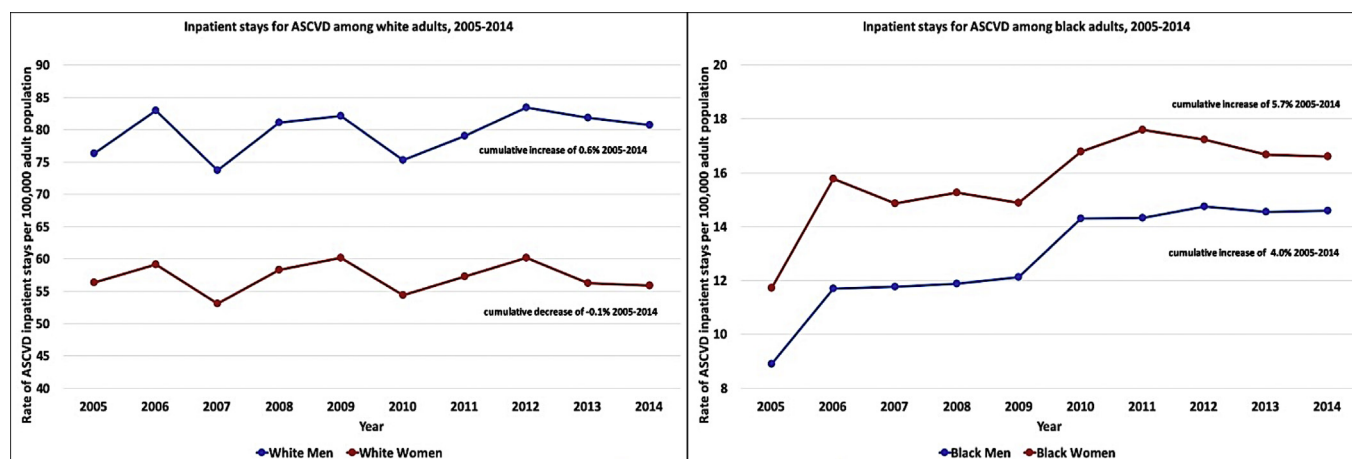


Fig. 2.

major limb amputation during an ASCVD hospitalizations.

### 3.6. ASCVD hospitalizations: racial and sex differences in in-hospital mortality and length of stay

In-hospital mortality was calculated based on comorbid risk factors adjusted to age, comorbidities, median zip code income, and primary insurance payor using complex samples regression probabilities. White and Black Women had the highest incidence of ASCVD related in-hospital mortality, while the in-hospital mortality rate was similar amongst white and black men (Table 3). In-hospital length of stay for ASCVD was less in white hospitalizations compared to black hospitalizations (4.7 days vs. 5.6 days,  $p < 0.001$ ).

## 4. Discussion

Macrovascular complications of diabetes, namely ASCVD, are the leading cause of morbidity and mortality in the U.S [11,12]. In the cross-sectional analysis of a nationally representative database, we document an overall significant cumulative increase in the rate of hospitalizations for ASCVD for the black population with diabetes compared to the white population. This contrasts with the current literature, which reports an overall decrease in ASCVD related hospitalization burden [13]. When we evaluated all-cause diabetic hospitalizations, they reflected a higher burden of black hospitalizations with no insurance status and represented relatively younger patients. Also, we noted a higher incidence of comorbid hypertension and renal failure. Black Hospitalizations for ASCVD with diabetes were driven by a higher incidence of stroke. In-Hospital mortality for ASCVD related hospitalizations was the highest amongst white women.

Previous population cross-sectional studies have reported a declining trend in hospitalization rates for ASCVD related conditions for people with comorbid diabetes [14–17]. This outcome is derived despite an improvement in cardiac biomarker inpatient testing profiles, imaging diagnostics, and inpatient triage modalities [17,18]. Improvement in ASCVD related morbidity may be secondary to better control of modifiable risk factors, namely diabetes, obesity, renal failure, hypertension, smoking, and dyslipidemia.

Burrows et al. [17], on an evaluation of hospitalization trends for cardiovascular conditions from 1998 to 2014, reported an overall decline in trends of hospitalizations for heart failure, ischemic heart disease, dysrhythmias, and stroke. However, they did notice a significant increase in hospitalizations for cardiovascular conditions from 2006 onwards for non-Hispanic black, not dissimilar from our analysis. Notably, there was a concerning increase coming from the population with diabetes. The reasons for the difference may reflect a disparity in primary preventive

treatment upstream, poor risk factor control, and other unforeseen factors [19]. Notably, we report a higher proportion of black hospitalizations with stroke, with a concomitant higher incidence of comorbid hypertension.

Our findings are in concert to a recent evaluation of rehospitalization black patients had a higher risk of readmission compared with white patients (OR, 1.15; 95% CI, 1.12–1.18;  $P < 0.001$ ). An administrative claims data set of commercially insured and Medicare Advantage beneficiaries across the United States was used. Data analysis took place between October 2016 and February 2019.

We also noticed a concerning trend of a higher proportion of black women hospitalizations compared to black men. This contrasted with white men who had a higher proportion of hospitalizations compared to white women. Our findings are in concert to a recent evaluation of rehospitalization [20]. Black patients had a higher risk of readmission compared with white patients (OR, 1.15; 95% CI, 1.12–1.18;  $P < 0.001$ ). An administrative claims data set of commercially insured and Medicare Advantage beneficiaries across the United States was used. Data analysis took place between October 2016 and February 2019. Black and Hispanic patients tended to be younger and female and have lower annual household incomes than white or Asian patients (annual household income  $< \$40,000$ : black patients, 50,590 [56.2%]; Hispanic patients, 16,852 [44.2%]; white patients, 131,071 [39.8%]; Asian patients 2895 [29.1%];  $P < 0.001$ ).

The incidence of risk adjusted in-hospital mortality was the highest for white women. This may primarily reflect a higher incidence of primary ASCVD presentation as AMI in the white population compared to stroke in the black population. The causation remains elusive, with a higher association of reduced preventive medication prescription, advanced disease at presentation, and less intensive care as pertinent predictors in whites [21,22]. The Multi-Ethnic Study of Atherosclerosis reported white women had the highest percentiles of coronary artery calcium and Hispanics had the lowest, with Chinese and black women in the middle [23]. A higher calcium score with concomitant diabetes could potentially explain the disparate outcome. Additionally, there was a higher prevalence of Medicaid insurance status and living in a low-income zip code in the blacks. A population analysis of the Atherosclerosis Risk in Community study reports living in disadvantaged location to be associated with a higher incidence of heart disease [2,24]. Similarly, the Jackson Heart Study has elucidated an association between neighborhood disadvantage and cumulative biologic score, which represents cardiovascular, metabolic, inflammatory, and neuroendocrine biomarkers [25]. Furthermore, we report a lower association of obesity with ASCVD presentation with diabetes. The TECOS randomized trial data reports similar findings [26]. The sub-study evaluated to determine the association of obesity with cardiovascular outcomes in patients with

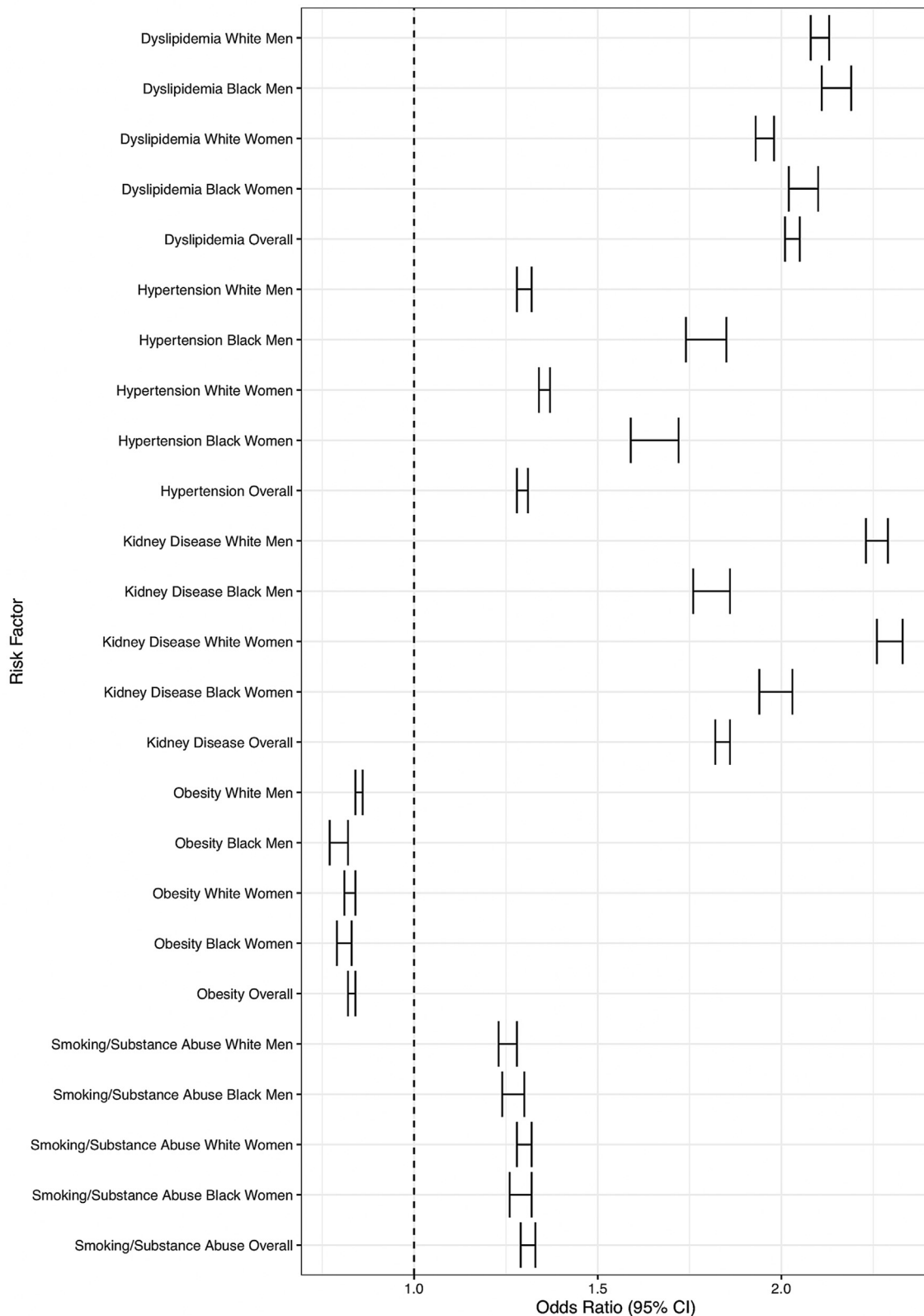


Fig. 3. Odds of Hospitalization with ASCVD related principal diagnosis in patients with diabetes.

type 2 diabetes and cardiovascular disease. Obese individuals had a lower CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina compared to normal/underweight individuals.

Overall, there has been a higher noticeable usage of statin

medications and cholesterol control in patients with diabetes than in patients without diabetes [27]. However, percolation of a primary prevention strategy in patients with diabetes may not be that prominent in the black population. For instance, one study evaluated the 2015 outpatient registry data on statin prescription trends on goal-directed

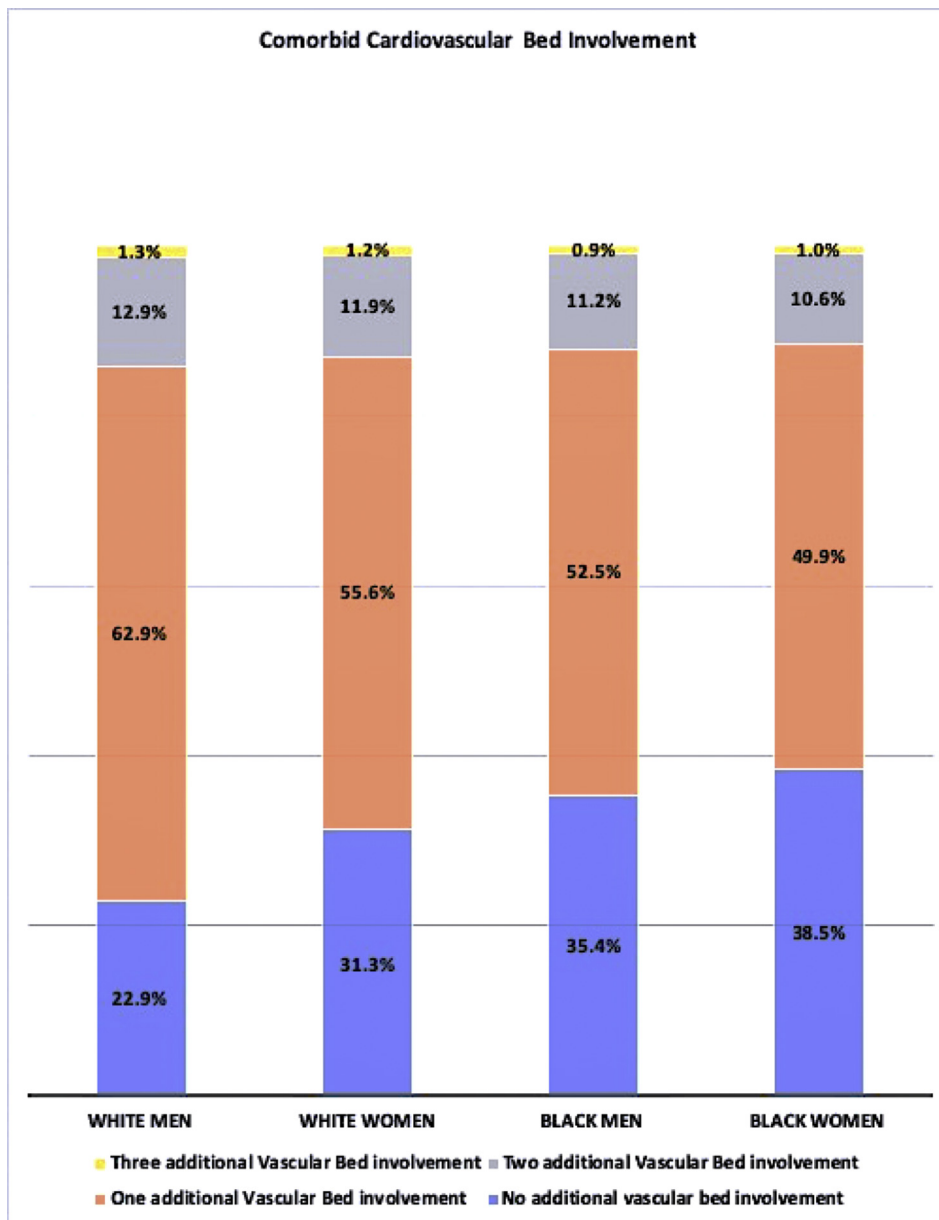


Fig. 4. ASCVD hospitalizations with comorbid vascular bed involvement.

therapy reported significant undertreatment of A.A. with statin therapy [28]. Interestingly, we report that white patients with diabetes have higher odds of having an ASCVD related co-discharge diagnosis of dyslipidemia compared to black patients with diabetes. Concomitantly, we report a higher relative comorbid hypertension and renal disease in the black population with diabetes presenting with ASCVD compared to whites. Our study highlights greater polyvascular bed involvement in hospitalized white compared to black. We believe this is attributed to increased re-hospitalization of whites with known stable ASCVD. Comparatively, the increasing monovascular involvement in blacks probably reflects the increasing recognition of undiagnosed worsening ASCVD in this population. Additionally, blacks hospitalized with ASCVD were of a younger age compared to whites. Pathobiology of ASCVD in blacks is multifactorial with epigenetic proinflammatory arteriosclerotic mechanisms, reflected by a higher level of hsCRP, increased carotid intima thickness, and prediabetic renal injury with documented glomerular hyperfiltration [29–32]. Kataoka et al., in an ultrasound-guided study of atheroma progression using data from multiple trials of anti-atherosclerotic therapies, reported U.S. blacks having more

significant atheroma progression and less optimal risk factor control [33]. Concomitantly, there continues to be a disparity in procedural selection and outcomes for ASCVD hospitalizations. Pertinently, there was a higher burden of major limb amputation in blacks in our study. We attribute this finding to the presentation with more advanced disease in blacks, with further vulnerable prognostic manifestations.

To date, there now exist multiple oral medications for diabetes, which demonstrate a significant reduction in cardiovascular event rates [34]. In fact, the primary outcome of these trials is a composite endpoint, which typically includes evaluation for a reduction in hospitalizations for cardiovascular events [35]. However, the majority of the large-scale trials have a poor track record of black representation, with a recent meta-analysis demonstrating major diabetes trials on cardiovascular outcomes to enroll on an average less than 5% of blacks [7]. Significant evidence to date exists on the difference of anti-diabetic drug pharmacokinetics stratified by race and sex [1,36–38]. Lower participation of minorities in these trials is worrisome, as it hinders a broader interpretation of the available data. Multiple reasons for the low enrollment exist, common amongst them low socio-economic status, poor health literacy,

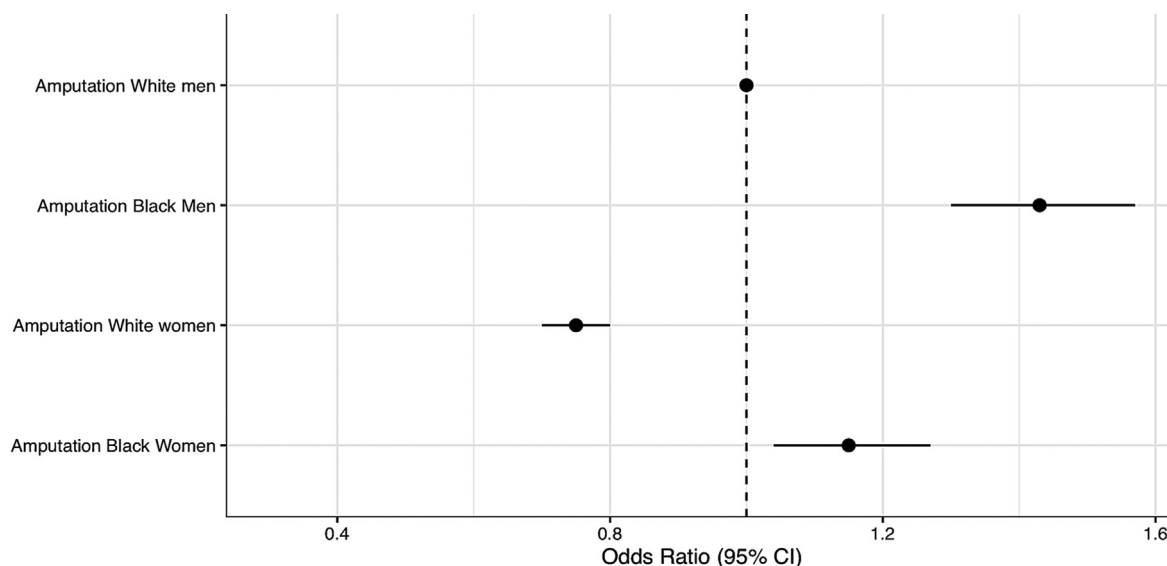


Fig. 5. Odds of in-hospital procedures during ASCVD hospitalization in patients with diabetes.

Table 3

Racial and Sex Disparity in ASCVD in-hospital hospitalizations per principal admission diagnosis, in-hospital mortality and length of stay.

	White Male	Black Male	White Female	Black Female
ASCVD estimate	2604339	427437	1858970	518699
Myocardial Infarction	31.3%	25.3%	30.1%	24.0%
Coronary Artery Disease	40.4%	30.9%	33.1%	29.8%
Stroke	20.1%	34.8%	26.3%	36.2%
Peripheral Arterial Disease	8.2%	9.0%	10.5%	10.0%
ASCVD risk adjusted In-Hospital Mortality	3.6%	3.5%	4.2%	3.9%
ASCVD Length of Stay (Days)	4.7	5.5	4.8	5.6

and fear of abuse [39]. With the advent of precision medicine, the approval of newer therapies allows for an essential role in the understanding of its application in subpopulations [36]. As new anti-diabetic drugs with cardiovascular benefits arrive [34], there needs to be a strategy to ensure the enrollment of minorities to measure benefit directly. As newer treatments come with an increasing cost, health systems and insurers may well require strong evidence of value for use within minority populations.

The major strength of our study is that we used a nationally representative survey to examine trends in ASCVD hospitalizations amongst whites and blacks with diabetes. However, our study has significant limitations. First, our findings should be translated with caution as health care practices have continued to evolve from 2005 to 2015. In the data we analyzed, race is self-reported, rather than based on biomarkers or genetic testing. Second, the NIS is a sample of hospital discharges and not individual patients; the rate of events may not genuinely reflect rates per individual. Patients got counted multiple times if they got hospitalized more than once in a calendar year. Third, we cannot differentiate discharges with prior known ASCVD from those with new-onset ASCVD. Multiple hospitalizations for the same condition can skew in-hospital procedural and mortality data. Fourth, improved, and widespread testing may have resulted in a wider net of individuals with milder disease getting detected earlier, which may correlate with our results. Fifth, admission and discharge medications, particularly statins, newer anti-diabetic medications, labs, Hemoglobin A1c, low density lipoprotein cholesterol levels, vital signs, body weight and imaging characteristics were not available. Sixth, comorbid data is obtained from ICD-9 codes, which are based on administrative claims. Nevertheless, the NIS database

allows for the evaluation of a comprehensive, diverse sampling of real-world hospitalizations, which should regulate the above inherent confounding variables.

To conclude, it is well-known race and ethnicity are crude proxies for any disease and are social constructs rather than scientific categories [40]. Despite substantial and growing heterogeneity in the contemporary American society, including mixed ancestry, the present findings may elucidate clinically significant differences based on race, in addition to sex, and potentially reveal significant areas that must be addressed to curtail increases in diabetes-related ASCVD burdens.

#### Authorship declaration

The authors report no conflict of interest. All authors have participated in this work and have reviewed and agree with the content of this article. None of the contents are under consideration for publication in any other journal. No portion of the text has been copied from other material in the literature.

#### Disclosures

None.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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