REVIEW

OPEN

Are the current evaluation tools for advanced therapies biased?

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Purpose of review
Despite attention to racial disparities in outcomes for heart failure (HF) and other chronic diseases, progress against these inequities has been gradual at best. The disparities of COVID-19 and police brutality have highlighted the pervasiveness of systemic racism in health outcomes. Whether racial bias impacts patient access to advanced HF therapies is unclear.

Recent findings
As documented in other settings, racial bias appears to operate in HF providers' consideration of patients for advanced therapy. Multiple medical and psychosocial elements of the evaluation process are particularly vulnerable to bias.

Summary
Reducing gaps in access to advanced therapies will require commitments at multiple levels to reduce barriers to healthcare access, standardize clinical operations, research the determinants of patient success and increase diversity among providers and researchers. Progress is achievable but likely requires as disruptive and investment of immense resources as in the battle against COVID-19.

Keywords
heart failure, heart transplantation, left ventricular device, racial bias, racism

INTRODUCTION

Decisions about whether a patient should receive advanced heart failure (HF) therapy, and which type – heart transplant (HT) or left ventricular assist device (LVAD) – require considering a complicated slate of risks and benefits. Whether the metrics HF practitioners use to evaluate patients for advanced therapy are universally appropriate, and whether therapies are distributed fairly, are areas that need discussion and investigation. The following review considers possible bias in evaluating patients for advanced therapy largely through the lens of American anti-Black racism and its consequences. I discuss the potential for biased risk estimates based upon standard assessments of medical and psychosocial factors, negative impacts of provider bias, and the need to be serious about addressing disparities and improving diversity in clinical research.

HEART FAILURE DISPARITIES IN THE CURRENT LANDSCAPE OF ADVANCED THERAPIES

African-Americans and other marginalized groups bear a disproportionate burden of chronic diseases, including HF. From 2002 to 2013, age-standardized HF hospitalization rates for African-Americans were more than twice that for any other group [1]. Analysis of Centers for Disease Control data shows that age-adjusted excess Black HF deaths have decreased overall since the late 1960s, but over the past two decades have increased nearly twofold (Fig. 1A) despite a cascade of landmark HF trials— erasing 30 years of progress. The crude excess Black HF death rate has increased since 1999 in every age group between 25 and 84 (Fig. 1B), ages in which HF patients might benefit from advanced therapies.

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KEY POINTS

- Despite advances in the management of various stages of heart failure, excess age-adjusted deaths among African-Americans have risen substantially over the past two decades.
- Multiple elements of the advanced HF therapy evaluation process are vulnerable to bias.
- The impact of biases on advanced therapy evaluation is unclear and requires dedicated research.
- Progress toward equity and justice will require enhanced diversity among research subjects, investigators, journal editors, and providers.
- Professional societies should develop guidelines for researching and reducing heart failure disparities.

One-year post-HT survival is roughly comparable regardless of race, but Black recipients have higher long-term rates of death or graft failure in most United Network for Organ Sharing (UNOS) registry analyses [2–5], including that presented in Fig. 2. Linked UNOS and Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry data prior to HeartMate 3 LVAD (HM3) availability show superior survival for patients bridged to HT with an LVAD (BTT) than those receiving an LVAD as provisional destination therapy (DT) [3]. Survival after HM3 implantation in the MOMENTUM 3 trial was roughly 87% at 1 year and 79% at 2 years regardless of intent (BTT, DT, or bridge to candidacy) as compared to 90% and 85% one- and three-year post-HT survival, respectively [6]. LVAD implantation or HT should yield similar one-year survival for patients suitable for either strategy. However, while an LVAD can be implanted on-demand, time to HT depends upon multiple factors including ABO blood type, waitlist priority, UNOS region, pulmonary hypertension (HTN), sensitization, and body size. Only half of candidates have undergone HT by 1 year after listing, and roughly 22% have experienced death or delisting [7]. Compared to White BTT patients, African-Americans are more likely to die or be delisted and less likely to receive HT [2]. The 2018 revision to the UNOS heart allocation strategy additionally advantages patients on temporary mechanical circulatory support. In response, centers are bridging fewer

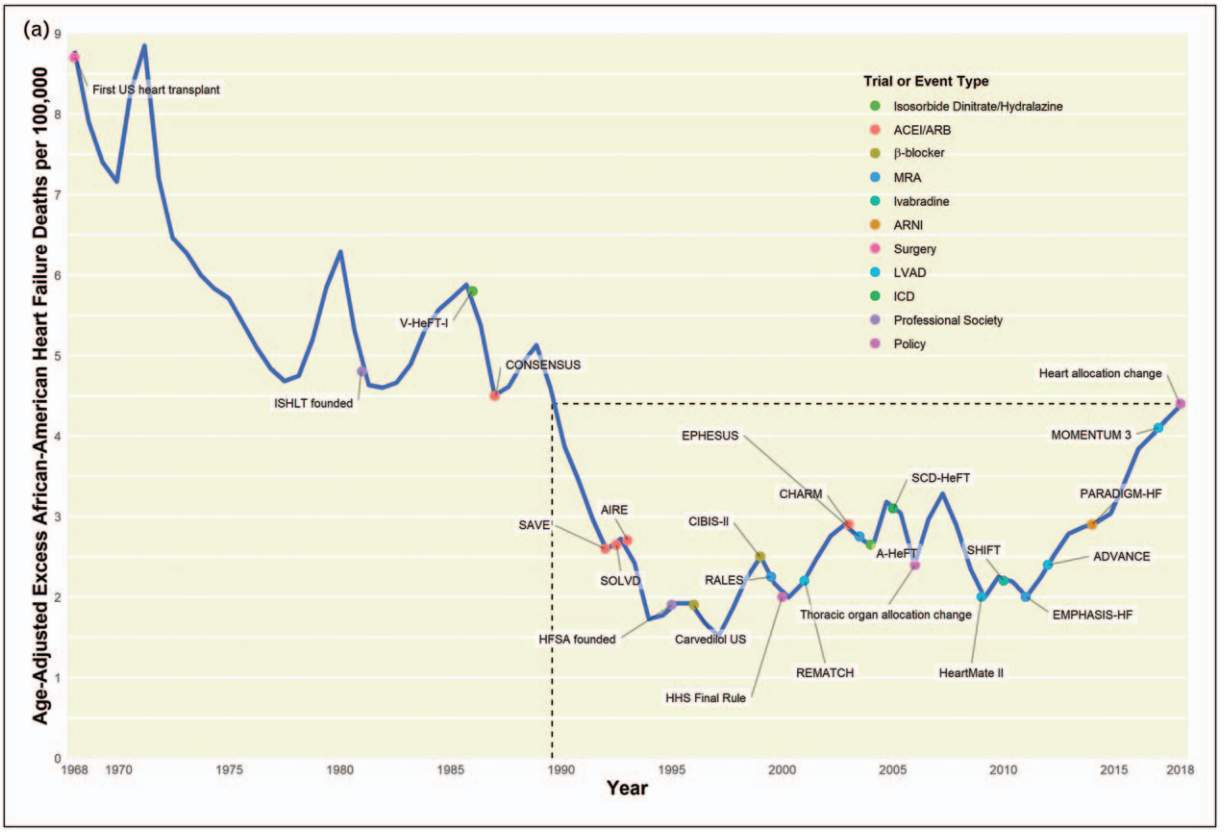

FIGURE 1. Excess African-American Heart Failure Deaths. A: Trend in annual age-adjusted excess deaths among African-Americans compared to the non-Black population. B: Annual number of crude excess African-American heart failure deaths compared to the non-Black population in 10-year age intervals from 25 to 84.

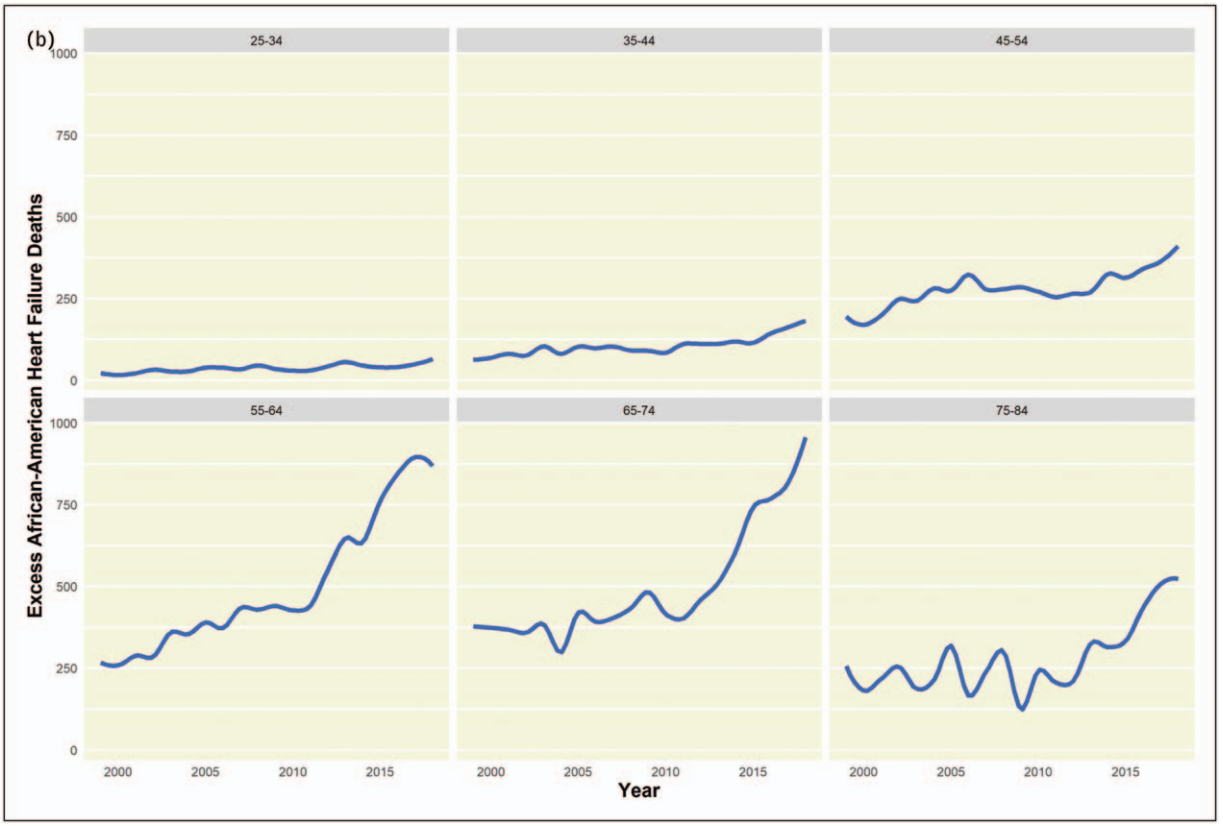

FIGURE 1. (*Continued*).

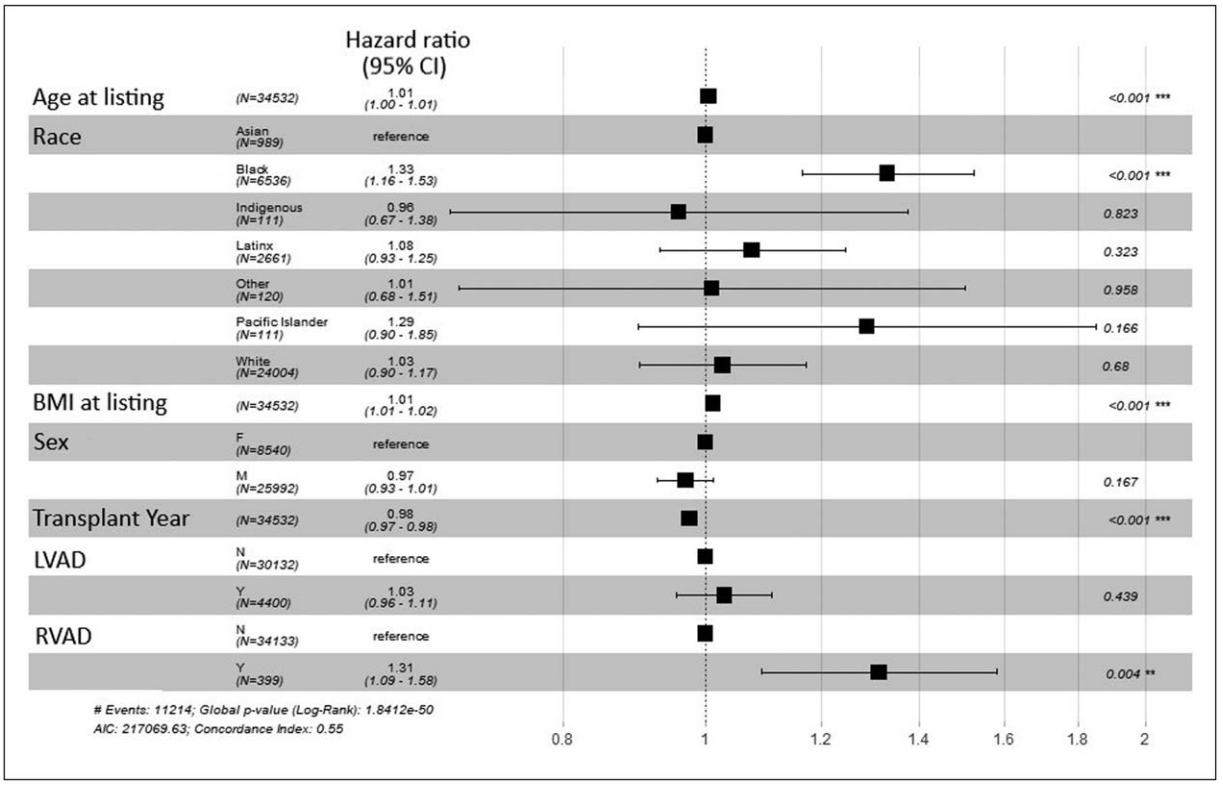

FIGURE 2. Multivariable hazard of graft failure or death among first-time heart-only recipients (2000–2016).

candidates with durable devices and more with temporary support [8–10]. Optimal strategies for supporting diverse patients with advanced HF in the current era of organ allocation and durable LVAD have not been explored.

ADVANCED HEART FAILURE THERAPY EVALUATION

Common indications for advanced therapy include intractable symptoms such as angina, manifestations of low cardiac output, and electrical or hemodynamic instability despite the maximum achievable pharmacologic and interventional therapy [11,12]. Advanced HF programs must be prudent in evaluating how to allocate limited resources based upon patients' medical and psychosocial risk. But select elements of typical evaluation processes appear vulnerable to bias.

Medical factors

Several factors would predict a higher likelihood of Black patients being declined for advanced therapy or receiving an LVAD before or instead of HT. The distributions of these factors by race among patients evaluated for advanced therapies, prior to candidacy, are unclear. Additionally, data directly establishing their contribution to bias in the evaluation are lacking.

Immunology

A higher prevalence of O blood type among Black and Latinx people in the general US population and on HT waitlists would predict longer wait times and thus higher LVAD placement rates than for White people [13,14]. Patients who are sensitized against donor antigens may also require LVAD bridging until a suitable donor can be identified or appropriate desensitization is completed. But LVAD surgery conveys a risk of additional sensitization because of transfusion needs, and thus may further delay HT.

Morris *et al.* found in a UNOS registry analysis that Black candidates had higher peak panel reactive antibody (PRA) levels that predict graft failure, and are the most likely ethnic group to be sensitized-defined as having peak PRA $\geq$10% [14]. Known contributors to sensitization did not appear to explain these differences. Black candidates were less likely than others to have previously received blood transfusions. Black candidates were more likely to have had prior pregnancies, but this difference appears to reflect the higher proportion of women among Black candidates than among other groups. Whether sensitization influences equity in the allocation of LVAD and HT is unexamined. Morris *et al.* additionally showed in a single-center retrospective study that Black HT recipients were more likely to develop *de novo* donor-specific antibodies (DSAs), independently of pre-HT sensitization [15]. LVAD placement as a bridge to HT was marginally predictive of *de novo* DSA development.

Hemodynamics

Pulmonary vascular resistance (PVR) $\geq$3 Wood units (WU) is a common contraindication to HT. Perhaps owing to later referral, Black and Latinx candidates are more likely than White candidates to have a PVR $>$3 WU [16,17]. If the PVR cannot be lowered pharmacologically, LVAD implantation may be considered until hemodynamics are more suitable for HT listing.

A peak oxygen consumption (VO_2) $\leq$14 mL/kg/min on cardiopulmonary exercise testing is a well-known indication for advanced therapy. Black HF patients have lower average peak VO_2 compared to White patients despite similar β-blocker use [18,19]. This difference may reflect later referral, but peak VO_2 is lower for African-Americans without HF [20,21]. Lower cardiorespiratory fitness among African-Americans is unexplained. Researchers have invoked lower hemoglobin levels and muscle oxidative capacity due to a lower abundance of mitochondria-rich type I muscle fibers, but race independently predicts peak VO_2 after adjustment for these factors among subjects without HF [22–24]. A higher prevalence of obesity and chronically lower access to physical activity opportunities for African-Americans may also be explanatory. Ventilatory efficiency, as indicated by the minute ventilation/carbon dioxide slope (VE/VCO_2), is strongly predictive of a combined endpoint of HT, LVAD, or cardiac death in multiple studies [25,26]. Peak VO_2 was not significantly prognostic in a multicenter study for HF Black patients, particularly for Black women, but VE/VCO_2 appeared to be predictive regardless of race or sex [27]. Whether preferential use of VE/VCO_2 versus peak VO_2 would affect equity in advanced therapy deserves additional study.

Metabolism

Black HT candidates have a higher average body mass index (BMI) than other groups. Increasing BMI at listing predicts declining likelihood of HT, including nearly 50% reduction for candidates with BMI $\geq$35 [28]. Neither BMI at listing or at transplant predicts one-year post-HT survival, though high-priority recipients with BMI $\geq$35 have reduced three-year survival [28,29]. Obesity is associated with elevated risks of non-HM3 LVAD thrombosis, device-related infection and right HF, but lower one-year and equivalent two-year mortality [30]. For BTT

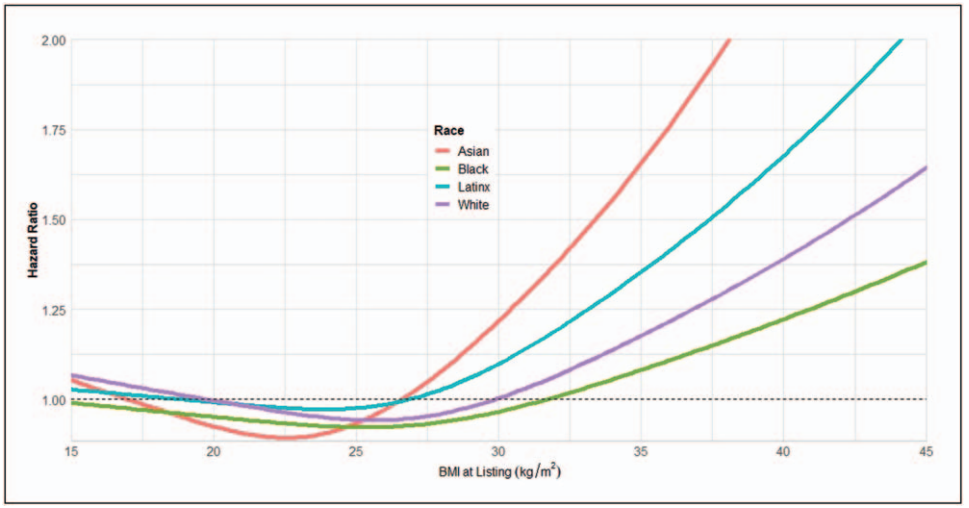

FIGURE 3. Race-specific hazards of graft failure or death as a function of BMI among first-time heart-only recipients (2000–2016). Hazards are adjusted for age at listing, sex, year of transplant, LVAD prior to transplant and RVAD prior to transplant. BMI, body mass index; LVAD, left ventricular assist device; RVAD, right ventricular assist device.

patients, obesity, even at a BMI >40, does not predict post-HT survival despite higher risk profiles [31]. A single-center study found no impact of extreme obesity (BMI >40) on survival at one year after LVAD implantation, despite more pump thrombosis among obese patients [32]. Figure 3 shows J-shaped hazards of graft failure or death among first-time heart-only recipients as a function of BMI at listing- after adjustment for age, sex, UNOS region, year of transplant, and LVAD or right ventricular assist device (RVAD) at listing. The risk for Black patients rises at higher BMIs than for other groups and is only 10% above baseline at a BMI of 36. These differences mirror epidemiologic findings of ethnic-specific all-cause mortality hazards due to BMI [33,34].

BMI firmly associates with the risk of diabetes mellitus (DM), which is more prevalent among non-White people in the general population [35]. Despite a negative impact on a wide range of health outcomes, DM does not consistently associate with post-LVAD mortality, infection, stroke, or pump thrombosis [36]. A beneficial effect of LVAD placement on glucose metabolism may explain this null association [37,38]. The impacts of DM and glycemic control on the allocation of advanced therapy by race are unclear.

Renal function

Early chronic kidney disease (CKD) prevalence is similar among American ethnic groups but CKD progression is more common among non-White groups. Black, Latinx, and Indigenous Americans have a higher prevalence of end-stage renal disease (ESRD) than do White people [39]. In addition to likely socioeconomic contributors, elevated frequencies of high-risk *apolipoprotein L1* gene alleles among African-Americans appear to explain a substantial proportion of excess ESRD risk [40]. In a prospective cohort, Black subjects with an estimated glomerular filtration rate (GFR) between 20 and 70 mL/min/1/73 m^2 were more likely to have HF at study entry and a 60% higher risk of HF events over a median follow-up of 6.6 years [41]. Among patients with established HF, CKD is more common among Black patients with HF with preserved ejection fraction than among White patients [42]. Black HT recipients are more likely than White recipients to have also received a simultaneous kidney transplant [43]. A small single-center retrospective study indicates greater declines in estimated GFR after solitary HT for Black recipients compared to non-Black recipients despite similar maintenance calcineurin inhibitor levels [44]. For patients with reduced GFR in the setting of HF, LVAD placement results in early improvement in renal function that returns to the pre-LVAD baseline after one year, for reasons that are unclear [45]. The degree to which advanced therapies affect renal disease progression among different ethnic groups deserves further study. Whether CKD has differential impact on advanced therapy candidacy by race is unknown. Recent debate that remains unsettled surrounds whether race should be included in the estimation of GFR. Both the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations incorporate Black race. Concerns that inclusion of race in clinical equations may be counterbalanced by underestimation of GFR for most African-Americans

if the race parameter were to be removed [46]. The magnitude of difference is small for patients whose true GFR is lower than 30 [47].

Psychosocial factors

Standardized pretransplant psychosocial assessments have been tested in diverse cohorts [48–53]. Each rates candidates in domains that include social support, psychological illness, and stability, readiness for therapy, illness management including adherence, and substance use. Each of these domains, perhaps excluding substance use, is vulnerable to bias. The abilities of these factors to predict advanced therapy outcomes are inconsistent, and whether they perform similarly for different ethnic groups is unclear.

Nonadherence

Given a need for patients to adhere faithfully to heavy drug regimens after advanced therapy, nonadherence should raise concerns, especially for HT. There is evidence of less-consistent pill-taking among privately insured Black, Latinx, and Asian patients compared to White patients prescribed medications for HTN, DM, and hyperlipidemia after controlling for socioeconomic status and out-of-pocket costs [54]. At a large HF clinic, non-White patients were likelier to arrive late for appointments, but the effect was confined primarily to younger patients scheduled for early morning appointments [55]. Adherence varies among racial groups, but the contribution of provider bias to the existence and perception of nonadherence may be underappreciated. Pro-White implicit bias among providers is associated with the quality of patient interactions, treatment decisions, quality of care, treatment adherence and outcomes [56–58]. Patient mistrust of providers predicts lower adherence among Black men with HIV [59]. Perceived discrimination predicts lower adherence for Black patients with HTN, an association mediated partly by patient stress and depression [60]. Providers' implicit bias may contribute to patient nonadherence and helps determine which patients they presume to be nonadherent [61–63]. Physicians seeing patients after coronary angiography rated Black patients as less likely to follow medical advice or participate in cardiac rehabilitation, and were less likely to rate them as 'the kind of person I can see myself being friends with.' They were less likely to rate Black patients as intelligent or educated, even after controlling for reported education [64]. Black patients with DM seen in clinics of a large health system were roughly three times as likely as White patients to be labeled nonadherent, even when hemoglobin A1c was at goal [65▪▪]. Every clinician in an era of 'copy forward' electronic records must understand the potential for labels such as 'nonadherent' or 'noncompliant' – whether accurate or not- to become fixed in patients' records and prejudice new providers.

Most studies of implicit bias testing among providers find that those with high levels of pro-White bias have greater difficulties with patient-provider communication [57]. Black cancer patients seen by providers with higher implicit bias had more difficulty remembering details of the interaction, lower confidence in prescribed treatments, and greater perceived difficulty in completing treatments [66]. The relevance of these findings to patients' medical adherence and engagement is clear.

Psychological illness

Racism may contribute to depression and anxiety among African-Americans. Black adolescents exposed to increasing levels of perceived discrimination have higher ratings of depressive and anxious symptoms [67]. Emergency visits for depression and self-reported burden of poor mental health spike among African-Americans after local police killings [68]. Black people with mental illness may face barriers to care such as insurance, but discrimination may also intervene. When psychotherapists receive voicemail messages featuring actors portraying people seeking help for depression or anxiety, all with the same commercial insurance plan, 'Black' callers are less likely to receive an appointment or callback [69]. Bias may affect clinician ratings of Black mental illness. African-Americans are particularly likely to receive a diagnosis of schizophrenia, a disparity possibly mediated by interviewers' perception of Black patients as less honest about their symptoms and by difficulties in patient-clinician relationships [70,71].

Social support

Studies of social support by race show mixed results. Data from the 1980s showed lower levels of instrumental and emotional support among African-Americans, for whom low instrumental support was associated with increased odds of HTN [72]. Nationally representative data show similar emotional and financial support for Black and White respondents, but Black respondents lacking both were likelier to have HTN [73]. Physicians in the postangiography study were more likely to rate Black patients as likely lacking social support, even after controlling for patients' self-reported social support [64].

Evidence of bias, biased evidence

A landmark 1999 study revealed bias among physicians randomized to video vignettes of actors

portraying patients with angina that differed only by race and sex. The physicians were less likely to refer Black and women actors for cardiac catheterization [74]. Building upon these methods, Breathett *et al.* conducted studies that randomized professionals involved in decision-making about advanced therapy allocation to standardized vignettes, showing that race figured prominently in thought processes about decision-making and that adherence and social history emerged as important factors in decisions about Black patients. Recurring themes included beliefs that Black patients were sicker and less likely to be adherent and that respondents might have difficulty forming rapport with Black patients. The White patient was more likely to be offered HT and the Black patient more likely to be offered LVAD. In a separate study, children were seen as particular liabilities for women - especially Black women, to whom respondents attached concerns about financial stability [75▪▪,76▪].

Bias in, bias out

Underrepresentation of non-White subjects in clinical studies is persistent and leads to biased risk prediction. Risk factors derived from the Framingham Heart Study underperform in predicting cardiovascular events among non-White patients [77]. HF guidelines recommend ancillary use of risk scores like the Seattle Heart Failure Model (SHFM) for advanced therapy decision-making. But SHFM, validated in largely White cohorts [78], underestimates risk for all patients but particularly for Black patients [79,80]. One group added Black race to a BTT risk score for 1-year post-HT outcomes and published an online calculator. The score also included recipient age, BMI, recent infection, serum bilirubin, and dialysis [5]. The model showed mildly improved concordance compared to one without race [81]. It is important to acknowledge the association of race with outcomes, but the wisdom of incorporating race itself as a 'risk factor' into a score intended to guide clinical decision-making must be pointedly questioned. Many single-center and multicenter studies fail to reproduce these findings [82].

UNOS analyses that demonstrate racial disparities in post-HT survival generally fail to account formally for center differences. Black patients disproportionately receive HT at centers that perform poorly based on score (IMPACT) that also includes Black race [83,84]. The BTT and IMPACT risk scores appeared in journals whose editorial boards had no Black editors at the time of publication [85,86], which is emblematic of diversity deficits throughout medicine - and in cardiology and HF specifically - that may facilitate inappropriate invocations of race and propagate racialized thinking. Even machine algorithms are vulnerable to the biases of their programmers. A prediction algorithm used by a large health system widely underperforms in predicting risk for Black patients, for whom risk is far higher than predicted [87]. It is possible to overcome these barriers but awareness and intention are required [88].

Bias reduction

Implicit bias has emerged as a target for improving equity and inclusion among clinical teams and for reducing healthcare disparities. Frequently cited research has suggested that neurobiological processes underlying biases consist of distinct components: implicit, explicit, and behavioral [89]. Implicit Association Test scores among healthcare providers are similar to the general population [58]. Brain regions implicated in implicit bias include the amygdala, dorsolateral prefrontal cortex, and fusiform gyrus [90]. In placebo-controlled studies, White volunteers treated with propranolol have reductions in implicit association scores and lower fusiform and thalamic activation when shown images of Black faces, implicating β-adrenergic pathways and potentially anxiety or fear mechanisms in mediating implicit cognition [91,92]. But a multitude of interventions aimed at reducing implicit bias are inconsistently associated with any impact on bias and less so with stable and durable change, in a literature largely plagued by low-quality study designs [56,93]. Credible evidence that implicit bias training or other bias-reduction and diversity practices reduce racial gaps in healthcare delivery and quality is nonexistent, as is a rigorous framework for generating such evidence [94]. Currently accepted practices for reducing the impacts of bias notably aim to change thinking, which is not easily or regularly measurable, as opposed to targeting quantifiable behavior such as individual providers' quality metrics.

A diversity mandate

Black and Latinx physicians each comprise roughly 5% of the HF physician workforce (Fig. 4), figures that are unrepresentative of the HF patient population. For Black patients, the availability of Black physicians may be profound. Messaging from Black physicians increases African-Americans' knowledge and information-seeking about COVID-19 [95]. In racially concordant interactions, Black patients were more likely to give their physicians the highest rating for 'likelihood of recommending this care provider to others' than in discordant encounters [96▪▪]. Black and Latinx patients are more likely than White patients to seek care from physicians of the same race

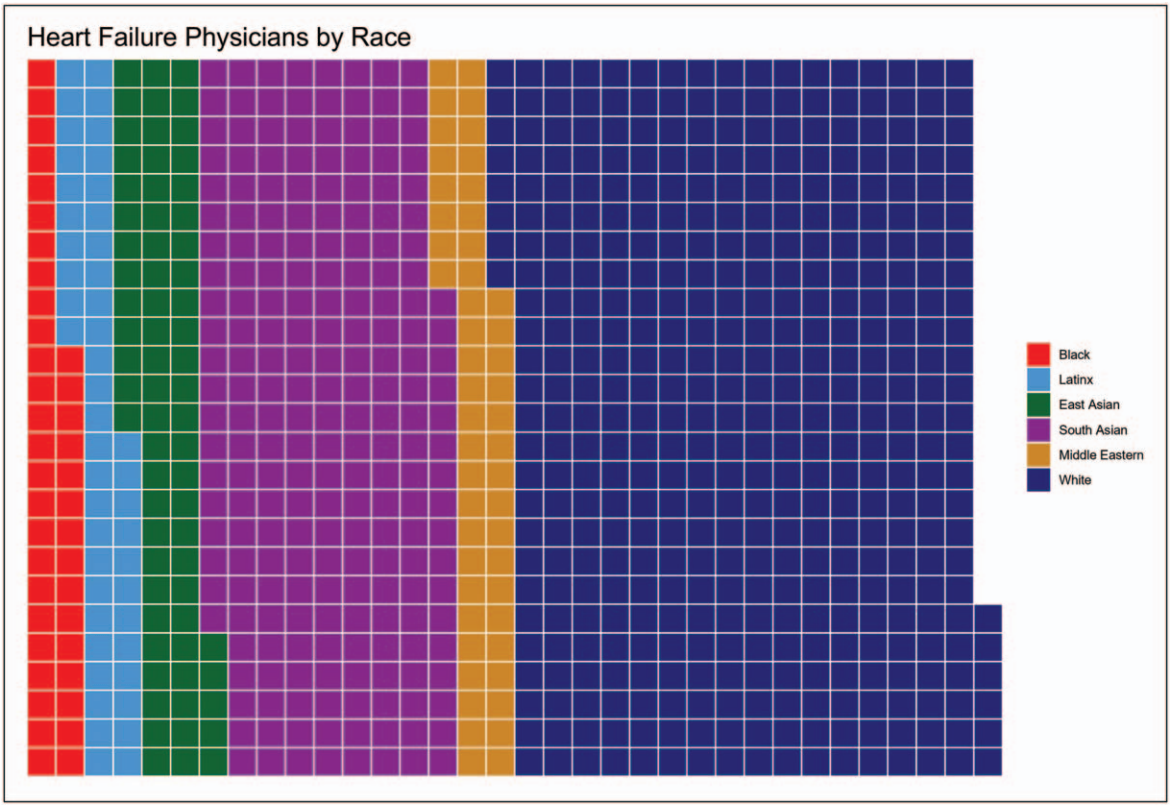

FIGURE 4. Racial diversity among US heart failure physicians. Each square represents one physician.

or ethnicity. Black patients are more likely to rate Black physicians as 'excellent' overall and to report that their doctor treats them with respect, explains problems, listens, and is accessible. Black patients with Black physicians are more likely than those with physicians who are not Black to report receiving preventive care and all necessary care [97]. Black neonates who receive care from Black doctors have a substantially reduced mortality, an effect even more apparent in complicated cases [98▪]. I suggest that diversity deficits on clinical and research teams contribute to fatal flaws that perpetuate bias and health disparities. In 2020, a respected cardiology journal, which at the time had one Black and Latinx editor each on a board or more than 40, published a 'white paper' expressing hostility to diversity efforts in cardiology [99,100]. The journal retracted the paper under pressure, noting critical factual inaccuracies and blandly promising 'a path forward to eliminate deficiencies in the peer review process' [101]. Diversifying its staff would be an obvious first step. The journal has several social media editors, as do many other journals, but no social justice editor.

A legacy of mistrust

A thorough examination of barriers to HF health equity created by implicit and 'unconscious' bias must acknowledge a history of explicit and fully conscious bias - and outright racism - in American healthcare. African-American mistrust of the medical establishment rightfully follows a long history of mistreatment that includes medical and surgical experimentation on enslaved people, theft of Black bodies for dissection and forced sterilization of Black women. The Tuskegee Project that studied the natural history of syphilis by withholding treatment from infected Black men is only the most prominent example of the medical abuse of African-Americans. The early era of American heart transplantation recapitulates this history. In 1968, the Medical College of Virginia (MCV), with its own history of racist grave robbing, admitted a Black man named Bruce Tucker after a traumatic brain injury. Without the knowledge or consent of Mr. Tucker's family, surgeons placed his heart in the body of a White patient—the first heart transplant in the segregated American South. The funeral director informed Mr. Tucker's family that his heart and kidneys were missing [102]. An all-White jury exonerated MCV of wrongdoing. MCV's successor, Virginia Commonwealth University (VCU), acknowledges this episode as an unfortunate part of its legacy and pledges to have conversations, learn, accept criticism and contribute to healing. It has not pledged to redress this crime with the family and community it harmed.

The disparities of the COVID-19 outbreak have sparked necessary discussion about the impacts of structural racism and systemic bias on healthcare access and outcomes [103]. VCU's response to its own racist history is emblematic of the gulf between medicine's well meaning promise of gradual change and the disruptive action needed to address the matter of Black lives- and save them.

CONCLUSION

Racial bias likely intervenes at multiple points and at various levels (provider, patient, institution, research) in the journey toward advanced HF therapy. Initial suggestions for mitigating bias (Table 1) build upon on work by Arriola addressing bias in kidney transplantation [104]. Building an equity culture will require emphasizing racism, not race, as an essential factor in disparities. Standardizing evaluation processes and reporting data to a central body, in addition to designing prospective multicenter investigations, would facilitate comprehensive and quantitative assessments of inequity in advanced therapy distribution. Psychosocial assessments must be culturally appropriate and should include details of patients'' trust in providers,

Table 1. Recommendations for addressing bias and improving equity in advanced heart failure therapy allocation

Action	Source of Bias	Recommendations
Provider determines suitability for referral to advanced care center	Provider	C- Educate community providers about guideline-directed HF therapy and timely recognition of triggers to refer for advanced therapy evaluation C- Participate in interventions that raise awareness of the impact of bias on medical care R- Expand research on the role of unconscious bias in dialysis and transplant settings
Patient expresses interest in advanced therapy	Internal	C- Educate patients about options, with sensitivity to histories of medical abuse, healthcare inequalities, and medical mistrust among Black and other marginalized patient groups P- Establish core elements of patient education on advanced HF options
Provider refers patient to advanced care center	Provider	C- Acknowledge that we live in a race-conscious society C- Participate in interventions that raise awareness of the impact of bias on medical care R- Expand research on the role of bias in LVAD and HT settings P- Partner with community practices serving vulnerable populations to increase referral rates P- Financially incentivize dialysis facilities to decrease racial disparities in referral
Patient visits advanced care center	Internal	C/R- Implement and test patient navigation to enhance completion of the evaluation process C- Educate patients about evaluation, with sensitivity to histories of medical abuse, healthcare inequalities, and medical mistrust among Black and other marginalized patient groups R- Assess patient perceptions of barriers to completing evaluation and collect data to understand characteristics of patients who are unable to complete evaluation
Center conducts evaluation	Institutional Provider	C/R- Develop and test patient navigation to help patients complete the evaluation process C/R- Create dashboards of determinants and trends of patients' ability to proceed to candidacy C- Intensify efforts to recruit diverse trainees and practitioners P- Expand access to quality public health insurance P- Health centers invest in community-level interventions to address social determinants of health including safety, pollution, transportation, and housing and food security P/R- Professional societies such as HFSA, ACC and AHA should convene writing groups to summarize the literature, set research agendas and issue guidelines to address disparities in advanced therapy R- Conduct center-level and multicenter research on the potential disparate impact and fairness of medical and psychosocial items used in evaluation
Center accepts patient as advanced therapy candidate	Institutional Provider	C- Enhance support services for patients who are face barriers to being a successful candidate C- Demonstrate cultural sensitivity in care delivery during the evaluation process P- Expand coverage for immunosuppressant medications R- Collect center-level quality improvement data about disparities in advanced therapy access among patients who begin evaluation
Patient is listed for HT and/or scheduled for LVAD	Institutional Provider	R- Conduct mixed-methods research to understand barriers and facilitators of access P- Financially incentivize centers to improve equity in advanced therapy access and outcomes
Patient undergoes LVAD placement or HT	Institutional Provider Research	R- Conduct mixed methods research on factors associated with advanced therapy outcomes R- Establish standards for analysis and reporting of race disparities in registries P- Improve diversity of HF journal editorial boards

ACC, American College of Cardiology; AHA, American Heart Association; C, Care; HF, heart failure; HFSA, Heart Failure Society of America; HT, heart transplantation; LVAD, left ventricular assist device; P, Policy; R, Research.
Adapted from reference [79].

perceived discrimination and understanding of barriers to adherence. Professional societies such as the Heart Failure Society of America, the American College of Cardiology, the American Heart Association and the Association of Black Cardiologists should convene writing committees to review the best available literature, suggest research agendas, issue clinical guidelines and best practices, and develop metrics and targets for patient access and outcomes. The unprecedented speed of COVID-19 vaccine development should prompt restlessness about the pace of our progress against HF disparities, which is dangerously behind and damnably slow. The evidence vacuum for efficacy in reducing bias and promoting equity is intolerable. All who are dedicated to improving health equity and justice must demand more targeted research and funding, more provider diversity, and a serious focus on eliminating health disparities.

Supplemental Data Information for Figures

Figure 1: Heart failure (HF) death data were obtained from the Centers for Disease Control (CDC) Wide-ranging ONline Data for Epidemiologic Research (WONDER) database (wonder.cdc.gov). Age was adjusted to the US 2000 standard population. Annual excess age-adjusted African-American HF death rate (Fig. 1A) is the difference between the age-adjusted death rate due to HF (ICD-10 150.0, 150.1 or 150.9) among Black people and the age-adjusted rate among the non-Black population. Annual crude excess Black HF deaths in each 10-year age group (Fig. 1B) is the number of HF deaths among Black people in each age group minus the product of the crude non-Black HF death rate and the Black population in that age group.

Figures 2 and 3: Data are from the UNOS registry from 2000 through 2016. First-time heart-only recipients with BMI at listing <60 (to reduce the likelihood of miscoding) were selected (N = 34,532). Figure 2 shows the contribution of age, race, BMI, sex, year of transplant, and presence of an LVAD or and RVAD prior to transplant to the hazard of graft failure or death. Figure 3 displays race-specific hazards of graft failure or death as a function of BMI at listing with adjustment for the remaining variables examined in Figure 2. Confidence bands have been removed for visual clarity.

Figure 4: Data on HF physicians were obtained from the Centers for Medicare and Medicaid Services National Downloadable File (https://data.cms.gov/provider-data/sites/default/files/resources/de04109ea8ad84f5d82cf77674f8d76c_1604886408/mj5m-pzi6.csv) and from the Heart Failure Society of America membership directory (https://members.hfsa.org/individual-directory). Race and sex were assigned based upon visual inspection of publicly available photographs, the typical sex suggested by the first name, the typical race or geographic origin suggested by the surname, the actual geographic origins for physicians born outside the US and/or personal knowledge of the physician's identity.

All analyses and all figures were created in R 4.0.1.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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