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ORIGINAL RESEARCH

Real-World Racial Variation in Treatment and Outcomes Among Patients with Peripheral Artery Disease

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ABSTRACT

Introduction: Prior studies have found considerable disparities in prevalence and outcomes for patients with peripheral arterial disease (PAD). This study compared rates of diagnostic testing, treatment patterns, and outcomes after diagnosis of PAD among commercially insured Black and White patients in the United States.
Methods: Optum's de-identified Clinformatics® Data Mart Database (1/2016–6/2021) were used to identify Black and White patients with PAD; first PAD diagnosis was deemed study index date. Baseline demographics, markers of disease severity, and healthcare costs were compared between cohorts. Patterns of medical management and rates of major adverse limb events (MALE; including acute or chronic limb ischemia, lower-limb amputation) and cardiovascular (CV) events (stroke, myocardial infarction) during the available follow-up period were described. Outcomes were compared between cohorts using multinomial logistic regression models, Kaplan–Meier survival analysis, and Cox proportional hazards models.
Results: A total of 669,939 patients were identified, with 454,382 White patients and 96,162 Black patients. Black patients were younger on average (71.8 years vs. 74.2 years), but had higher comorbid burden, concomitant risk factors, and CV medication use at baseline. Prevalence of diagnostic testing, revascularization procedures, and medication use was numerically higher among Black patients. Black patients were also more likely than the White patients to receive medical therapy without a revascularization procedure [adjusted odds ratio with 95% confidence interval (CI) = 1.47 (1.44–1.49)]. However, Black patients with PAD had higher incidence of MALE and CV events than White patients [adjusted hazard ratio for composite event (95% CI) = 1.13, (1.11–1.15)]. Except myocardial infarction, the hazards of individual components of MALE and CV events were also significantly higher among Black patients with PAD.

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Conclusions: Results of this real-world study suggest that Black patients with PAD have higher disease severity at the time of diagnosis and are at increased risk of experiencing adverse outcomes following diagnosis.

Keywords: Cardiovascular events; Diagnostic testing; Medical management; Peripheral artery disease; Race; Disparities; Variation; Treatment patterns

Key Summary Points

Why carry out this study?

Peripheral artery disease (PAD) is a common condition with significant racial variation in the rate of diagnosis, treatment, and outcomes.

To build upon the existing literature, we conducted a comprehensive, retrospective study evaluating trends in diagnostic testing, treatment patterns, and patient health outcomes after diagnosis of PAD between commercially insured Black and White patients in the United States.

What was learned from the study?

Compared to White patients, Black patients were observed to have higher disease severity leading up to the PAD diagnosis and increased risk of long-term cardiovascular and limb complications, despite increased diagnostic testing and medication use following PAD diagnosis.

The findings suggest that Black patients with PAD experience substantial disease burden under the current standard of care. Future interventions should be tailored to facilitate earlier diagnosis of PAD and to improve the standard of care for Black patients with PAD, which, in turn, could reduce disparate adverse outcomes following diagnosis.

INTRODUCTION

Peripheral artery disease (PAD) is a common condition in which vessels of the lower limb are narrowed due to atherosclerotic occlusion. In the United States (US), approximately 8.5 million people live with PAD [1]. The disease is associated with elevated risks of major adverse cardiovascular (CV) events, including stroke, myocardial infarction (MI), or CV death; and major adverse limb events (MALE), including acute limb ischemia (ALI), chronic limb threatening ischemia, and limb amputation [2, 3].

Management of PAD is critical to minimizing future risk of adverse CV events, and may involve pharmacologic options and/or revascularization therapies [4, 5]. Pharmacologic treatment includes antiplatelet agents (e.g., aspirin) and anticoagulant agents (e.g., vitamin K antagonist), or a combination of the two (i.e., dual pathway inhibition). In recent years, direct-acting oral anticoagulants, such as direct Factor Xa inhibitor, have also emerged as promising options [6–9]. As PAD progresses, endovascular or surgical revascularization may be required [4, 5].

Recent studies have shown significant differences in the rate of PAD diagnosis, treatment, and outcomes by race. Matsushita and colleagues found that the lifetime risk of PAD was significantly greater among Black Americans than those with White or Hispanic ethnicity [10]. Moreover, Soden and colleagues found that Black Americans with PAD interventions have more severe disease at the time of initial major vascular operation compared to non-Hispanic White Americans [11]. Studies have also found that Black Americans are less likely to be offered and to undergo revascularization procedures to salvage the effected limb and avoid amputation [12–15].

In addition, studies have documented that Black patients with PAD have worse clinical outcomes than White patients with PAD. For example, a study by Chen and colleagues reported that, compared with non-Hispanic White Americans, Black patients with PAD had nearly 50% higher odds of PAD with chronic limb ischemia (CLI), and over 70% higher odds

of major limb amputation [16]. Fanaroff et al. similarly reported that markers of lower socioeconomic status and Black race were associated with higher rates of major lower extremity amputation [17]. Black patients with PAD may also be at an even greater risk of adverse CV events due to atherosclerotic occlusion [18]. A prospective study of patients with stable CAD found that symptomatic PAD was associated with a 70% increased risk of subsequent CV events, after adjustment for traditional risk factors [19].

The current study builds upon the existing literature by conducting a comprehensive evaluation of the trends in diagnostic testing, treatment patterns, and outcomes after diagnosis of PAD between commercially insured Black and White patients in the US.

METHODS

Data Source

Optum's de-identified Clinformatics® Data Mart (CDM) Database, spanning from January 1, 2016 to June 30, 2021, was used to meet the study objectives. Optum CDM includes 12–14 million annual covered lives in all census regions in the United States. The claims data contain more than 36 months of historical data on patient demographics, dates of eligibility and death, claims for inpatient and outpatient (OP) visits, costs of services, and laboratory tests and results. Race and ethnicity are reported based on a propriety algorithm derived using member geographic location and name. The Optum CDM data also include information on patients' socio-economic characteristics, such as education level, federal poverty status, home ownership, household income, net worth, and occupation.

All patient data are de-identified and comply with the requirements of the Health Insurance Portability and Accountability Act. Because the current study relied exclusively on de-identified patient records and did not involve the collection, use, or dissemination of individually identifiable data, institutional review board approval was not necessary. Permission to access and use the data was granted by Optum.

Study Design and Population

A retrospective study design was used to evaluate and compare treatment patterns, diagnostic testing, revascularization procedures, and adverse outcomes among Black and White patients with PAD (Fig. 1). Patients were included if they had ≥ 2 medical visits with a diagnosis of PAD (the first visit was defined as the index date), ≥ 6 months of continuous health plan enrollment before the index date (i.e., baseline period), and ≥ 1 months of continuous health plan enrollment after the index date (i.e., follow-up period). Patients were also required to be ≥ 18 years of age and have complete information on race and geographic region. Patients were excluded if they had ≥ 1 diagnosis for major CV events (i.e., all-cause stroke, MI, ALI, and CLI), or lower limb amputation within 1 month prior to the index date, or ≥ 1 dispensing for oral anticoagulant therapy during the baseline period. Patients who met the selection criteria were stratified into mutually exclusive cohorts based on their race (Black or White race).

Study Outcomes

Demographics, comorbidities, healthcare resource use (HRU), healthcare costs, and severity profile at baseline [as inferred by the composite of the Quan–Charlson comorbidity index (Quan-CCI), PAD diagnosis with ALI, CLI, both, or neither at the index date, as well as the prevalence of PAD risk factors, baseline CV-related procedures, medication use, and level of diagnostic testing; with higher indices and prevalence indicating more severe disease] were reported. The specific outcomes evaluated were patterns of care and medical management before and after diagnosis, lower-limb amputation (overall and by high and low amputation), MALE (comprising of ALI, CLI, and lower-limb amputation), and CV events (MI and all-cause stroke) following the PAD diagnosis. Each study

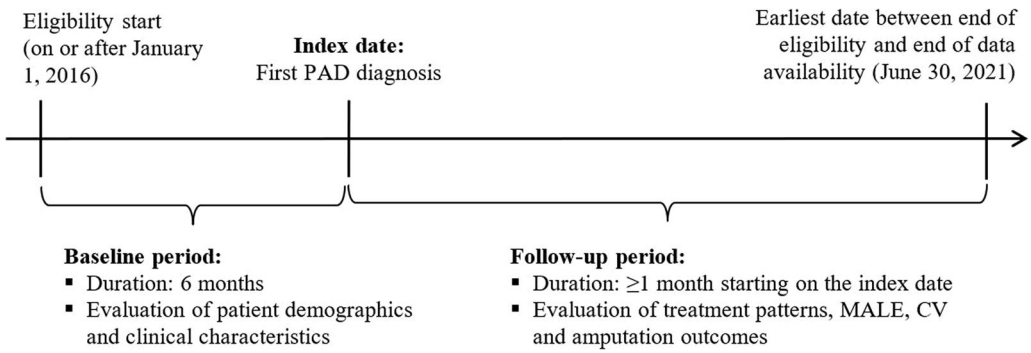

Fig. 1 Study design scheme. *CV* cardiovascular, *MALE* major adverse limb events, *PAD* peripheral artery disease. Source: Optum's de-identified Clinformatics® Data Mart Database with variables from January 1, 2016 to June 30, 2021

outcome was compared between Black and White patients.

Statistical Analysis

Differences in baseline characteristics between Black and White patients were assessed using standardized differences, with a standardized difference of less than 10% considered not clinically relevant. Descriptive statistics included mean, standard deviation (SD), and median values for continuous variables, and relative frequencies and proportions for categorical variables.

Medical management at 3-, 6-, 9-, and 12-month timepoints following the diagnosis of PAD was described to understand any changes in treatment patterns leading up to key outcomes of interest. Specifically, proportions of patients with PAD treated with prescription medications, revascularization, or both were described and compared using Chi-square tests. In addition, to minimize potential confounding, multivariable models were used to assess the statistical significance of differences in outcomes between cohorts, adjusting for age, gender, geographic region, Quan-CCI, PAD diagnosis type, and the number of concomitant comorbidities and risk factors for PAD. Proportions of patients receiving revascularization or medications were compared using multinomial logistic regression models, and odds ratios (ORs) with 95% confidence interval (CI) were reported. The frequency and type of diagnosis testing performed were also described.

Frequency and rates of revascularization, MALE, and CV events during the follow-up period were reported. Rates were calculated as the number of events divided by the patient-years of observation and reported per 100 person-years. For each outcome, time to first event was assessed with Kaplan–Meier survival analysis. Patients who did not experience the event were censored at the end of their observation period. Time to first event was also modeled with multivariable Cox proportional hazards regression. The models adjusted for differences in age, gender, geographic region, Quan-CCI, PAD diagnosis type, and the number of concomitant comorbidities and risk factors for PAD. The probability of each outcome was expressed as a hazard ratio (HR), accompanied by 95% CI and *P* values to assess the statistical significance of the results.

RESULTS

Study Population

After applying all eligibility criteria, 669,939 patients were included in the study population (Fig. 2). Patients were further stratified by race, with 454,382 (68%) categorized as White and 96,162 (14%) categorized as Black.

Baseline Patient Characteristics

Mean age at PAD diagnosis was lower among Black patients relative to White patients (71.8

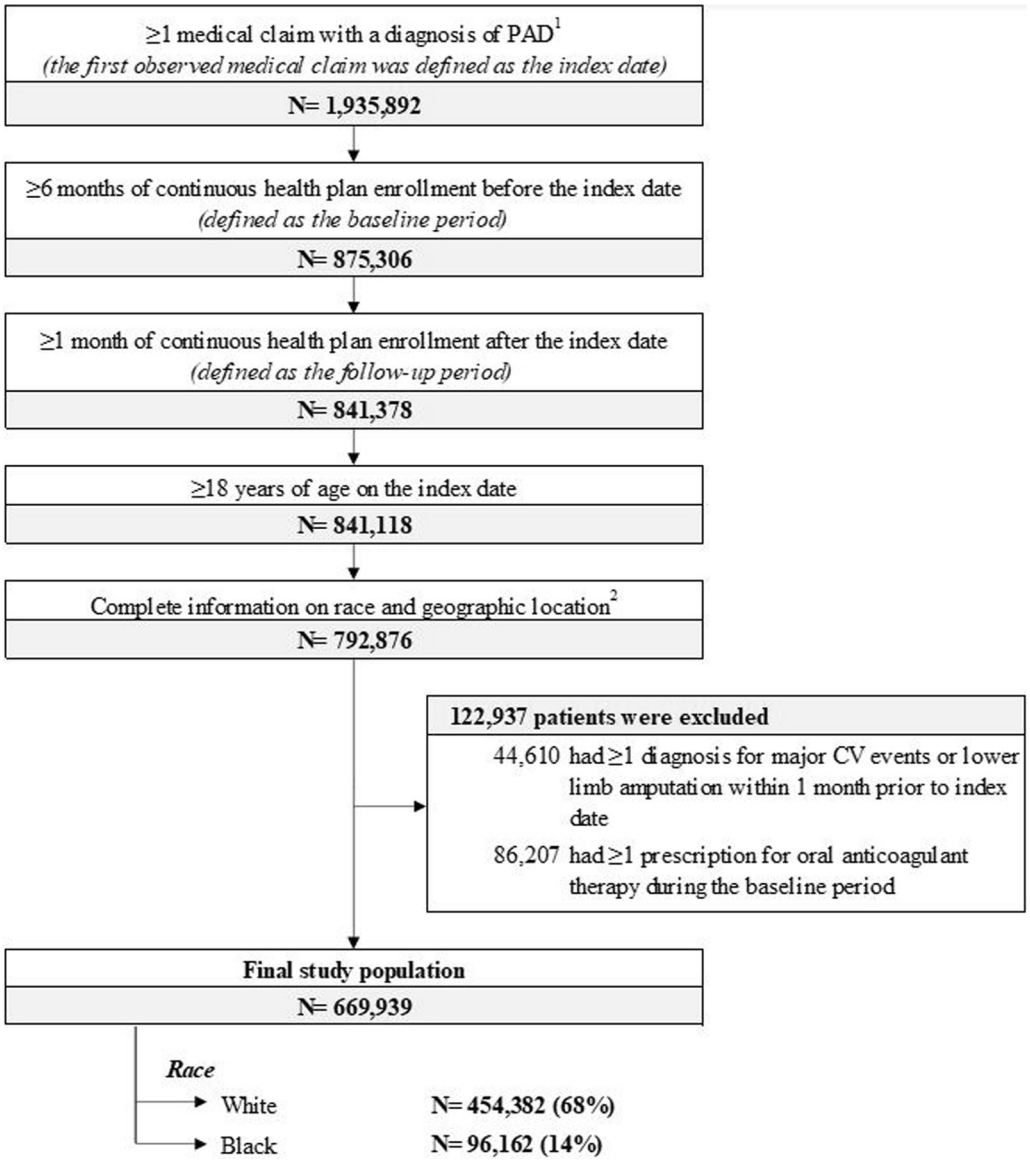

Fig. 2 Patient disposition. *CV* cardiovascular, *PAD* peripheral artery disease [1]Medical visits may have occurred in the inpatient or outpatient setting [2]Information on race and geographic region was not associated with a specific date in the database

vs. 74.2 years; standardized difference = 22.2%), and a higher proportion of Black patients were female (61.3% vs. 53.3%; standardized difference = 15.7%; Table 1). Socioeconomic factors, including education level (bachelor's degree or higher: 4.1% vs. 15.2%; standardized difference = 37.5%) and household income (< $40 K: 54.6% vs. 31.7%; standardized difference = 46.4%) were largely different between Black and White patients, respectively. Mean Quan-CCI was higher among Black patients relative to White patients (1.7 vs. 1.5; standardized difference = 10.1%). The prevalence of several comorbidities and risk factors for PAD were also higher among Black patients, including hypertension, diabetes, renal failure or end stage renal disease (eGFR < 60 mL/min), and obesity (standardized difference > 10%). Moreover, the proportion of patients with three or more concomitant comorbidities and risk

Table 1 Baseline demographics and characteristics

Characteristics	White patients [A] (n = 454,382)	Black patients [B] (n = 96,162)	Std. diff.[a,b] (%) [A] vs. [B]
Observation period[c], days, mean ± SD [median]	581 ± 414 [500]	588 ± 419 [508]	1.6
Demographics[d]			
Age, years, mean ± SD [median]	74.2 ± 10.7 [75]	71.8 ± 10.9 [72]	22.2
Female, *n* (%)	243,271 (53.5)	58,959 (61.3)	15.7
Geographic region, *n* (%)			
South Atlantic	109,332 (24.1)	45,565 (47.4)	48.7
West South Central	58,660 (12.9)	15,866 (16.5)	10.1
East North Central	65,465 (14.4)	8966 (9.3)	15.7
Pacific	50,403 (11.1)	2525 (2.6)	33.5
Middle Atlantic	47,902 (10.5)	9191 (9.6)	3.3
Mountain	44,093 (9.7)	1753 (1.8)	33.8
West North Central	38,385 (8.4)	3599 (3.7)	19.7
East South Central	20,220 (4.5)	7525 (7.8)	14.1
New England	19,922 (4.4)	1172 (1.2)	19.2
Insurance plan type, *n* (%)			
Medicare advantage	400,882 (88.2)	86,782 (90.2)	6.5
Commercial insurance	53,500 (11.8)	9380 (9.8)	6.5
HMO	6180 (1.4)	1456 (1.5)	1.3
POS	37,329 (8.2)	6203 (6.5)	6.8
PPO	685 (0.2)	88 (0.1)	1.7
EPO	5968 (1.3)	1411 (1.5)	1.3
IND	3022 (0.7)	228 (0.2)	6.4
Other	473 (0.1)	22 (0.0)	3.2
Education level, *n* (%)			
Less than 12th grade	937 (0.2)	299 (0.3)	2.1
High school diploma	119,083 (26.2)	52,052 (54.1)	57.0
Less than bachelor's degree	264,512 (58.2)	39,727 (41.3)	33.8
Bachelor's degree or higher	69,245 (15.2)	3975 (4.1)	37.5
Unknown	605 (0.1)	109 (0.1)	0.6
Household income, *n* (%)			
< $40K	143,824 (31.7)	52,529 (54.6)	46.4

Table 1 continued

Characteristics	White patients [A] (n = 454,382)	Black patients [B] (n = 96,162)	Std. diff.[a,b](%) [A] vs. [B]
$40K–$49K	41,041 (9.0)	10,521 (10.9)	6.4
$50K–$59K	43,000 (9.5)	8872 (9.2)	0.8
$60K–$74K	52,763 (11.6)	7366 (7.7)	13.4
$75K–$99K	67,341 (14.8)	6147 (6.4)	27.4
≥ $100K	82,842 (18.2)	4210 (4.4)	43.8
Unknown	23,571 (5.2)	6517 (6.8)	6.7
Year of index date[d], *n* (%)			
2016	72,134 (15.9)	14,971 (15.6)	0.8
2017	120,798 (26.6)	25,588 (26.6)	0.1
2018	112,054 (24.7)	23,308 (24.2)	1.0
2019	97,089 (21.4)	20,619 (21.4)	0.2
2020	49,504 (10.9)	10,925 (11.4)	1.5
2021	2803 (0.6)	751 (0.8)	2.0
Total healthcare costs[e,f], US$ 2021, mean ± SD [median]	$17,578 ± 40,980	$19,425 ± 47,531	4.2
Quan-CCI[c,g], mean ± SD [median]	1.5 ± 1.8 [1]	1.7 ± 1.9 [1]	10.1
PAD diagnosis type[d], *n* (%)			
ALI only	9510 (2.1)	3082 (3.2)	6.9
CLI only	4440 (1.0)	1045 (1.1)	1.1
ALI and CLI	247 (0.1)	81 (0.1)	1.1
No ALI or CLI	440,185 (96.9)	91,954 (95.6)	6.6
Selected comorbidities and risk factors for PAD[c,g], *n* (%)			
Hypertension	311,622 (68.6)	76,928 (80.0)	26.1
Diabetes	145,969 (32.1)	45,574 (47.4)	31.2
Coronary artery disease (polyvascular diseases)	108,874 (24.0)	20,704 (21.5)	5.8
Current or prior tobacco	100,014 (22.0)	21,353 (22.2)	0.5
Renal failure or end stage renal disease (eGFR < 60 ml/min)	82,507 (18.2)	22,302 (23.2)	12.4
Obesity	54,612 (12.0)	15,387 (16.0)	11.5
Cerebrovascular disease	58,055 (12.8)	11,931 (12.4)	1.1
Heart failure	53,282 (11.7)	13,557 (14.1)	7.1
Atrial fibrillation	43,611 (9.6)	5576 (5.8)	14.3
Venous thromboembolism	23,213 (5.1)	5167 (5.4)	1.2

Table 1 continued

Characteristics	White patients [A] (n = 454,382)	Black patients [B] (n = 96,162)	Std. diff.[a,b](%) [A] vs. [B]
Transient ischemic attack	7471 (1.6)	1466 (1.5)	1.0
Intracranial hemorrhage	442 (0.1)	83 (0.1)	0.4
Concomitant comorbidities and risk factors			
0	83,652 (18.4)	11,122 (11.6)	19.2
1	97,297 (21.4)	17,472 (18.2)	8.1
2	103,931 (22.9)	24,693 (25.7)	6.5
≥ 3	169,502 (37.3)	42,875 (44.6)	14.8
CV-related medication use[c], n (%)			
Antihypertensives	231,119 (50.9)	61,881 (64.4)	27.3
Antihyperlipidemic agents	207,965 (45.8)	49,890 (51.9)	12.2
Antihyperglycemic agents	72,046 (15.9)	22,709 (23.6)	19.5
Antiplatelet agents	44,862 (9.9)	11,015 (11.5)	5.1
Other CV agents	116,302 (25.6)	38,478 (40.0)	30.7
CV procedures[c], n (%)			
Cardiography procedures	169,433 (37.3)	37,900 (39.4)	4.4
Echocardiography procedures	68,670 (15.1)	15,499 (16.1)	2.8
CV monitoring devices, services, and evaluations	27,899 (6.1)	4952 (5.1)	4.3
Cardiac catheterization procedures	10,544 (2.3)	2048 (2.1)	1.3
Percutaneous coronary intervention	4162 (0.9)	731 (0.8)	1.7
Coronary bypass graft	906 (0.2)	171 (0.2)	0.5
Non-invasive physiologic studies and procedures	372 (0.1)	58 (0.1)	0.8
Home and outpatient INR monitoring services	347 (0.1)	20 (0.0)	2.5
Therapeutic CV services and procedures (excluding PCI)	1799 (0.4)	326 (0.3)	0.9
Other CV procedures	1563 (0.3)	216 (0.2)	2.2
Other selected procedures[c], n (%)			
Dialysis	4035 (0.9)	2477 (2.6)	12.9
Non-traumatic lower limb amputation	890 (0.2)	202 (0.2)	0.3
Foot and ankle (minor)	775 (0.2)	165 (0.2)	0.0
At and below knee (major)	101 (0.0)	29 (0.0)	0.5
Above knee (major)	43 (0.0)	14 (0.0)	0.5
Knee replacement	1754 (0.4)	300 (0.3)	1.3

Table 1 continued

Characteristics	White patients [A] (n = 454,382)	Black patients [B] (n = 96,162)	Std. diff.[a,b](%) [A] vs. [B]
Hip replacement	1493 (0.3)	210 (0.2)	2.1
Kidney transplant	485 (0.1)	184 (0.2)	2.2
Diagnostic testing[c], *n* (%)			
ABI	11,808 (2.6)	3353 (3.5)	5.2
Vascular ultrasound	11,876 (2.6)	2890 (3.0)	2.4
Angiography	3168 (0.7)	789 (0.8)	1.4
Aortography	147 (0.0)	34 (0.0)	0.2

ABI ankle brachial index, *ALI* acute limb ischemia, *CLI* chronic limb ischemia, *CV* cardiovascular, *EPO* exclusive provider organization, *HMO* health maintenance organization, *IND* indemnity, *INR* international normalized ratio, *PAD* peripheral artery disease, *POS* point of service, *PPO* preferred provider organization, *Quan-CCI* Quan-Charlson comorbidity index, *SD* standard deviation, *Std. diff.* standardized difference, *US* United States

[a]For continuous variables, the standardized difference is calculated by dividing the absolute difference in means of the control and the case by the pooled standard deviation of both groups. The pooled standard deviation is the square root of the average of the squared standard deviations

[b]For dichotomous variables, the standardized difference is calculated using the following equation where P is the respective proportion of participants in each group: $|(P_{case}\text{-}P_{control})|/\sqrt{[(P_{case}(1\text{-}P_{case}) + P_{control}(1\text{-}P_{control}))/2]}$

[c]The observation period spans from the index date up to the earliest of the end of eligibility or end of data availability

[d]Evaluated on the index date (i.e., first diagnosis of PAD)

[e]Evaluated during the 6-month baseline period, not including the index date

[f]Costs were inflation-adjusted to the 2021 US dollar (i.e., average over the entire year) using the medical care component of the Consumer Price Index from the US Bureau of Labor Statistics

[g]Reference: Quan H et al. (2005) Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Medical Care 43(11): 1130–39

factors for PAD was higher among Black patients relative to White patients (44.6% vs. 37.3%; standardized difference = 14.8%). Use of CV-related medications was also higher among Black patients relative to White patients; with some of the largest differences observed in the use of antihypertensives and other CV agents (standardized difference = 27.3% and 30.7%, respectively). The most common CV procedures during the baseline period were cardiography and echocardiography procedures for both Black and White patients (39.4% and 37.3%, respectively), with similar prevalence of CV procedures between both cohorts. Prevalence of other selected procedures and diagnostic testing were low during the baseline period and largely similar between cohorts, with only dialysis procedures being more prevalent among Black patients relative to White patients (2.6% vs. 0.9%; standardized difference = 12.9%). Likewise, baseline HRU and costs were generally similar between both cohorts.

Medical Management

While prevalence of revascularization procedures was generally low across both cohorts and at all time intervals (range 0.6–3.4%), Black patients with PAD had a significantly higher prevalence of revascularization procedures relative to White patients across all time intervals (Table 2; $P < 0.05$). Diagnostic testing with vascular ultrasound, ankle brachial index, angiography, or aortography was numerically more prevalent among Black patients relative to

Table 2 Medical management over time, stratified by 3-month intervals[a,b]

Treatments	From 0 to 3 months		From 3 to 6 months		From 6 to 9 months		From 9 to 12 months	
	White patients (n = 454,382)	Black patients (n = 96,162)	White patients (n = 414,085)	Black patients (n = 87,650)	White patients (n = 361,709)	Black patients (n = 76,520)	White patients (n = 322,029)	Black patients (n = 68,214)
Revascularization procedures, n (%)	12,610 (2.8)	3262 (3.4)*	3864 (0.9)	1043 (1.2)*	2242 (0.6)	601 (0.8)*	1808 (0.6)	522 (0.8)*
Diagnostic testing, n (%)								
Vascular ultrasound	71,117 (15.7)	18,200 (18.9)*	9287 (2.2)	2387 (2.7)*	7934 (2.2)	2072 (2.7)*	7261 (2.3)	1918 (2.8)*
ABI	70,695 (15.6)	18,856 (19.6)*	7297 (1.8)	2340 (2.7)*	6336 (1.8)	1975 (2.6)*	6012 (1.9)	1779 (2.6)*
Angiography	22,729 (5.0)	5419 (5.6)*	4951 (1.2)	1351 (1.5)*	3231 (0.9)	854 (1.1)*	2704 (0.8)	775 (1.1)*
Aortography	2838 (0.6)	738 (0.8)*	598 (0.1)	169 (0.2)*	344 (0.1)	95 (0.1)*	244 (0.1)	71 (0.1)*
Medication use, n (%)								
Antihypertensives	217,166 (47.8)	57,228 (59.5)*	188,512 (45.5)	49,659 (56.7)*	166,077 (45.9)	43,784 (57.2)*	149,684 (46.5)	39,375 (57.7)*
Antihyperlipidemic agents	195,181 (43.0)	45,756 (47.6)*	168,891 (40.8)	39,196 (44.7)*	148,866 (41.2)	34,818 (45.5)*	135,355 (42.0)	31,787 (46.6)*
Antihyperglycemic agents	63,410 (14.0)	19,456 (20.2)*	55,211 (13.3)	16,956 (19.3)*	48,600 (13.4)	14,840 (19.4)*	44,089 (13.7)	13,406 (19.7)*
Antiplatelet agents	53,375 (11.7)	13,103 (13.6)*	44,957 (10.9)	11,037 (12.6)*	38,874 (10.7)	9578 (12.5)*	35,047 (10.9)	8665 (12.7)*
Anticoagulant agents	11,335 (2.5)	2090 (2.2)*	11,136 (2.7)	2107 (2.4)*	10,857 (3.0)	2100 (2.7)*	10,966 (3.4)	2093 (3.1)*
Other cardiovascular agents	108,337 (23.8)	35,045 (36.4)*	92,537 (22.3)	30,149 (34.4)*	81,577 (22.6)	26,794 (35.0)*	74,586 (23.2)	24,300 (35.6)*

ABI ankle brachial index, *SD* standard deviation

*$P < .05$

[a]All patients are included in the "From 0 to 3 months" interval. For the subsequent interval, each includes patients with at least one day of eligibility at the start of the interval

[b]Cohorts were compared using Chi-square tests

Table 3 Patterns of care during the full observation period

Treatments[a]	Race[b]	PAD patients (n = 550,544)	Adjusted OR[c] (95% CI)
Medication use only[d], *n* (%)	White patients	313,664 (57.0)	–
	Black patients	75,649 (13.7)	1.47 (1.44–1.49)*
Both revascularization procedures and medication use[d], *n* (%)	White patients	18,200 (3.3)	–
	Black patients	5231 (1.0)	1.26 (1.22–1.31)*
Revascularization procedures only, *n* (%)	White patients	3284 (0.6)	–
	Black patients	408 (0.1)	0.67 (0.60–0.74)*
No revascularization or medication[d], *n* (%)	White patients	119,234 (21.7)	–
	Black patients	14,874 (2.7)	0.60 (0.59–0.61)*
Lower-limb amputation[e], *n* (%)	White patients	7518 (1.4)	–
	Black patients	2449 (0.4)	1.36 (1.30–1.43)*
High amputation, *n* (%)	White patients	3620 (48.2)	–
	Black patients	1525 (62.3)	1.74 (1.64–1.86)*
Low amputation, *n* (%)	White patients	5726 (76.2)	–
	Black patients	1630 (66.6)	1.18 (1.11–1.25)*
High-to-low amputation ratio	White patients	0.63	–
	Black patients	0.94	–

CI confidence interval, *OR* odds ratio, *PAD* peripheral artery disease, *Quan-CCI* Quan-Charlson comorbidity index
*P value $< .001$
[a]Evaluated during the observation period, which spans from the index date to the earliest date between end of eligibility and end of data availability (i.e., June 30, 2021)
[b]The cohort of White patients with PAD served as the reference category for the calculation of ORs, 95% CIs, and P values
[c]ORs, 95% CIs and P values were generated from multinomial logistic regression models. Adjusted models controlled for the following baseline demographics and clinical characteristics: age, gender, geographic region, Quan-CCI, PAD diagnosis type, and the number of concomitant comorbidities and risk factors for PAD
[d]Medication include antihypertensives, antihyperlipidemic agents, antihyperglycemic agents, antiplatelet agents, anticoagulant agents, and other cardiovascular agents
[e]Lower-limb amputation was identified during the observation period

Table 4 Rates of MALE, CV events, and lower-limb peripheral revascularization during the full observation period

Outcomes[a]	Event		Adjusted hazard ratio[b,c] (95% CI)	*P* value
	Frequency	Rate (per 100 person-years)		
MALE				
Acute limb ischemia				
White patients	5431	0.75	Reference	
Black patients	2019	1.30	1.56 (1.48–1.64)	< 0.001
Chronic limb ischemia				
White patients	3923	0.50	Reference	
Black patients	1208	0.80	1.33 (1.24–1.42)	< 0.001
Lower-limb amputation				
White patients	7518	1.00	Reference	
Black patients	2449	1.60	1.32 (1.26–1.39)	< 0.001
High amputation				
White patients	3620	0.50	Reference	
Black patients	1525	1.00	1.68 (1.58–1.79)	< 0.001
Low amputation				
White patients	5726	0.80	Reference	
Black patients	1630	1.10	1.15 (1.09–1.22)	< 0.001
CV outcomes				
Myocardial infarction				
White patients	19,342	2.70	Reference	
Black patients	4150	2.70	1.00 (0.97–1.04)	0.840
All-cause stroke				
White patients	26,106	3.60	Reference	
Black patients	6439	4.20	1.19 (1.16–1.23)	< 0.001
Composite (MALE or CV)				
White patients	52,627	7.30	Reference	
Black patients	12,727	8.20	1.13 (1.11–1.15)	< 0.001
Revascularization procedures				
White patients	21,484	3.00	Reference	

Table 4 continued

Outcomes[a]	Event		Adjusted hazard ratio[b,c] (95% CI)	*P* value
	Frequency	Rate (per 100 person-years)		
Black patients	5639	3.60	1.16 (1.13–1.20)	< 0.001

CI confidence interval, *CV* cardiovascular, *MALE* major limb adverse event, *Quan-CCI* Quan-Charlson comorbidity index, *PAD* peripheral artery disease

[a]Acute limb ischemia, chronic limb ischemia, myocardial infarction or stroke events were identified with a primary diagnosis during an inpatient stay, or an emergency room visit

[b]Hazard ratios were calculated using multivariable Cox proportional hazards regression, adjusting for the following baseline demographics and clinical characteristics: age, gender, geographic region, Quan-CCI, PAD diagnosis type, and the number of concomitant comorbidities and risk factors for PAD

[c]Evaluated during the observation period, which spans from the index date to the earliest date between end of eligibility and end of data availability (i.e., June 30, 2021)

White patients across nearly all time intervals. A substantial decrease in prevalence of diagnostic testing with vascular ultrasound, ankle brachial index, or angiography was observed across both cohorts in the 3–6 months following the PAD diagnosis (White patients: 1.2–2.2%; Black patients: 1.5–2.7%) relative to the 0–3 months prior (White patients: 5.0–15.7%; Black patients: 5.6–19.6%). The prevalence of diagnostic testing continued to decrease in the 6–9 and 9–12 months following the initial PAD diagnosis in both cohorts. Medication use was significantly higher among Black patients relative to White patients across all time intervals ($P < 0.05$), and prevalence remained generally consistent across all time intervals for both cohorts.

After adjusting for baseline differences, Black patients with PAD had significantly higher odds of being treated with only medications [OR (95% CI) = 1.47 (1.44–1.49); $P < 0.001$; Table 3] compared to White patients with PAD. Moreover, Black patients with PAD had double the odds of high amputations compared to White patients with PAD [OR (95% CI) = 2.01 (1.89–2.13); $P < 0.001$], significantly higher odds of low amputations [OR (95% CI) = 1.35 (1.28–1.43); $P < 0.001$], and numerically higher high-to-low amputation ratio (0.94 and 0.63, respectively; Table 3).

Incidence of MALE and CV Events

Kaplan–Meier estimates of time to first MALE or CV event overall in the 12 months following PAD diagnosis were low across both cohorts, but numerically higher among Black patients relative to White patients and by individual MALE and CV events (Supplementary Figs. 1–6). Compared to White patients, the adjusted hazard of any MALE or CV event was significantly higher among Black patients [HR (95% CI) = 1.13 (1.11–1.15); $P < 0.001$; Table 4]. Except myocardial infarction, the adjusted hazards of all CV and limb events were also significantly higher among Black patients than White patients (Table 4). Black patients with PAD had a significantly higher hazard of both high and low amputations compared to White patients with PAD [high amputation: HR (95% CI) = 1.68 (1.58–1.79); $P < 0.001$, low amputation: HR (95% CI) = 1.15 (1.09–1.22); $P < 0.001$; Table 4]. Incidence of events of interest were further supported by numerically higher rates per 100 person-years among Black patients with PAD relative to White patients.

DISCUSSION

Compared to White patients, Black patients were observed to have higher disease severity leading up to the PAD diagnosis and worse long-term CV and limb complications following the PAD diagnosis. More specifically, Black patients

had a numerically higher Quan-CCI on average, a higher prevalence of comorbidities and PAD risk factors, as well as more widespread use of CV medications relative to White patients prior to diagnosis with PAD. Following PAD diagnosis, prevalence of medical management with diagnostic testing, revascularization procedures, and medication use was numerically higher among Black patients across all time intervals for up to 12 months post-diagnosis relative to White patients. Black patients were more likely than the White patients to receive medical therapy without a revascularization procedure. Black patients with PAD also had numerically higher time to first lower-limb revascularization and significantly higher hazards of lower-limb peripheral revascularization compared to White patients, further suggesting that Black patients present with more severe disease requiring earlier interventional management, which is recommended for patients with inadequate response to guideline-directed management and therapy, including structured exercise and pharmacotherapy (Class 1) [5]. With the exception of myocardial infarction, Black patients with PAD consistently had higher Kaplan–Meier rates of time to first MALE and CV events compared to White patients, which was further corroborated by significantly higher hazards of each outcome after adjusting for baseline confounders as well as higher rates of each outcome per 100 person-years.

Contrary to prior studies [12, 20, 21], this study found that Black patients had higher rates of diagnostic testing, CV medication use, and revascularization procedures than White patients, both before and after the diagnosis of PAD. This finding may be explained by the fairly homogenous population of commercially insured patients who were evaluated in this study, and all of whom had continuous health plan coverage during the study period. In a retrospective study of racial disparities in PAD before and after the 2006 Massachusetts health reform, which provided the framework for the Affordable Care Act, disparities in the probability of receiving revascularization procedures between non-White and White patients admitted with PAD were no longer statistically significant after insurance expansion as they were prior to expansion, underscoring the impact that inequities in health insurance coverage have on racial disparities in healthcare [22]. A different study of more than 115,000 hospitalizations among racial and ethnic minorities with lower extremity complications of diabetes reported a 33% reduction in high level amputations amongst early adopting Medicaid expansion states versus non-adopters [23]. Additional exploration is needed to further understand the implications of the synergy between ethnicity, diabetes, vascular disease, and access to care on medical management and outcomes among people with PAD [24].

Furthermore, Black patients were observed to have a higher severity of disease (as indicated by higher Quan-CCI scores and greater proportions of patients with multiple risk factors for PAD), and higher likelihood of all adverse outcomes over time (except for myocardial infarction), even after adjusting for baseline confounders. Similar findings were observed in a registry study of Black and non-Hispanic White Americans with infrainguinal PAD interventions, where Black patients presented with more advanced disease, including more diabetes, hypertension, congestive heart failure, and dialysis dependence, at time of initial major vascular operation [11]. Another registry study of the 1-year risk of MALE, major amputation, and death for patients undergoing elective revascularization for claudication or chronic limb-threatening ischemia found that the hazards of MALE and amputation were significantly higher among Black patients relative to White patients [25]. A different study of claims data from fee-for-service Medicare beneficiaries $\geq$ 66 years of age also found that Black beneficiaries were significantly more likely to experience adverse events after peripheral endovascular intervention compared to White beneficiaries [26].

Taken together, these findings suggest that increased diagnostic testing and/or medication use—potentially due to access to insurance coverage—may not always be indicative of better care. On the contrary, Black patients continue to be diagnosed at more advanced stages of the disease and have higher concomitant risk factors for PAD, potentially limiting the

effectiveness of subsequent medical interventions. Other reasons for the persistent differences in health outcomes after adjustments in observable characteristics could be attributable to institutional barriers, individual provider issues, and patient issues [27]. For example, Black patients may have suboptimal health insurance coverage before and/or during the study period compared to White patients, which could result in the adverse outcomes observed in this study. Factors such as lower education and household income observed among Black patients could also contribute to reduced awareness about PAD and its management, all of which could result in worse outcomes over time. For example, one cross-sectional survey study of adults $\geq$ 50 years of age found that only 13.0% of Black Americans were aware of PAD, compared to 25.7% and 16.6% of non-Hispanic White Americans and Hispanic Americans, respectively. Moreover, awareness of PAD was consistently lower among individuals with lower income and education level [28]. Future interventions should be tailored to facilitate earlier diagnosis of PAD and improve the standard of care for Black patients with PAD, which, in turn, could reduce disparate adverse outcomes following diagnosis.

The present study should be viewed in the context of certain limitations. Analyses of administrative claims data depend on correct diagnosis, procedure, and drug codes, and coding inaccuracies may lead to case misidentification. Race may be misclassified due to the imputation method, which had a sensitivity of 48% [29]. However, the method was validated and demonstrated 97% specificity and 71% positive predictive value for estimating Black race [29]. While the study evaluated patient comorbidities and risk factors for PAD as potential markers of disease severity, the data lack clinical information, and therefore limit the ability to assess certain metrics, such as disease severity inferred by the physician using laboratory and imaging results. In addition, the data may not contain all prescription-related information, particularly medications administered in inpatient settings, and over-the-counter medications, such as aspirin. Moreover, the data do not contain information on reasons for loss of follow-up, which may introduce informative censoring bias. Clinical events following the end of data availability or patient healthcare coverage were not observed in the data. The study used robust statistical methods to control for observable differences across patient cohorts, including markers for disease severity and CV medication use. However, these techniques cannot account for unobserved heterogeneity (e.g., in diet and exercise, details regarding insurance coverage before and during the study period) which could in turn affect the outcomes. Results are representative of the commercial and Medicare Advantage population in the US and, therefore, may not be generalizable to other patient populations (e.g., those enrolled in Medicaid or those without health insurance).

CONCLUSIONS

Results of this real-world study highlight the substantial disease burden experienced by Black patients with PAD compared to White patients with PAD, including a high prevalence of comorbidities and risk factors of PAD, as well as an increased risk of adverse outcomes following diagnosis. The findings underscore the need for timely diagnosis and more effective management of PAD among Black patients.

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Compliance with Ethics Guidelines. Since this study relied exclusively on de-identified patient records which were compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act and did not involve the collection, use, or dissemination of individually identifiable data, approval from an ethics committee was not required. Permission to access and use of the data was granted by Optum.

Data Availability. The datasets generated and analyzed during the current study are not publicly available, as they are subject to a data use agreement between Analysis Group, Inc., and the data provider. The data are available through requests made directly to Optum.

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