Phase II: Literature Review: Racial Disparities in Use of Selected Medical Technologies

Prepared For:

Advanced Medical Technology Association (AdvaMed)

Prepared by:

Inna Cintina, Ph.D.
Robert C. Saunders, Ph.D.
Jermaine Piper
Elizabeth Hamlett
Lane Koenig, Ph.D.
KNG Health Consulting, LLC

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KNG HEALTH CONSULTING LLC

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Executive Summary

Racial and ethnic healthcare disparities in access to advanced interventions have stubbornly persisted for decades in U.S. healthcare, with lower use of advanced cardiovascular and neurovascular technologies among Black populations relative to White.

This report is the second of a three-phase series investigating the prevalence of racial and ethnic disparities in the use of selected medical technologies. In Phase I, we presented initial evidence of gaps in access for a broad range of cardiovascular, neurovascular, orthopedic, respiratory, and preventive interventions. Phase III will provide a more in-depth analysis to include the impact of clinical and community factors on differences in access to cardiovascular and neurovascular interventions across groups.

In this Phase II analysis, we set out to understand from the medical literature the factors that contribute to racial and ethnic disparities in utilization for five procedures from the initial Phase I gap analysis—three cardiovascular procedures (cardiac ablation, angioplasty, transcatheter aortic valve replacement) and two neurovascular procedures (mechanical thrombectomy and thrombolysis).

Our review applied a lifespan lens to consider how disparities at the point of care reflect not just issues for providing the specific service but arise over time through the interplay of disease progression and treatment decisions before and after the point of care. That is, racial differences in risk factors for medical conditions, accessibility of services, and decision making with respect to diagnosis and treatment influence how to interpret both the magnitude of disparities observed for specific services and the potential opportunities to intervene to address those disparities.

Key Findings

Disparities arise due to a multitude of factors at the patient, community, provider, and treatment level. For both cardiovascular and neurovascular procedures, our analysis identified two main themes: accessibility-related factors, which create delays and barriers pre-treatment, and treatment-related factors, which contribute to delays and disparities around the selected procedure.

- Key accessibility issues were geographic factors and, for cardiovascular procedures, referral sensitivity. The five services studied typically require specialists' referrals, but access by Black patients is hampered by access to smaller referral networks, which leads to fewer referrals and fewer visits to cardiologists.

- Diagnosis delays, which is one of the main treatment-related factors, occur due to differences in disease pathophysiology, help-seeking behaviors, and implicit provider biases.
    - Treatment guidelines are shaped by clinical trials evidence, and Black patients are underrepresented in clinical trials.
    - Implicit biases, which refers to the attitudes or stereotypes that affect our understanding, actions and decisions in an unconscious manner (The Joint Commission, n.d.), in the provision of medical care around diagnosis, symptom, and severity assessment contribute to lower utilization rates for these conditions generally (e.g., there is evidence of a referral bias for cardiac surgeries specifically for treatment of aortic valve disease

(Rodriguez et al., 2017) as well as lower prescription of direct-acting oral anticoagulants for Black patients with arrhythmias (Bhave et al., 2015)).

- For time-sensitive procedures like stroke, pre-hospital delays in symptom recognition and presenting to the hospital reduce chances of clinical eligibility (i.e., patients present outside of the therapeutic window).

Our review concludes that multiple factors impede access and contribute to treatment delays in both pre-admission and post-admission time intervals. We identified three broad areas for interventions: early detection and timeliness of diagnosis; guidelines and treatment protocols; and treatment eligibility and provider biases.

I. Introduction

Healthcare technologies can improve patients' recovery time and health outcomes and reduce the adverse effects and long-term consequences associated with common cardiovascular and neurovascular conditions. Despite these advantages, recent studies have demonstrated persistent disparities in access to innovative technology and advanced procedures among minority racial and ethnic groups and other populations.

Phase I of our analysis documented differences in use rates for selected cardiovascular, neurovascular, orthopedic, spinal, and respiratory treatments and selected cancer screenings among Medicare beneficiaries. With respect to the cardiovascular and neurovascular procedures—1) cardiac ablation for arrhythmias and atrial fibrillation, 2) angioplasty for acute myocardial infarction (AMI) or angina, 3) transcatheter aortic valve replacement (TAVR) for aortic stenosis, and 4) mechanical thrombectomy and 5) thrombolysis for ischemic stroke—we found:

- Despite higher risk factors, Black beneficiaries and other racial minorities were identified with arrhythmias, AMI or angina, and aortic stenosis at lower rates than White beneficiaries. As a result, Black Medicare beneficiaries and Other race beneficiaries had lower utilization rates of cardiac ablation relative to Whites: a 32% difference for Black non-dual eligible patients and a 19% difference for Other non-dual eligible patients. Similarly, in the indicated TAVR population, White non-dual patients were 50% more likely to receive TAVR than Black non-dual patients.
- We found a difference in the rate of mechanical thrombectomy in favor of minorities, with Black Medicare beneficiaries 18-20% more likely to receive the procedure relative to Whites. In contrast, Black non-dual and dual eligible beneficiaries, as well as Other race beneficiaries, were less likely to receive thrombolysis than White beneficiaries.

In this Phase II report, we reviewed the literature on a subset of cardiovascular and neurovascular procedures. The objective of the literature review (Phase II) was to understand the factors that drive disparities in these five procedures and guide selection of procedures for Phase III analysis, and to determine which factors to include in Phase III statistical models. The literature review illustrates how disparities arise over the course of a patient's treatment experience globally and not just at the point of care. While the primary focus is racial/ethnic disparities, similar issues apply to disparities by gender and other patient attributes and are discussed for some conditions where the evidence was especially strong.

The rest of the report is organized as follows. First, in Section II we provide a background on the disparities framework that covers healthcare from a lifespan perspective and factors that may influence the disparities observed in the literature and our Phase I results. That is, how might differences by race/ethnicity in diagnosis and prior service utilization contribute to the differences observed at the point-of-care where these technologies are available to eligible patients? In Section III, we summarize the methodology behind the literature review. Sections IV and V document disparities in the use of cardiovascular and neurovascular procedures, respectively. Discussion and potential interventions designed to decrease gaps in medical technology use are presented in Section VI, and Section VII concludes.

II. Background

The Institute of Medicine report *Unequal Treatment* (2003) raised the profile of research on racial disparities in the use and outcomes of medical services. The authors documented then-recent evidence of racial differences, primarily between Black and White patients, in the use of services across a range of medical conditions, including cardiovascular and neurological disorders. These differences persisted even after reasonable efforts to adjust for differences in access, financial constraints, and other individual and community factors.

Their work called attention to both the direct and indirect effects of historical factors in service delivery and access to medical coverage and treatment; the contributions of patient and health-system factors; micro-level decision making at the point of care by clinicians under time and information constraints; and, patients' mistrust of providers and the healthcare system. Importantly, the report sparked improvements in the capture of data on race, expansion of research into disparities including for other races and the role of additional factors in shaping disparate utilization and outcomes, and systematic thinking about how unequal treatment arises within the US medical system.

Twenty years after the publication of *Unequal Treatment*, differences in healthcare utilization and outcomes remain a critical concern. In addition to documenting what is known about the magnitude of disparities at the point of care, we discuss how factors prior to the point of care (e.g., access to specialists or primary care providers), at the point of care (e.g., likelihood of treatment recommendations), and post-point of care (e.g., adherence to treatment follow-up) may shape interpretation of observed differences and how or whether they represent a disparity.

Framework

Differences between racial groups in utilization are an indicator of potential disparity. A difference rises to the level of disparity "after demonstrating that racial differences are not attributable to treatment eligibility, clinical contraindications, patient preferences, or confounding by other clinical factors and are associated with adverse consequences." (Rathore & Krumholz, 2004).

There are considerable opportunities for differential treatment decisions and health outcomes in patients with the same nominal health condition (Rice & Institute of Medicine, 2003). Although some differences in utilization may be appropriate, more often they arise from the combination of individual decisions by patients, providers, and utilization managers (Rice & Institute of Medicine, 2003). Healthcare providers make judgements about treatment choices given a patient's presenting symptoms and history but also their personal and/or professional experience, clinical uncertainty, and risk aversion. Further, with the prominent role of third-party payment, utilization managers operate according to a mix of clinical and business guidelines that may result in different approvals for similar cases.

As a result, identifying differences at a point in time is usually not sufficient to determine the causes of disparities, and one must consider a "lifespan developmental framework" to study causes, modifiers, trajectories, and outcomes related to health and disease (Bogard et al., 2017). A lifespan perspective accounts for differences by age as well as health contributors for a given person across time and

incorporates an understanding of how prior life experiences and human development influence subsequent treatment options.

While a full assessment of these factors is beyond the scope of this review, we can expand beyond a narrow assessment of gaps in utilization rates of a service to consider how factors upstream and downstream from use of these specific services influence interpretation of disparate use of specific services. For example, equal treatment rates across racial groups could still be indicative of a disparity if there are unequal rates of diagnosis between those groups (Green et al., 2007).

At the point of care, physicians and other clinical decisionmakers must make time-dependent medical decisions based on patient-reported and clinical information. Although these decisions are shaped by the practitioner's experience and skills, they are also shaped by their expectations about whether a patient will benefit from treatment and comply with follow-up care (Rice & Institute of Medicine, 2003). Doctors deal with cognitive challenges caused by uncertainty and time pressure using what the Institute of Medicine (IOM) calls "cognitive shortcuts." When the rationale guiding these shortcuts correlate with race, gender or other social traits, disparities can arise in the healthcare received.

- Diagnosis. How healthcare providers diagnose and evaluate certain conditions may be affected by these shortcuts. For example, doctors routinely underdiagnose cardiovascular diseases in women and understate their severity. This results in fewer visits to electrophysiologists, lower likelihood of being given oral coagulant medication, and fewer cardiac ablations among women (Mosca et al., 2005).

- Treatment. Healthcare providers may recommend (or fail to recommend) treatment options based on assumptions related to a patient's race, ethnicity, gender, or other characteristics. For example, a widely used kidney function test for determination of kidney failure and kidney transplant eligibility for years overestimated kidney function in Black patients. As a result, doctors have underestimated kidney disease severity, which has delayed proper diagnosis and transplant referrals (OPTN, 2022).

- Quality of care. A physician's race, ethnicity, or gender may influence clinical assessments of patients and their willingness to allocate treatment based on the physician's perceived beliefs. A review of 15 studies found that most healthcare providers may have implicit bias in terms of positive attitudes toward White patients and negative attitudes toward Black patients and other people of color, which affect patient-provider interactions, treatment decisions and adherence, and patient health outcomes (Hall et al., 2015). An experimental study assessing race-related implicit bias in provider assessment of angina symptoms, as presented by Black female and White male actors portraying "patients", found non-minority medical students were more definitive in diagnosing symptoms of White male "patients" as angina relative to Black female "patients" while rating the Black female "patients" to have worse health status despite presenting with identical symptoms (Rathore et al., 2000). Racial minority students did not exhibit the same discrepancies in diagnosis.

Differences in treatment rates are also influenced by whether a patient ever makes it to the point of care and the impact of delays in treatment on the patient's health status once evaluated. Patient preference

or patient mistrust of providers due to experiencing discrimination may result in lower likelihood of help-seeking behaviors or seeking a treatment. For example, medical mistrust among Black Americans has a long history (Hostetter & Klein, 2021) and specific to underlying conditions of interest, there is evidence of non-Hispanic Black patients being more likely to decline tissue plasminogen (tPA) for acute ischemic stroke in the emergency department (Mendelson et al., 2018; Zha et al., 2021).

Structural capacity, such as where treatment centers are located or the number of available practitioners, can also contribute to these differences. For example, the number of TAVR hospitals doubled from 2012 to 2017 with an overall increase in the proportion of the U.S. population living within a driving distance of 100 miles of a TAVR hospital (Mentias et al., 2021) and with 90% of the Medicare-age population living in a hospital referral region with a TAVR center (Marquis-Gravel et al., 2020). In fact, relative to White and Hispanic populations, a higher share of the Black population lives within 100-miles of a TAVR-eligible hospital (Mentias et al., 2021). Despite improved spatial access, lower utilization rates for Black patients persist, with lower rates of TAVR being documented within major metropolitan regions in zip code areas characterized by lower median household incomes, higher proportion of population who are dually eligible for Medicare and Medicaid services, higher Distressed Communities Index scores, and with predominantly Black and Hispanic Medicare populations (Nathan et al., 2022). Rates of access are lower, not just in rural areas, but also in communities with a lower socio-economic status. That could be a reflection of the initial expansion of TAVR programs predominantly in metropolitan areas (i.e., 98% of 583 hospitals that developed new TAVR program between 2012 and 2018) and to hospitals serving wealthier patients (Nathan et al., 2021).

Finally, lower utilization rates could be due to Medicare TAVR reimbursement limitations that create unintended access barriers (e.g., Medicare restrictions on which hospitals may perform TAVR) (The Advisory Board, 2018). Hospitals have to balance high TAVR costs with the ability to offer a complete array of state-of-the-art therapies for aortic stenosis (Reddy et al., 2022). This could lead to decreased access to TAVR services by patients cared for in hospitals that cannot afford these services or have difficulty meeting procedural requirements, recruiting skilled physicians, and initiating and then maintaining a functioning TAVR program (Reddy et al., 2022). These findings suggest that factors beyond distance influence access to advanced-technology therapeutics such as TAVR.

One such factor is dependence upon providers to refer patients for treatment. As our literature review of particular interventions showed, Black patients often have less access to specialists. Even with access, treatment delays may also arise from the differential impact of seemingly neutral policies associated with utilization review, prior authorization, and other cost controls (Rice & Institute of Medicine, 2003). Delays in treatment may result in more advanced progression of disease once a patient is ultimately seen, which may restrict the range of services that are clinically appropriate (e.g., patient is too severely ill to qualify for an otherwise appropriate intervention) and may impact patient outcomes.

Understanding the root causes of disparities that manifest in gaps in utilization rates is imperative in designing effective interventions that target underserved populations. Such interventions, if incentivized and structured appropriately (i.e., target specific factors that impede utilization), could increase the number of diagnosed cases (i.e., an increase in the size of population that is indicated for treatment), improve referral completeness processes (i.e., an increase in access to diagnosis, providers, and ultimately treatment), and increase utilization of procedures leading to alleviation of disparities in use of

these select procedures. Provider level interventions could also target clinical processes (e.g., tailoring treatment guidelines for various populations) and post point of care follow-up behavior (e.g., post-discharge follow-up contacts).

After presenting the methods for conducting the literature review, the next sections address the two key questions for the cardiovascular and neurovascular conditions investigated in this report:

1) What is known about differences in the use of these procedures across various populations? and
2) What factors may be important for determining how these differences, both in the literature and those observed in the Phase I analysis, may represent disparities in care?

To address these questions, we first summarize what the literature says about existing disparities for each of the five procedures at the point of service (i.e., differences in utilization rates) and how they compare to our findings in the Phase I analysis. The five procedures are:

Cardiovascular	• Ablation • Angioplasty • TAVR
Neurovascular	• Mechanical thrombectomy • Thrombolysis

With this report, we aim to raise awareness of contextual factors that shape how to interpret differences in utilization at one point in the care process and how or where to intervene. We focus primarily on differences in race between Black and White non-Hispanic populations but include some information on gender differences. The Phase I report used a three-level categorization of race (Black non-Hispanic, White non-Hispanic and Other Race[1]) to accommodate Medicare data's combined racial and ethnic classification categories and avoid issues with small sample sizes. In this Phase II report, we also will use the terms Black and White to mean Black non-Hispanic and White non-Hispanic. However, when describing findings from specific studies, we used the racial categories used by the author (e.g., if the study identifies differences between African American race or Hispanic ethnicity individuals then we use the original author's terms).

We then summarize factors in the literature that influence interpretation of the point-of-care utilization differences based on the broader lifespan framework. Specifically, we identified two themes affecting disparities in utilization of those five procedures of interest:

- Accessibility issues, such as geographic variation in provider access and feasibility of treatment at the facility given referral sensitivity; and,
- Factors related to the treatment itself (e.g., timeliness of diagnosis, feasibility of treatment at the facility given time since the onset of symptoms, patient involvement).

[1] The race categories in Medicare claims data are: White, Black, Other, Asian, Hispanic, North American Native, and Unknown. When we use Other race, we mean to refer to any race/ethnicity other than non-Hispanic White and non-Hispanic Black.

It should be noted that these factors are intertwined. For example, cardiovascular procedures require specialist visits, timely diagnosis, and a referral for the treatment. Neighborhoods with predominantly minority populations are at a higher risk of never having or losing access to ambulatory care centers (Tsui et al., 2020). The lack of local health centers introduces barriers to necessary basic healthcare resources. If a patient does not have access to basic "entry-level" providers such as primary care doctors (e.g., no providers within geographic area, no providers that take new patients, etc.), there will be delays in obtaining a referral to a specialist such as a cardiologist that could provide a referral to a TAVR specialist. Further, the pathway to certain procedures can be shaped by the scope of physician referral networks, with smaller networks contributing to racial disparities in the provision of TAVR (Bob-Manuel et al., 2018). Thus, lower utilization of TAVR procedure among Black patients could reflect challenges in accessing appropriate specialists despite geographic proximity to numerous facilities.[2]

[2] Over 90% of US population aged 65 years and older live in a hospital referral region with a TAVR center (Marquis-Gravel et al., 2020).

III. Methods

To understand the reasons and root causes of disparities in utilization, we conducted a literature review that targeted peer-reviewed articles that documented various aspects of racial/ethnic disparities related to use of five select procedures: cardiac ablation for atrial fibrillation and arrhythmias; angioplasty for AMI or angina; TAVR for aortic stenosis; and, mechanical thrombectomy and thrombolysis for ischemic stroke.

The procedures included in this literature review were chosen based on three criteria: high mortality from and prevalence of the underlying condition in the overall population and documented racial/ethnic disparity in utilization of novel procedures in Phase I. These conditions have high mortality rates. According to the Centers for Disease Control and Prevention (CDC), over 877,500 Americans die from heart disease, stroke, or other cardiovascular diseases every year (*Heart Disease and Stroke | CDC*, 2022). Heart disease and stroke are among the leading causes of death in the U.S., ranked at first and fifth respectively (*Heart Disease and Stroke | CDC*, 2022). Cardiovascular disease leads to 1 in 3 deaths each year in the U.S. Thus, interventions tailored to increase equitable access to related cardio- and neurovascular technology would reduce disease burden both overall and for minority communities.

In addition to their underlying prevalence, the interconnectedness of cardiovascular and neurovascular risks led us to focus on these conditions. The risk factors that shape cardiovascular disease simultaneously shape neurovascular disease progression (Arboix, 2015). Undiagnosed and untreated cardiovascular diseases such as atrial fibrillation, for example, may progress to neurovascular conditions such as stroke. More than half of undiagnosed atrial fibrillation cases have a moderate to high risk for stroke (Turakhia et al., 2018).

We also considered what is known about racial/ethnic disparities in utilization of these procedures. The American Heart Association and American Stroke Association have noted a number of issues including: minorities' decreased likelihood to receive thrombolysis for acute ischemic stroke, lowered participation in clinical research, mistrust of the healthcare system, and the possibility of bias in the delivery of care (Cruz-Flores et al., 2011). This study provides further insight into the factors that influence health care decisions and lead to observed racial/ethnic disparities in utilization of these procedures.

The literature review process included several phases: defining appropriate search terms/keyword combinations, title screening, abstract screening, and in-depth review of full text that passed title and abstract screening. We searched PubMed for relevant recently published peer-reviewed articles of existing literature related to cardiovascular and neurovascular racial/ethnic disparities among our selected procedures.

Our keyword strategy focused on combinations of cardiovascular and neurovascular medical procedures and the procedures' respective underlying conditions (see Table 1). For example, a search term query for cardiac ablation would be composed of terms such as: "cardiac ablation," "atrial fibrillation", "cardiac arrhythmia", "race", "racial", "difference", and "disparity". Only articles that were published in English and after January 2010 were included in our search. Additionally, we limited our search to articles based on data from the United States of America.

Table 1. Primary Search Terms Used in the Literature Review

Related Diagnoses/Condition	Select Procedure	Disparity Keywords
"atrial fibrillation" or "cardiac arrhythmia"	"cardiac ablation"	"race" and "disparity" or "rac*" and "dispar*"
"aortic stenosis"	"transcatheter aortic valve replacement" or "TAVR"	"race" and "disparity" or "rac*" and "dispar*"
"acute myocardial infarction" or "AMI" or "angina"	"angioplasty"	"race" and "disparity" or "rac*" and "dispar*"
"ischemic stroke"	"mechanical thrombectomy"	"race" and "disparity" or "rac*" and "dispar*"
"ischemic stroke"	"thrombolysis"	"race" and "disparity" or "rac*" and "dispar*"

During the title screening, we reviewed the titles of articles flagged by our search strategy and inclusion/exclusion criteria, and determined which articles to move forward to abstract screening (see Table 2). We reviewed the abstracts of articles chosen from the search results and then based on a relevance assessment decided if the article should be moved to the next phase. The full-text review phase involved retrieving and analyzing the full-text of articles deemed relevant to our proposed research questions. Because there were so few final reviews, we repeated this process for the articles identified before limiting it to meta-analyses and systematic reviews. We additionally searched through the citations of articles that made it to the full-text screening to identify additional relevant literature that warranted inclusion.

Table 2. Attrition Chart Used in the Literature Review

Search Criteria	Atrial Fibrillation OR Cardiac Arrythmia with Cardiac Ablation	Aortic Stenosis with Transcatheter Aortic Valve Replacement	Acute Myocardial Infarction with Angioplasty	Ischemic Stroke with Mechanical Thrombectomy	Ischemic Stroke with Thrombolysis
Related Diagnoses/Condition, Select Procedure, English, 2010 – 2023	21,006	11,583	4,451	3,476	6,951
… AND Disparity Keywords	117	118	65	66	66
… AND Meta Analysis/ Systematic Review	3	3	2	1	2
Final Review	3	3	0*	1	1**

*Our team removed two of the articles due to a lack of applicability: (1) not a meta-analysis and is centralized in Canada, (2) focus is on use of revascularization procedures among people with severe mental illness (SMI) and does not mention race-related disparities.

**Our team removed one of the articles due to a lack of applicability: does not pertain to race-related differences; RACE is the name of the stroke assessment tool mentioned in the article.

IV. Disparities in Selected Cardiovascular Procedures

In this section we begin by summarizing what is known about the magnitude of differences in use of cardiac ablation, angioplasty, and TAVR in the U.S. We then summarize findings from the literature review on differences related to diagnosis, inclusion in the indicated population, and use of these procedures at various points of the healthcare decision process that contribute to the observed differences.

A. Overview of Existing Differences

Cardiac Ablation. Recent research has identified lower rates of cardiac ablation among racial and ethnic minorities. Using the AHRQ National Inpatient Sample (NIS) for 2001-2011 researchers reported that among patients with heart failure and atrial fibrillation, Black, Hispanic, and Asian patients were 17%, 22%, and 62% less likely, respectively, to receive catheter ablation compared to White patients (Bhatia et al., 2016). A lower utilization of cardiac ablation among minorities is documented in other studies. For example, the adjusted hazard ratio for cardiac ablation utilization was significantly lower among Hispanic Medicare patients when compared to White patients (Bhave et al., 2015). In our analysis of 2018-2019 Medicare fee-for-service claims data, we found that Black Medicare beneficiaries with atrial fibrillation or other cardiac arrhythmias had 28% lower odds and Other race had 9% lower odds of receiving cardiac ablation relative to Whites.

Angioplasty. Analysis of NIS data from 2017 found the population-adjusted incidence rate of angioplasties for men was 202.8 per 100,000 persons for White patients and 130.3 per 100,000 persons for Black patients and 94.3 and 89.9 respectively for women (Best et al., 2021). These rates represent an improvement of 20.1 per 100,000 for men and 4.2 per 100,000 for women (Best et al., 2021). Others also have documented racial and ethnic disparities in several post-myocardial infarction interventions (Bolorunduro et al., 2016). In 2018-2019 fee-for-service Medicare data, we found that White beneficiaries were more likely to be identified with a primary diagnosis of acute myocardial infarction or angina than Black beneficiaries. However, the access rate differences within indicated population between Black and White beneficiaries were relatively small (2% higher among White non-dual eligible patients and Black dual eligible patients having a 7% higher access rate than White dual eligible patients). Despite these relatively minor differences in access rates, after adjusting for cofounders beyond age and gender, Black Medicare beneficiaries had 30% lower odds of angioplasty and Other race had 26% lower odds relative to their White peers.

Transcatheter Aortic Valve Replacement (TAVR). The FDA approval of TAVR in 2011 resulted in a paradigm shift in how severe aortic stenosis is treated. Despite these advances in treatment of aortic stenosis, disparities in the management and treatment of aortic stenosis are widely recognized and persistent (Ahmed et al., 2023). Beydoun and colleagues (Beydoun et al., 2016), using data from the NIS, found that Black patients had 32% lower risk-adjusted odds of being diagnosed with aortic stenosis when compared with White patients. This trend was consistent with previous studies that used medical record data to identify aortic stenosis (Novaro et al., 2013). Utilization rates of TAVR among Black patients with aortic stenosis were also lower relative to Whites. Based on NIS data, among patients who underwent aortic valve replacement between 2011 and 2014, the rates of TAVR utilization increased from 0.32% to 7.6% in

Black patients and from 0.4% to 8.8% in White patients (Alqahtani et al., 2018). Underrepresentation of racial minorities in the population of patients that undergo TAVR has been documented in other studies (Alkhouli et al., 2019; Kulkarni et al., 2022; Yeung et al., 2013).

Our Phase 1 results were consistent with this literature. We found that, compared to Black and Other race beneficiaries, more White Medicare beneficiaries were included in the indicated population. After adjusting for age, gender, and dual-eligibility status, Black and Other race Medicare beneficiaries had lower odds of TAVR relative to Whites (36% and 31% lower odds respectively for Black patients and Other race patients).

B. Trajectories over the Healthcare Lifespan

Accessibility

Referral Sensitivity. Another factor affecting accessibility of treatment at the point of care is "referral sensitivity" of the procedure (Bolorunduro et al., 2016). For example, patients are required to have a referral for procedures like angioplasties and valve replacements. White Medicare beneficiaries had the highest access to services such as cardiologist visits, catheter ablations, oral anticoagulants, and other essential atrial fibrillation treatments (Bhave et al., 2015), and Black patients are less likely to receive referrals to cardiology for severe aortic stenosis (Sleder et al., 2017).

There is evidence that specialist networks available for White patients are larger than referral networks for Black patients as measured by two metrics: the number of other primary care physicians whom each physician was connected to and the number of shared patients per connection (Landon et al., 2021). Limited referral networks for Black patients could explain fewer referrals and cardiologist visits, which in turn leads to lower access to cardiac ablation services.

The lowered referral rates (Mentias et al., 2021) and smaller physician referral networks (Bob-Manuel et al., 2018) observed for Black patients with aortic stenosis also may contribute to lower TAVR utilization rates. Lower utilization of TAVR in Black populations with severe aortic stenosis was related to a disproportionately lower likelihood of referral to specialty cardiologists, a higher likelihood to decline intervention, or lack of follow-up by providers (Sleder et al., 2017). Similar findings, with fewer cardiac referrals and follow-up appointments, were made for Hispanic patients and those with lower socioeconomic status (Cook et al., 2009).

Treatment

Diagnosis. There is evidence that Black patients are less likely to be aware of their atrial fibrillation (Meschia et al., 2010). As we noted in our Phase I analysis, the Black population has a higher prevalence of risk-factors such as hypertension and diabetes for cardiovascular diseases like atrial fibrillation. However, the risk- and age adjusted prevalence of atrial fibrillation in the White population aged 60 years and older is twice as large (2.5% vs 1.2%) as for the Black population (Lahiri et al., 2011). This phenomenon is known as the "racial paradox of atrial fibrillation risk" (Nanda & Kabra, 2019): despite greater risk of arrhythmias and negative health outcomes (e.g., heart failure, stroke) that could be alleviated by cardiac ablation procedures, the Black patient population is less often diagnosed with

arrhythmias (Nanda & Kabra, 2019). Some of the paradox may be mediated by genetics: having European ancestry increases risk for atrial fibrillation (Magnani et al., 2011). Our Phase I gap analysis also found that White beneficiaries were identified with arrhythmias at a higher rate than Black and Other race beneficiaries.

A timely referral to a specialist could increase the detection of the disease, but timeliness of the diagnosis also depends on the diagnostic techniques used. There is some evidence that diagnostic tools may be unreliable (Magnani et al., 2011). For example, the likelihood of receiving an appropriate echocardiogram is significantly reduced for Black patients, women, older patients, and patients receiving Medicaid (Tanguturi et al., 2019), which also could reflect lower referral rates for Black populations to cardiovascular procedures such as echocardiography (Hyland et al., 2022). Lower use of transthoracic echocardiography was most prominent amongst non-White Medicare-beneficiaries, especially Black females and persisted despite adjusting for the competing risk of mortality (Hyland et al., 2022). Additionally, the proportion of provider-detected atrial fibrillation differed between White and Black patients whereas the proportion of monitor-detected (i.e., using a wearable (patch) ambulatory electrocardiographic (ECG) monitor) atrial fibrillation did not (Heckbert et al., 2020).

This issue is especially common in the case of gender disparities for arrhythmias and other cardiac care. Doctors are more dismissive of and downplay the importance of women's cardiac symptoms (McSweeney et al., 2016). The difference in utilization of cardiac ablations relates to how providers assign severity of atrial fibrillation (e.g., CHADS2 stroke risk score). Results from an experimental case study indicate that primary care providers assigned a greater portion of women (20%) to lower risk categories than men (13%) with identical risk profiles and were significantly less likely to categorize intermediate-risk women to higher-risk categories compared to their male counterparts (Mosca et al., 2005). Based on findings in the literature, providers tend to be less aggressive in their assessment of risk severity and treatment options for women. A systematic review of sex-related differences amongst patients with atrial fibrillation indicated that women experience higher patient-rated burden of illness, reduced quality of life, more severe strokes, yet were less likely to be prescribed anti-arrhythmic medications or receive invasive treatment strategies such as cardiac ablations relative to men (Moqeem et al., 2020). As a result, women regardless of race/ethnicity are underdiagnosed (e.g., have fewer visits to electrophysiologists and are less likely to receive oral anticoagulation medication) and have a lower likelihood of being included in the indicated for treatment population for cardiac ablations (i.e., have fewer cardiac ablations).

One study on prevalence of aortic stenosis found that Black populations have 32% lower risk-adjusted odds of aortic stenosis than White populations (Beydoun et al., 2016). A systematic review of racial and ethnic differences in aortic stenosis noted a lower incidence of certain types of aortic stenosis among racial and ethnic groups relative to White patients (Wilson et al., 2020). More recent evidence suggests age-adjusted rates of severe aortic stenosis are comparable for Black and White populations (Ambrosy et al., 2023). However, it is crucial to note that aortic stenosis is underdiagnosed in the Black population despite observing echocardiographic evidence of aortic stenosis, which contributes to reduced follow-up, and appropriate treatment in the future (Crousillat et al., 2022).

Effectiveness of treatment. Black patients are underrepresented in clinical trial studies (Alegria et al., 2021). In the case of medications, such underrepresentation may result in inaccurate dosage guidelines for racial subgroups, especially if a drug has a narrow therapeutic range, its efficacy is sensitive to dosage (i.e., high variability in dosing range across patients that relies on dose-predicting algorithms and the clinical benefit achieved only within the target therapeutic range), or it requires routine clinical monitoring (Asiimwe et al., 2020). For example, Black patients with atrial fibrillation are at the greatest risk for Warfarin-related intracranial hemorrhages, which are the likely result of a dosage that was too high and has surpassed therapeutic ranges (Akinboboye, 2015) due to dosing based on algorithms developed largely in White patients. Poor anticoagulation control, measured by the percent of time a patient spends within the therapeutic range, can increase a risk of thromboembolism (international normalized ratio below 2) or bleeding (international normalized ratio exceeds 3) (Zirlik & Bode, 2017). From a biological perspective, Black patients require a higher dosage of Warfarin relative to the dosage for White patients (Akinboboye, 2015), with some evidence from pharmacogenetic studies that differences in genetic polymorphisms between White and Black populations could be affecting stable therapeutic Warfarin dose (Wadelius, 2014).

Finally, atrial fibrillation is an age-progressive disease that tends to become more persistent and more difficult to treat over time. Hence, patient demographics such as age at the time of procedure and disease duration are likely to influence the treatment path and outcomes such as a possibility of reoccurrence of atrial fibrillation after cardiac ablation (Bunch et al., 2016). While there is evidence that cardiac ablation is safe in older patients, larger absolute and relative benefits from the procedure are observed in younger patients (Bahnson et al., 2021). Thus, if timing of diagnosis varies across races (e.g., diagnosing Black populations at a more advanced age and potentially with higher progression of the disease), then that could contribute to racial differences observed in utilization of cardiac ablation.

This resonates with the scenario for patients with aortic stenosis. Aortic stenosis is underdiagnosed in the Black population despite clinical evidence (i.e., even when tested, their findings in the echocardiograms that indicated diagnoses were recorded as such diagnoses less frequently than in White patients), contributing to patients not being followed over time to monitor disease progression, further missing the opportunity to identify the right time to intervene (Crousillat et al., 2022). Evidence has shown that the risk of mortality post-TAVR increases with delayed treatment, thus highlighting the need for timely intervention (Roule et al., 2022) .

Treatment adherence. Nonadherence to anticoagulants for stroke prevention such as Vitamin K antagonists can lead to inferior outcomes like higher risk of death, stroke, and major bleeding (Haas et al., 2016). Reinitiating the therapy after several missed doses of vitamin K antagonists (which include Warfarin) may also result in a pro-thrombotic state (Zirlik & Bode, 2017). There is evidence of general suboptimal adherence to anticoagulant treatment regardless of race: 1 in 3 patients with atrial fibrillation adhere to direct-acting oral anticoagulants less than 80% of the time leading to poor clinical outcome in non-adhering patients (Ozaki et al., 2020), although adherence for direct-acting oral anticoagulants is better than for Warfarin (Yao et al., 2016).

Patient preferences also play a role in non-adherence. According to the Global Anticoagulant Registry in the Field-Atrial Fibrillation (GARFIELD-AF) registry, 7.2% of patients with atrial fibrillation and CHADS score exceeding 1 refused vitamin K antagonist treatment citing inconvenience of regular blood tests, dietary

restrictions, bleeding risk, and an under-appreciation or lack of knowledge regarding the risk of stroke (Zirlik & Bode, 2017). Poor adherence to oral anticoagulants is also linked to education and accuracy of guidance (Park & Jang, 2021). However, there is little evidence of racial differences in adherence for use or patient refusals of anticoagulants.

Undertreatment of aortic stenosis remains significant, however. The introduction of TAVR and the rapid adoption of TAVR by the Black population has reduced racial differences in treatment rates for aortic stenosis. Thus, availability of a minimally invasive option to treat aortic stenosis (e.g., TAVR) incentivizes those initially unwilling to consider treatment to access care (Matthew Brennan et al., 2020).

Provider bias. Among those patients who are aware of their atrial fibrillation, the odds of Black patients being treated with Warfarin were only one quarter as great as that for White patients (Meschia et al., 2010). Black and Hispanic patients with atrial fibrillation are also significantly less likely to receive direct-acting oral anticoagulants, which are more expensive but easier to use than Warfarin (Essien et al., 2018). In contrast, White Medicare beneficiaries have the highest access to oral anticoagulants and other essential atrial fibrillation treatments (Bhave et al., 2015). Additionally, when atrial fibrillation was treated, the quality of outcomes associated with anticoagulant use in Black and Hispanic patients was inferior relative to use in Whites, with lower time in the therapeutic range values in those taking Warfarin and modestly greater underdosing in those taking direct oral anticoagulants (Essien et al., 2018).

Although provider bias is presented as potential explanation (e.g., in Bhave), the authors did not test for such effects. A study by Blair and colleagues examining a similar medication-sensitive cardiovascular condition (i.e., hypertension) did not detect a relationship between medication adherence among Black and Latino patients, and implicit provider bias (Blair et al., 2014).

There is evidence of referral bias for cardiac surgeries. Relative to White patients, Black patients were less likely to be referred for treatment of aortic valve disease (Rodriguez et al., 2017; Sleder et al., 2017). Referral bias could also lead to lower numbers of Black patients admitted into a hospital with any diagnosis of aortic stenosis, as aortic stenosis is largely diagnosed in the outpatient setting and treated in the inpatient setting (Czarny et al., 2021).It is also known that for a closely related condition such as heart failure, primary care by a cardiologist improves in-hospital survival regardless of race/ethnicity. However, Black patients have a higher risk of progression of left ventricular systolic dysfunction than Whites, and thus have a greater need for a specialist's care to help reduce progression of disease and provide options for end-stage care (Dries et al., 1999). Even in the intensive care unit, this population is less likely to be seen by a cardiologist (Breathett et al., 2018).

Follow-up / Re-intervention. The majority of elderly patients will experience recurrences of atrial fibrillation and atrial flutter, as age-based substrate for arrhythmia is likely to progress (Bunch et al., 2016). While studies indicate that approximately 90% of patients are alleviated from symptomatic atrial fibrillation/atrial tachycardia/atrial flutter within a single cardiac ablation procedure without the use of antiarrhythmic medications within 1 year of follow-up (Calkins, 2019), the benefits of cardiac ablation diminish over time. However, ablations (similar to angioplasty) require continuous care with about 1 in 8 patients undergoing a repeat procedure within 1-year of index cardiac ablation (Al-Hijji et al., 2016) to maintain the therapeutic benefits. Repeated cardiac ablations were more common in younger patients (i.e., Medicare patients less than 80 years old underwent twice as much repeat ablation as patients older

than 80 years) and White patients, indicating that demographic characteristics, particularly age rather than clinical characteristics (e.g., comorbidities as gauged by the CHA2DS2-Vasc scores or the Charlson comorbidity index) affect the probability of repeat ablation (Al-Hijji et al., 2016). The age difference may be due to lower utilization by older patients due to increased age-related procedure complication risks.

Repeat ablation is not the only type of follow-up. Renin-angiotensin system inhibitors (RASIs) have been utilized in clinical trials and have been shown to be effective in preventing atrial fibrillation recurrence following a cardiac ablation (Peng et al., 2020). However, current literature indicates that the utilization of RASIs in African American patients is uncommon due to the population having a low renin profile and their historically not being recommended as an initial treatment for those with hypertension (Williams et al., 2014). Further clinical trials have suggested, that RASIs have become increasingly effective in improving clinical outcomes of African Americans with hypertension and comorbidities related to cardiovascular health (Williams et al., 2014). While patient-specific factors can contribute to discrepancies in hypertension control (i.e., medical adherence), physician-related factors contribute to worse outcomes (e.g., failing to escalate therapy, unfamiliarity with antihypertensive regimen complexity for minority populations) (Gu et al., 2017).

Although not specific to AMI or angina, there is evidence of differential reintervention needs for minority populations that receive angioplasty. Among patients with endovascular peripheral arterial disease, reintervention within 365 days was more likely in Black and Hispanic populations at a faster rate than White populations (Loja et al., 2015). Black and Hispanic populations also have a substantially increased likelihood of major amputation within 365 days and heightened all-cause mortality within 365 days compared to their non-Hispanic White counterparts (Loja et al., 2015). Even with this elevated risk of reintervention, Black patients were less likely than Whites to receive preventive revascularization efforts preceding amputation, limb-related treatments, or wound debridement prior to amputation (Loja et al., 2015). These differences in reintervention may reflect the influence of race-based bias at the time of initial intervention, in patient severity, or in the quality of care provided.

V. Disparities in Selected Neurovascular Procedures

In this section we begin by summarizing what is known about the magnitude of differences in use of mechanical thrombectomy and thrombolysis procedures in the U.S. We then summarize findings from the literature review on differences related to diagnosis, inclusion in the indicated population, and use of these procedures throughout the healthcare decision process that may influence the observed differences.

A. Overview of Existing Differences

Mechanical Thrombectomy. A systematic review of disparities in stroke treatment between racial minorities found that rates of mechanical thrombectomy utilization were lower among minority patient populations, with 13 of the 18 studies reporting lower rates of mechanical thrombectomy and thrombolysis use in racial minorities. (Ikeme et al., 2022). Analysis of 2006-2014 data from the NIS, showed that Black patients, and to a lesser degree Hispanic patients, had a significantly lower adjusted rate of thrombectomy utilization compared to non-Hispanic White patients (Black and Hispanic patients had 33% and 6% lower odds, respectively) (Esenwa et al., 2020). Another study using 2013-2018 data from the same database found that while the difference in utilization between Whites and non-White patients persisted across years, the gap was closing (Wahood et al., 2021). Specifically, Black patients had 17% lower risk-adjusted odds of receiving mechanical thrombectomy relative to Whites. The decrease in differential is in line with 12% lower odds for Black patients reported in an analysis of 2016-2017 national inpatient data (Golnari et al., 2021). In our analysis of more recent data from 2018-2019 fee-for-service Medicare claims, we found that Black Medicare beneficiaries diagnosed with ischemic stroke (i.e., beneficiaries who are included in the population indicated for mechanical thrombectomy) had similar risk-adjusted odds of receiving the procedure relative to Whites. The odds for Other race relative to White were higher at 17%. The use of mechanical thrombectomy has increased over time (Wahood et al., 2021). Therefore, a change in the utilization pattern over time may indicate improved access to mechanical thrombectomy among minorities as the procedure has become a standard of care for acute ischemic stroke since 2015.

It was noted in the literature that utilization of mechanical thrombectomy between 2006-2014 varied greatly by insurance type, with Medicaid beneficiaries experiencing the lowest rates of utilization (13% lower odds of utilization) and private insurance holders having the highest rates of utilization (24% higher odds) (Esenwa et al., 2020). However, insurance differential was not statistically significant in the 2013-2018 cohort (Wahood et al., 2021). Though our work, focused on the fee for service (FFS) Medicare population, which has a common standard of coverage, we also identified lower rates of access among dual-eligible Medicare-Medicaid beneficiaries (14% lower odds relative to non-duals).

Thrombolysis. In a study utilizing the 2011-2012 NIS, among patients with a primary diagnosis of acute ischemic stroke, Black patients were 16% less likely to be treated with thrombolysis relative to White patients (Kumar et al., 2016). In a systematic review, White patients (2.8%) were more likely to receive the most common thrombolysis medication (tissue plasminogen activator) than African American (2.3%), Hispanic (2.6%), and Asian (2.3%) patients (Ikeme et al., 2022). This aligns with our Phase I findings that

Black non-dual and dual eligible beneficiaries were slightly less likely to receive thrombolysis than White beneficiaries, with the White to Black access rates in the non-dual population being 7% higher and 1% higher in the dual-eligible population. Our risk-adjusted results indicate that in 2018-2019 Black Medicare beneficiaries had 14% lower odds of receiving thrombolysis relative to White patients.

B. Trajectories over the Healthcare Lifespan

Accessibility

Geography. Access to thrombolysis and thrombectomy for patients with acute ischemic stroke is a "postcode lottery" (Walter et al., 2021). While recent estimates indicate that 91% of the US population can reach an acute stroke ready hospital or stroke center within an hour by ambulance, the percent of population without access to such centers varies substantially by region (Zachrison et al., 2022). There are additional benefits associated with the proximity to larger hospitals and comprehensive stroke centers, as those are predictors of receiving thrombolysis treatment within 60 minutes (Oluwole et al., 2017).

With respect to endovascular treatment centers (EVT) that provide services such as mechanical thrombectomies, nearly a third of the US population are located beyond an hour drive to their nearest EVT center (Aroor et al., 2022). It has been shown that rural areas suffer from delayed EVT access thereby reducing benefits of this time-sensitive procedure for otherwise eligible patients (Yan et al., 2022). It also has been shown that the Southeast region of the U.S., which has both a high Black population and higher relative risk of stroke, has the lowest utilization rate for thrombectomy (Suolang et al., 2021).

Access to care. Staffing differences and whether a patient has been seen/evaluated by a specialist could also affect utilization rates. For example, the presence of stroke specialists and neurologists in the emergency department and treatment by an attending physician could contribute to faster thrombolytic treatment administration (Oluwole et al., 2017). Similarly hospitals with vascular neurology consultation capacities have higher intravenous thrombolysis rates relative to hospitals that do not have such capacity (Prabhakaran et al., 2012). Since being seen by a specialist is imperative to successfully treating some conditions, provider biases with respect to "standard of care" and who is being seen by a specialist could affect utilization of certain services creating racial disparities.

Treatment

Clinical Eligibility. Mechanical thrombectomy is targeted to patients with large vessel occlusion in the anterior circulation and the National Institutes of Health Stroke Scale (NIHSS) score above 5 (Mokin et al., 2019). That is, indication for the procedure depends on the time from the onset of symptoms, severity of stroke (higher NIHSS score indicate higher severity), and location of large vessel occlusions (LVO; intracranial and extracranial occlusions of the internal carotid artery, including tandem or isolated occlusion of the M1 and M2 segments of the middle cerebral artery). However, there are no known patterns of differences by race in the likelihood of LVO. For example, due to the time-sensitive nature of mechanical thrombectomies, providers have a clinical eligibility threshold that accounts for time since the onset of stroke symptoms. The latest guidelines indicate this procedure for select patients up to 16 hours

for unwitnessed strokes and in select patients up to 24 hours of symptom onset (Mokin et al., 2019), reflecting evidence that showed no differences in recanalization rates and safety outcome between patients treated within 6 hours and beyond 6 hours from onset (Casetta et al., 2020).

Lower utilization of mechanical thrombectomy in Black patients could be due to delayed presentation to the hospital. Black patients had almost twice the average time from stroke onset to hospital presentation relative to White patients (Catapano et al., 2021). The delays were especially pronounced between Black men who were 72% more likely to arrive 3 hours or later from the onset of symptoms relative to White men, with no significant differences in arrival times for women (Springer et al., 2017). Delayed presentation leads to an increase in the size of the ischemic core and reduces the radius of the salvageable penumbra, which reduces efficacy of mechanical thrombectomy (Saver, 2006). As a result, delayed presentation to stroke centers after stroke onset also can explain higher mortality rates among Black patients after mechanical thrombectomy (Catapano et al., 2021).

Some of the differences in utilization may reflect accessibility or availability differences, as described above; however, it may also result from differences in help-seeking and symptom recognition between Black and White patients. Delayed presentation to the hospital among Black patients is related to low awareness of heart disease, low recognition of stroke symptoms, and the lower propensity to seek help (Farcas et al., 2022; McSweeney et al., 2016).

Even in specialized centers that offer mechanical thrombectomy services, Black patients' rate of utilization is less than half of White patient populations (Brinjikji et al., 2014). Authors note that differences in rates can be attributed to a multitude of barriers, such as geographic access challenges (i.e., lack of access to centers offering thrombectomy treatments), socio-economic reasons (i.e., delays in seeking treatment, education level), and differences in stroke etiology. With respect to stroke etiology, there is evidence that high ischemic stroke incidence among Black patients is due to higher rates of all ischemic stroke subtypes, but especially intracranial atherosclerotic and lacunar stroke (White et al., 2005). These differences in ischemic stroke subtype distribution and incidence are thought to be due to variations in risk factor burden and possibly in genetic susceptibility (White et al., 2005). However, only a few genetic studies focus on Black populations with a majority focusing on people of European descent (Keene et al., 2020).

Delays in getting to the hospital do not stop at delayed recognition of symptoms. It has been documented that there are barriers to access to essential services for all populations and specific barriers to communities of color. For example, the utilization of transport services and emergency transport also differ by race and ethnicity, with minority communities less likely to call 9-1-1 (Aroor et al., 2022). A systematic review of disparities in stroke treatment between racial minorities found White patients utilized emergency medical services at a greater rate (59.8%) than African American patients (55.6%) and other racial and ethnic minorities (Ikeme et al., 2022). Utilization of EMS could affect utilization rates for thrombolysis as there is a positive association between arriving by ambulance transport to the hospital and receiving thrombolytic treatment within 60-minutes (Oluwole et al., 2017). There are lost opportunities in pre-admission care (e.g., rapid triage and critical care) for patients arriving in private vehicles (Kunz et al., 2020). However, there is also evidence of provider bias at the EMS clinician level

with respect to correctly diagnosing stroke in minorities and using pre-arrival stroke notifications (Farcas et al., 2022). Provider implicit bias could also create delays even when health care is sought in a timely manner. There is some evidence that providers may under-identify stroke symptoms in women (McSweeney et al., 2016), even though there are typically not differences in presenting typical stroke symptoms by gender (Beal, 2010; Beal et al., 2012; Stuart-Shor et al., 2009).

Thrombolysis is even more time-sensitive, with a door-to-needle time of less than 60 minutes being the standard of care for the optimal efficacy of the procedure. Less than half of acute ischemic stroke patients (42%) receive treatment within 60 minutes of hospital arrival, with Black patients less likely to be treated within 45 minutes during off hours (e.g., nights and weekends) (Oluwole et al., 2017). However, controlling for lower use of emergency medical services (EMS) by Black patients, adjustments for EMS prenotification (i.e., call-ahead to the receiving hospital), and adjustments for stroke severity (i.e., a larger proportion of Black patient had NIHSS score above five indicating higher severity) did not fully account for longer door-to-needle time (Oluwole et al., 2017).

The severity of neurological presentation at the time of admission also affects the likelihood of treatment. Hospitals are more likely to immediately begin thrombolysis in response to more severe stroke symptoms. Specifically, the likelihood of thrombolytic administration was higher for younger, White, Hispanic, and Other patients, who arrived at the hospital early with severe neurological presentation (Asdaghi et al., 2018). Finally, Black patients have lower rates of documented acute large vessel occlusion which could lead to lower utilization rates of mechanical thrombectomy (Wallace et al., 2022). It is noted that differences in utilization could be because of differences in stroke cause, including a higher prevalence of cardioembolic stroke in White patients and a higher prevalence of intracranial atherosclerosis in Black patients.

An additional consideration is the history of prior treatment. A recent review found that 40% of ischemic stroke patients were already on antiplatelet regimens (Sun et al., 2019). Sub-group analyses found that Asian populations were more likely to have prior treatment with antiplatelet medication and were more likely to experience symptomatic intracerebral hemorrhage. Given the time urgency for intervention, provider awareness of relationships between prior treatment history and race may be important to consider when initiating treatment in current stroke presentation (Brandel et al., 2020).

Provider bias. Uneven population distribution, with demographic clustering and residential segregation by race across regions, results in clustering of minority patients in a relatively small number of minority-serving hospitals (Farcas et al., 2022; Himmelstein et al., 2023). Minority patients are also more likely to be transported by EMS to safety net emergency departments relative to White patients (Hanchate et al., 2019). However, even in predominantly minority serving hospitals, minority men had significantly lower odds of intravenous thrombolysis administration relative to hospitals serving predominantly White patients (Faigle et al., 2017); there were no such differences for White men treated in either hospital type (predominantly minority or predominantly White hospitals).

Such biases are further propagated by clinical guidelines (e.g., therapeutic window) that may restrict access to thrombolytic procedures. For example, due to the longer time to reach the hospital for minority populations, they are more likely not to meet time-sensitive procedure eligibility restrictions (Asdaghi et al., 2018). Additionally, there are well-documented racial disparities in stroke prevention, treatment, and

recovery that have been attributed to implicit bias and structural factors affecting inequities in healthcare access (Skolarus et al., 2020). Black patients as a result are less likely to be deemed eligible for mechanical thrombectomy when presenting for ischemic stroke (Wallace et al., 2022).

VI. Discussion

Our analysis and the literature review revealed gaps in utilization of cardiovascular and neurovascular procedures by race/ethnicity and in some instances gender. There is consistent evidence of underutilization of cardiac ablation, angioplasty, and TAVR in Black populations relative to White populations. Utilization of neurovascular procedures was also lower among the Black population. For example, White men have the highest odds of receiving intravenous thrombolysis procedures at all hospitals irrespective of the hospital being predominantly White-serving or minority serving, when compared to women and ethnic minorities (Faigle et al., 2017). While there was a Black-White gap in utilization of mechanical thrombectomy in the past, it decreased over time. Moreover, in recent years, Black patients have higher rates of receiving thrombectomy compared to White Medicare fee-for-service beneficiaries.

Our review showed that factors affecting utilization cover a broad range of issues and contribute to delays in treatment in both pre-admission and post-admission time intervals. Given the multitude of factors leading to utilization disparities, there will not be a single solution that fits all, but rather a list of potential interventions that address specific factors. Interventions that optimize timelines and accuracy of the diagnosis and reduce diagnosis delays require understanding the diagnostic process and its components as well as factors affecting pre-admission and post-admission delays. Below, we discuss common themes that could create disparities and specific examples of factors linked to disparities in utilization of these procedures that can inform future interventions, pre- and post- hospital admission.

Interventions aimed at early detection and timely diagnosis.

One of the common themes for both the cardiovascular and neurovascular diseases of interest was delay in detection and obtaining a timely diagnosis. A variety of behavioral factors at the patient and provider levels begin with recognition of symptoms by patients and end with implicit biases that affect provider's decisions leading to differences in standards of care across populations.

For time-sensitive procedures for neurovascular diseases, early recognition of symptoms, seeking immediate emergency help, and presenting to the hospital as soon as possible is essential for treatment eligibility and treatment efficacy. There is evidence that at risk populations, with limited knowledge of stroke symptoms and the importance of contacting EMS, include men, racial and ethnic minorities, as well as people with lower levels of education (Jackson et al., 2020). Studies showed that while targeted campaigns to improve stroke symptom recognition and improved understanding of the reasons underlying the importance of rapid emergency response in the US (e.g., FAST campaign) improve general knowledge of stroke and the awareness of acute stroke interventions, resultant behavioral response has been suboptimal (Hickey et al., 2018). Some international studies have demonstrated some success in speeding access to stroke care (Berglund et al., 2014; Bray et al., 2011). This implies that public education campaigns can be successful in targeting at-risk populations. An additional component of a well-designed campaign is educating at-risk populations to recognize atypical symptoms or symptoms that could be similar to other comorbidities (e.g., the symptom of "sudden severe headache" had the lowest prevalence of awareness of being a stroke symptom) (Jackson et al., 2020).

Timely diagnosis in part depends on timely recognition of the disease by the patient or timely detection of the disease by a provider. Education and health literacy differences between Black and White patients

result from a combination of race-related structural and interpersonal biases (Muvuka et al., 2020). Improving stroke symptom recognition among at risk populations and communities may require targeted interventions that address racial differences in social isolation and living arrangements (Taylor et al., 2019), as well as health literacy.

With age-progressive diseases such as arrhythmias, disparities in treatment utilization can be reduced through earlier disease detection. That is, a wedge in access to early intervention and treatment for atrial fibrillation leads to negative health outcomes for minority patient populations compounding over time and leading to lower success rates of cardiac ablations. Interventions targeting early detection of the disease such as screening among racial minorities, as well as interventions that incentivize referrals to cardiologists could decrease delays and improve timely diagnosis. Given the under diagnosed/under recognized severity of atrial fibrillation in women, provider-specific intervention could prioritize "gender-blind" assessment of risk scores, severity, and medication protocols.

Black patients are less likely to be referred to specialty cardiologists even when they have severe aortic stenosis (Sleder et al., 2017). To increase TAVR utilization among Black Medicare populations and to increase their inclusion in the indicated for treatment population, intervention should target referral and follow-up processes to ensure that patients visit specialty cardiologists and follow pathways needed for TAVR treatment. Given that TAVR has complex treatments pathways, this could be achieved by hiring pathway navigators to guide patients through the process and to support post-treatment follow-up (e.g., reminders for upcoming appointments, transportation support).

Interventions related to guidelines and treatment protocols.

Black populations were less likely to receive prescription medications, such as Warfarin, that are required to manage their atrial fibrillation. They were also less likely to see therapeutic results and at elevated risk for negative side-effects when prescribed Warfarin due to suboptimal dosage. Improved dosage guidelines and algorithms, developed through targeted clinical studies and recruitment of understudied populations, may generate more appropriate dosage guidelines that maximize outcomes within these groups and reduce a key source of disparities.

A lack of revascularization efforts seen in Black and Hispanic communities correlate with disproportionately high rates of amputation within minority communities, and fewer limb salvaging procedures such as angioplasties or bypass surgeries. Alternative treatments and preventive interventions in Black populations, could reduce the adverse effects of angioplasty related to amputation.

Interventions aimed at reducing treatment eligibility bias and provider bias.

For time-sensitive procedures, underutilization of emergency services by populations of color can reduce chances of a presentation to the hospital within the therapeutic window and eligibility for administration of procedures such as mechanical thrombectomy and thrombolysis. Interventions focused on education regarding stroke-like symptoms, importance of immediate medical attention/intervention in addressing those symptoms, promoting use of emergency services via community-based interventions/events, or providing alternative solutions for emergency transportation could alleviate gaps in utilization of these procedures. Barriers in accessing the EMS system or utilizing 9-1-1 services could be related to distrust and financial concerns, and in some communities to limited English proficiency and immigration status (Farcas et al., 2022). These barriers suggest that efforts should be made to build trust between emergency services and communities of color through increased education and outreach to these populations. These trust building efforts could clarify the relationship between emergency response

services and immigration services and educate on the urgency of early EMS activation in treating neurovascular conditions.

Hospital transfers, long travel times, and lack of timely access to revascularization procedures lead to lowered eligibility and worsened outcomes for patients (Aroor et al., 2022). Transfers between hospitals to EVT centers are quite common, with 45% of transfers being for the purposes of mechanical thrombectomies. There are documented lower rates of utilization of EVT among Black patients, albeit the gap has narrowed since 2015 (Sheriff et al., 2022). The rate of transfers to EVT centers is lower among Black patients (Shah et al., 2019). Hospital-based and EVT-center based interventions could focus on reducing transfer time, decreasing time to treatment.

Measuring and addressing implicit biases at a provider level or healthcare system-wide level is difficult, and improving bias is similarly challenging. A first step in addressing implicit bias is a recognition that such bias exists. Implicit bias awareness training programs can educate healthcare providers and first responders. Workforce diversification, especially among EMS and paramedics, 70% of which are White (Ventura et al., 2022), is one potential strategy. However, as noted in the National Institutes of Health Scientific Workforce Diversity Seminar proceedings, implicit-bias training has limitations, even when well-designed, and should not be a one-time event but rather part of a broader institutional strategy (NIH, 2021).

VII. Conclusion

The differences in procedure utilization rates provide a starting point for uncovering disparities in treatment between patient populations. A lifetime approach that considers the many structural factors, including differential access to services, health status and complications, and social factors, that shape these observed differences in utilization, is needed to identify potential points of intervention to reduce them. This Phase II analysis addresses what is known about racial disparities for the specified cardiovascular and neurovascular conditions and identifies potential solutions/recommendations to reduce disparities.

The Phase II analysis focused on cardiovascular and neurovascular conditions for several reasons. Based on Phase I analysis, we concluded that the cardiovascular and neurovascular interventions exhibited a meaningful pattern of racial disparity compared to the other conditions examined. These services also had relatively high frequency of utilization for common conditions that translate into meaningful opportunity for improvement. Additionally, the eligible populations for the cardiovascular and neurovascular interventions are clinically related, which will allow us to examine a broader pattern of disparity.

Phase III will extend the Phase I analysis to address additional causes of utilization differences, including clinical factors beyond diagnosis (e.g., comorbid conditions) and community-level factors and will assess the causes of access differences to determine whether they are driving disparities.

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