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Women's Health (A Sarma, Section Editor)

Disparities in Cardiovascular Care and Outcomes for Women From Racial/Ethnic Minority Backgrounds

Sujana Balla, MBBS[1,2]
Sofia Elena Gomez, MD[3]
Fatima Rodriguez, MD, MPH[2,*]

Address
[1]Department of Medicine, University of California San Francisco-Fresno, 155 N Fresno St, Fresno, CA, 93701, USA
[*,2]Division of Cardiovascular Medicine and the Cardiovascular Institute, Stanford University, 870 Quarry Road, Falk CVRC, Stanford, CA, 94305-5406, USA
Email: frodrigu@stanford.edu
[3]Department of Medicine, Stanford University, 291 Campus Dr, Stanford, CA, 94305, USA

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Sujana Balla and Sofia Elena Gomez contributed equally to this work.
Sujana Balla and Sofia Elena Gomez are co-first authors.
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Abstract

Purpose of review Racial, ethnic, and gender disparities in cardiovascular care are well-documented. This review aims to highlight the disparities and impact on a group particularly vulnerable to disparities, women from racial/ethnic minority backgrounds.
Recent findings Women from racial/ethnic minority backgrounds remain underrepresented in major cardiovascular trials, limiting the generalizability of cardiovascular research to this population. Certain cardiovascular risk factors are more prevalent in women from racial/ethnic minority backgrounds, including traditional risk factors such as hypertension, obesity, and diabetes. Female-specific risk factors including gestational diabetes and preeclampsia as well as non-traditional psychosocial risk factors like depressive and anxiety disorders, increased child care, and familial and home care responsibility have been shown to increase risk for cardiovascular disease events in women more so than in men, and disproportionately affect women from racial/ethnic minority backgrounds. Despite this, minimal interventions to address differential risk have been proposed. Furthermore, disparities in treatment and outcomes that disadvantage minority women

persist. The limited improvement in outcomes over time, especially among non-Hispanic Black women, is an area that requires further research and active interventions.
Summary Understanding the lack of representation in cardiovascular trials, differential cardiovascular risk, and disparities in treatment and outcomes among women from racial/ethnic minority backgrounds highlights opportunities for improving cardiovascular care among this particularly vulnerable population.

Introduction

Cardiovascular disease (CVD) is recognized as the leading cause of death among both genders [1], but there are unique pathophysiological and clinical features of CVD in women [2, 3]. In the United States of America (USA), gender disparities in CVD are long-standing and persistent in time to diagnosis [4, 5], guideline-directed treatments [2, 3, 6–15], and outcomes [2, 3, 10–14, 16], although the overall prevalence of CVD in women is less than in men (44.7 versus 51.2%) [1]. When considering racial/ethnic CVD prevalence, the highest CVD prevalence rates are among Black males (60.1%) and Black females (57.1%), while the lowest prevalence rates are among NH Asian males (47.4%) and NH Asian females (37.2%) [1]. Additionally, disparities in CVD diagnosis, treatment, and outcomes disproportionately affect individuals from racial/ethnic minority backgrounds [1, 10, 16–22], and CVD disparities among women are amplified when they belong to minority racial/ethnic backgrounds.

In the USA, racial and ethnic diversity is growing rapidly [23]. The US Census Bureau predicts that by 2050, Whites will no longer be a majority population [24]. Thus, caring for women from racial/ethnic minority backgrounds is becoming increasingly important. Minority women experience disparities as both women and racial/ethnic minorities, but they also have different cardiovascular (CV) risk profiles which deserve better characterization and understanding. Importantly, delineating and addressing these risks along with appropriate representation may lead to improved outcomes, especially among women from racial/ethnic minority backgrounds.

Representation of women of racial/ethnic minority backgrounds in CV research

The representation of women in clinical CV trials has fluctuated over the past two decades, consistently remaining below 50% [25–27]. Studies investigating the representation of women in CV trials over the last decade have reported rates ranging from 33 to 38% [26, 27]. A 2019 study evaluating cohort demographics in CV clinical trials published in three major journals (*The New England Journal of Medicine*, *The Lancet*, *The Journal of the American Medical Association*) found that enrollment of women was 21% between 1986 and 1990 and 33% between 2011 and 2015, with a statistically significant increasing trend in enrollment [27]. Although we see absolute increases in female enrollment over time, participation prevalence ratios, a more accurate indication of appropriate representation, remain low [28]. Trials for hypertension, diabetes, hyperlipidemia, coronary artery disease, heart failure, and arrhythmia in recent years had

significantly lower participation of women relative to the prevalence of these diseases in women [27–33]. While some studies show improvement over time in the representation of women relevant to their disease prevalence in stroke and heart failure trials, a gender gap remains [26, 27]. Female enrollment also varies significantly with trial type, ranging from 31% in pharmacologic trials to 26% in procedural trials [27]. Representation of women is higher in international versus US-only trials (32.7% versus 26.7%) and comparable in government/foundation-funded versus industry-funded trials (31.9% versus 31.5%) [29]. Interestingly, Gong et al. reported differences in the representation of women between trials that reported statistically significant findings versus those that did not, with fewer women in significant trials [27]. While trials increasingly report gender distribution in their cohorts, discussions on gender-specific results are not as common [29].

Racial/ethnic minority populations are rapidly growing and experience a disproportionately and rising burden of cardiovascular disease. Despite this rise, their research enrollment rates remain low [1, 24]. Diabetes mellitus (DM) disproportionately affects racial/ethnic minority groups, especially African Americans [1, 35], yet this population is underrepresented in DM trials with most mega-trials of new therapies for type 2 DM having less than 5% African Americans participating [36]. Non-Hispanic (NH) Blacks are also disproportionately affected by hypertension [1], increasing their risk of CVD [37]. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), representation, while better, was not ideal: 47% NH White, 32% NH Black, and 19% Hispanic [38]. Studies have shown no significant improvement in minority representation over the past three decades [34, 39]. Apart from low enrollment, racial/ethnic reporting is often absent; for example, from 1985 to 1999, only 20% of heart failure trials reported their racial distribution [40]. In another study analyzing published CV trials from 1986 to 2018, only 56% of trials reported information on race [39].

The importance of improving representation and demographic reporting has been echoed by national organizations: In 1993, the National Institutes of Health (NIH) instituted a policy requiring women and minority representation in NIH funded trials, which fostered a culture of improving representation with contemporary US Food and Drug Administration (FDA) action plans [41] to reduce barriers for participation of both women and racial/ethnic minorities. Yet, close to three decades later, these disparities persist with contemporary trials continuing to underrepresent women and racial/ethnic minorities. For example, ISCHEMIA's cohort is only 32% women, and 66% of their cohort is White [42]. ERADICATE-AF has a similar representation of women but does not report their racial/ethnic composition [43]. This is a common theme in major trials across cardiology, making it difficult to generalize findings to women from racial/ethnic minority backgrounds. Underrepresentation of minority women in major CVD trials obscures management decisions for many clinicians, often leading to under-treatment of these groups [3].

Women from racial/ethnic minority backgrounds lie at the intersection of these categorizations and therefore face the amplified effects of inadequate representation as both women and racial/ethnic minorities in CV research. Currently, minority women are rarely evaluated independently apart from their larger categorizations as women and racial/ethnic minority groups. These women have unique risk profiles, face amplified diagnostic and treatment disparities, and deserve tailored research. An appropriate representation of women from

racial/ethnic minority backgrounds, especially relative to disease prevalence, in clinical registries and trials is crucial to understand and thereby mitigate healthcare disparities. However, in the interim, diverse cohorts of women like the Women's Health Initiative population [44] are crucial to increase the current database of literature on women from racial/ethnic minority backgrounds.

CV risk factors in women from racial/ethnic minority backgrounds

Women, in general, have a different CV risk burden compared to men, which impacts their CV care processes and outcomes. Few studies have focused specifically on women from racial/ethnic minority backgrounds or revealed which CV risk factors are particularly important to consider when caring for these populations.

Traditional CV risk factors

Hypertension is one of the traditional risk factors that affects women more severely than men. For example, it is estimated that eradicating hypertension could curtail CVD mortality by 38.0% among women, which is around 8% greater than the estimated reduction in CVD mortality among men (30.4%) [45]. Black women are further disproportionately affected by hypertension: The prevalence in 2011 to 2016 of hypertension in NH Black women was 53.2%, second only to NH Black men (57.6%) among race and gender-specific groups [1]. In 2016, death rates categorized as being attributable to hypertension were highest among NH Black males, followed by NH Black females [1]. The prevalence of hypertension among Hispanic women in the USA is thought to be lower but is heterogeneous based on Hispanic subgroup: Data range from 19.5 [46] to 38.8% [1] in Mexican-American women, 29.1% in Puerto Rican women, 26.4% in Cuban women, 26.1% in Dominican women, 25.6% in Central American women, and as low as 15.9% in South American women [46]. Furthermore, control of hypertension is lower in NH Black, Hispanic, and Asian women compared to NH White women, revealing an additional disparity [1]. Obesity, another important CV risk factor, is more prevalent in NH Black (56.1%) and Hispanic (48.4%) women, compared to NH White (38.8%) and Asian (13.6%) women [47]. Among Hispanic women, obesity has been found to be the most prevalent among Puerto Rican women (40.9%) and least prevalent among Central American women (32.7%) [46]. An association between obesity and food insecurity is thought to be a contributing factor, specifically among White and Hispanic women [48]. DM, known to be both a major overall risk factor for CVD [49] and a stronger risk factor in women [6], is most prevalent among Hispanic and NH Black women, followed by Asian and White women [1]. Among Hispanic women, DM prevalence from 2008 to 2011 was highest among those of Puerto Rican and mixed backgrounds, and lowest among South American women [50].

While hyperlipidemia and smoking are more prevalent in White women [1, 51], hypertension, obesity, and DM are more common in many groups of women from racial/ethnic minority backgrounds [1]. Additionally, the attributable risk for certain types of CVD, such as atrial fibrillation, from many of

these traditional risk factors is higher among women from racial/ethnic minority backgrounds [52].

Non-traditional CV risk factors

Psychological stress among minority populations [53] is associated with worse CV health, even after correcting for differences in socioeconomic status [54]. Psychosocial factors, like depressive and anxiety disorders and increased child care, familial and home care responsibility, have been shown to increase risk for CVD events in women more so than in men [3, 6, 55]. Another important consideration is varying gender roles across racial and ethnic groups. Among certain racial/ethnic minority groups, many women embrace their gender role as involving increased familial responsibility and emotional suppression [56], which can be linked to worsening CV health [57] and delays in seeking care [58]. Notably, stress in women from racial/ethnic minority backgrounds may be amplified by race-specific stressors [54, 59]. High rates of psychological distress related to interpersonal and structural discrimination, increased vigilance, acute life events, childhood adversity, and financial stressors have been associated with racial/ethnic minorities [54, 59]. Racial discrimination and related coping mechanisms have been associated with hypertension and higher LDL-C levels in African Americans, illustrating the direct link between race-related stress and CV health [57, 60, 61].

In these ways, the stacking of culturally specific gender roles and race-specific stressors may lead to exponentially increased psychosocial stress-associated risk among women from racial/ethnic minority backgrounds in the USA, further increasing their risk for CVD.

Female-specific CV risk factors

Common female-specific CV risk factors are early menarche and menopause, young maternal age, polycystic ovarian syndrome (PCOS), preeclampsia, gestational diabetes, preterm delivery, recurrent miscarriages, and obesity prior to pregnancy (Fig. 1) [62–64]. Many female-specific, CV risk factors disproportionately affect women from racial/ethnic minority backgrounds. The prevalence of gestational diabetes has been found to be highest among Asian women (11.1%), with more granular data showing that in this subgroup, Asian Indians (11.1%) have the highest prevalence, followed by Filipinas (9.6%) and Southeast Asians (8.8%) [65]. Among other broader racial/ethnic categories, lower prevalence rates are seen among Hispanic (6.6%), NH White (5.3%), and NH Black women (4.8%) [66]. Preeclampsia is known to be more prevalent in African American women than any other racial group [67]. In fact, all hypertensive disorders of pregnancy have been found to be most prevalent among Black women, with the disparity between Black and White women increasing over time [68]. Hispanic women have also been found to have higher rates of preeclampsia than White women; yet consistent with the "Hispanic paradox," they have better pregnancy outcomes despite disadvantageous socioeconomic determinants of health [69].

Other obstetric CV risk factors such as young maternal age, preterm birth, early menarche, and menopause are also more common in women from racial/ethnic minority backgrounds. Teen pregnancy rates, which may serve as a marker for younger maternal age, while declining across all racial/ethnic groups,

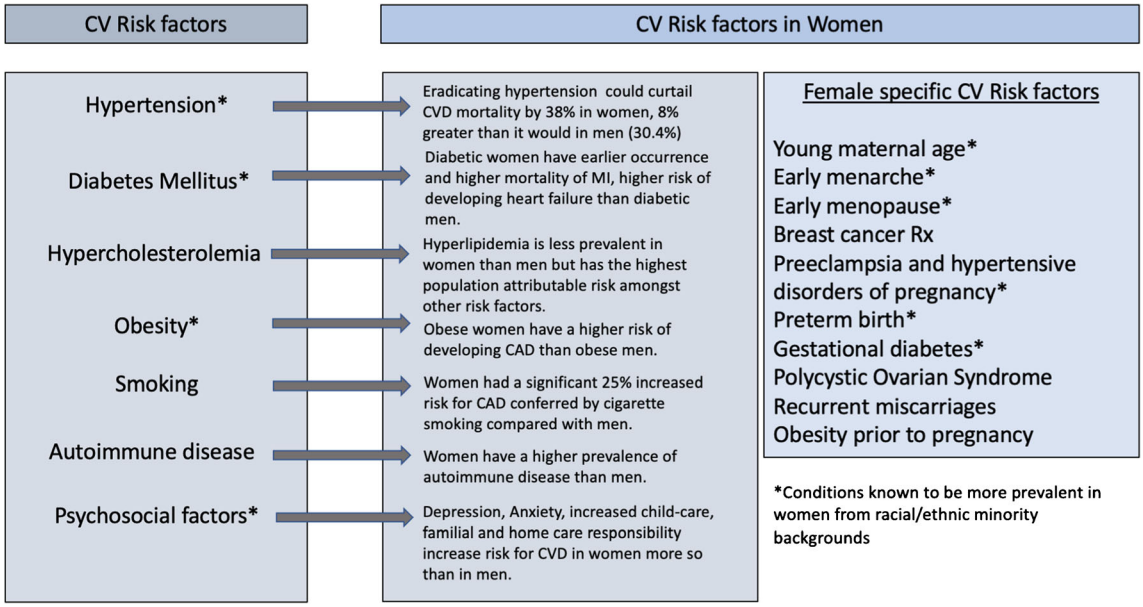

Fig. 1. Cardiovascular (CV) risk factors in women.

were higher in NH American Indian/Alaska Native (32.9%), Hispanic (28.9%), NH Black (27.5%), and NH Native Hawaiian/Pacific Islander (25.5%) women compared to NH White (13.2%) or NH Asian (3.3%) women [70]. Additionally, Black women are at increased risk for preterm birth, as well as recurrent preterm birth, in the USA; this finding persists even upon controlling for socioeconomic factors and maternal comorbidities [71]. The well-known increased risk of CVD and CVD mortality with early menarche [64] and menopause [72–74] is likely exacerbated in minority women: Hispanic and Black women have been shown to have menarche earlier in life compared to White and Asian women [75], while Black women have been found to have natural menopause at an earlier age than Hispanic or White women [76]. The field of cardio-obstetrics has recently developed to address the increasing prevalence of CVD in pregnancy, which is higher among women from racial/ethnic minority backgrounds [77]. However, formal training in cardio-obstetrics and exposure to CV disease in pregnancy is lacking in CV training programs across the USA [77].

Composite and alternate measures of increased CV risk

Apart from analyzing the impact of individual risk factors on women from racial/ethnic minority backgrounds, a handful of studies have investigated composite or alternate measurements of CV risk in this group. The pooled cohort equation (PCE) was evaluated using the Women's Health Initiative cohort, and it was found that PCE-predicted and observed event rates were comparable, albeit more variable, in women from racial/ethnic minority backgrounds [78]. Similarly, atrial fibrillation risk prediction models were evaluated using the same cohort, revealing that they perform equally well in women from racial/ethnic minority backgrounds, if not better [52].

Alternate measures like heart age, the predicted age of an individual's CV system based on their risk profile, across a diverse racial/ethnic population by gender [79] have been investigated in minority women. NH Black and Hispanic women had significantly greater average excess heart age (6.1 and 3.45 more years respectively) than their White female counterparts (2.3 years) [79].

Coronary artery calcium (CAC) measurements avoid many assumptions intrinsic to common risk calculators [80, 81], and have been used to assess risk in diverse racial/ethnic groups [19]. While women overall had lower rates of CAC than men, disparities emanated: Black women had the highest burden of CAC (50.6%), followed by White women (40.3%), Hispanic women (39.3%), and Asian women (35.5%) [19]. These composite and alternate measures of CV risk highlight the disproportionate burden of risk among Black women in the USA, while also re-affirming overall differences in risk among women from racial/ethnic minority backgrounds. They also provide new possibilities for risk assessment in this group that may improve risk categorization.

CV treatment disparities in women from racial/ethnic minority backgrounds

Women are more likely to be assigned a lower risk category of CVD [4] and receive overall less intensive CVD medical therapy, both pharmacologic and invasive, as well as lifestyle counseling compared to men [2, 6, 10–14, 82–84]. Disparities in treatment among racial/ethnic minority populations have also been reported, with lower statin and antihypertensive use as well as lower likelihood of escalation of care [1, 10, 18, 85–88].

Many studies have shown lower treatment rates of hypercholesterolemia and hypertension among both women and racial/ethnic minority backgrounds [18, 87]. Independently, women from racial/ethnic minority backgrounds have been shown to have lower rates of statin use (both for primary and secondary prevention) and cholesterol control than their White counterparts [7, 8, 86, 89]. Hispanic and Black populations have lower rates of antihypertensive use [1] as well as statin use [7, 8, 18, 87] than Whites. Black populations also have poorer LDL-C [86, 89, 90] and hypertension control [1] than Whites. Lifestyle interventions that have been shown to prevent type 2 DM [91, 92] are efficacious among racial/ethnic diverse populations as well [93]. Black and Hispanic individuals express the highest levels of interest in referral, yet less than 5% of eligible participants are being referred to these programs [94]. Postpartum screening rates in women with gestational diabetes are also low, especially among Black women, despite their increased risk of converting to type 2 DM [95, 96]. Similarly, Black women with pregnancy-related hypertension have more difficulty attending in-person postpartum visits, making postpartum treatment less accessible [97].

Studies show that women from racial/ethnic minority backgrounds have higher hospitalization and mortality rates compared to men and White women [13, 84, 98]. Black and Hispanic women are less likely to receive invasive management for coronary obstruction [13, 84, 99, 100], which has been correlated with in-hospital mortality [13, 84, 98]. Racial/ethnic minority women are also much less likely to receive implantation of a pacemaker or implantable cardioverter defibrillator, even after adjusting for baseline differences in

patient cohorts [101, 102]. Minority groups are also less likely to receive invasive cardiac procedures, implantation of pacemakers, transcatheter aortic valve replacement, and coronary artery bypass grafting [88, 101–104].

Treatment disparities have been associated with disruptions in care, single marital status, and lower education [18]. Other possible explanations for CV treatment disparities in racial/ethnic minority women range from socioeconomic factors such as lack of health insurance and lower income, to physician prescribing tendencies, lower rates of specialist referrals, inadequate risk assessment, and deficient patient-physician communication [86, 89].

CV outcomes in women from racial/ethnic minority backgrounds

Access to proper treatment and care is integral to outcomes: Unsurprisingly, CVD outcome disparities by gender and race/ethnicity exist. Women, especially younger women, have been found to have higher mortality rates from acute myocardial infarction (MI) [14, 105–108], especially in ST-elevation MI [109]. However, more recent studies show similar mortality outcomes among men and women, both before [110] and after adjusting for risk factors [111–113], suggesting that differing CV risk in women may be a driver of perceived mortality differences. Overall CVD mortality in 2016 in women (49.0%) was similar to that in men (51.0%) [1]. Despite this, significant outcome disparities persist: Women across all racial/ethnic backgrounds treated for atherosclerotic CVD (ASCVD) continue to report a lower-quality patient experience, poorer perception of their own health status, and decreased health-related quality of life [83].

CV outcomes analyses have shown persistent disparities among women from racial/ethnic minority backgrounds over time. In-hospital mortality for acute myocardial infarction is significantly higher in Hispanic and Black women than in men or White women [1, 84]. For example, one study found an odds ratio of 1.5 for in-hospital mortality among younger Hispanic women compared to younger White men after adjusting for age and comorbidities [84]. These disparities exist beyond coronary disease: Mortality due to heart failure was almost 3-fold higher in Black women compared to their White counterparts [114]. In accordance with this, hospitalization rates for heart failure are almost 2.5 times higher among Black women than NH White women; this disparity has not narrowed in the last 10 years [20]. Additionally, the outcomes of peripartum cardiomyopathy are worse in Black women than women from other racial/ethnic backgrounds [115]. Furthermore, NH Black and Hispanic women were 14.1% and 7.8% more likely to die from pregnancy-related CVD than NH White women [116].

The reasons for CV outcome disparities among women from racial/ethnic minority backgrounds are not well understood. They are most often attributed to the increased burden of CV risk factors in these groups including a higher burden of chronic stress, as well as discrimination in providing education, diagnosis, and treatment to this population [20, 116–119]. This highlights the importance of addressing differential risk among women from racial/ethnic minority backgrounds when initiating preventive care, as well as improving the delivery of appropriate diagnosis, risk assessment, and treatment in this underrepresented group.

Cardiac care for women beyond 2020

Despite recent efforts by federal agencies including the FDA [120] and NIH [121] to increase the representation of women and minority groups in CV clinical trials, these groups remain underrepresented and underreported [29, 122]. Initiatives like the Drug Trials Snapshots Program [123], the American Heart Association's Go Red For Women Campaign [124], Heart Health Centers for Women's healthcare delivery model proposal [125], and the Women's Health Initiative [44] have made efforts to encourage representation of women and racial/ethnic minorities in CV research. The Women's Health Initiative showcased the feasibility of enrolling large numbers of women in a CV trial registry that was diverse and representative [126]. Each of these serves as an example of effective initiatives that should continue to be developed to minimize the disparities in CV care and outcomes among women from racial/ethnic minority backgrounds. The authors additionally recommend accurate reporting of gender and racial/ethnic characteristics as well as of racial/ethnic subgroups within Black, Hispanic, and Asian categories to prevent homogenizing racial/ethnic groups and improve health disparities. Furthermore, we recommend that CV trials should aim to capture female-specific CV risk factors, especially age at menarche and menopause, preterm birth history, pregnancy-related hypertension, and gestational diabetes, to provide more substantial literature addressing the contributions of these factors to CV disease in women.

Data to guide trial enrollment to ensure recruitment of diverse populations is emerging [127–130], yet limited. One clear recommendation to improve diverse enrollment involves advocating for gender and racial/ethnic diversity among the physician workforce. A recent study found that heart failure trials published by a female first or senior author showed increased enrollment of women [131]. Cultural competence is also a key driver of minority recruitment that we highly recommend incorporating among research groups: Incremental increases in minority recruitment have been reported following appropriate training [132].

Given the important role that differential risk plays in the CV health of women from racial/ethnic minority backgrounds [20, 116–119], we recommend developing clinical, community, and virtual interventions to target risk factors in this group. These types of initiatives have proven effectiveness with respect to mortality and cost reduction [133]. While lifestyle and community interventions related to reducing the burden of type 2 DM [91–94], hypertension [134], and obesity [135] have been shown to be effective in women from racial/ethnic minority backgrounds, widespread incorporation of such initiatives is lacking [17]. Furthermore, effective interventions to address the female-specific, pregnancy-related CV risk factors in minority women are needed [136–140] and represent a worthwhile target for improving outcomes in these patients. Growth in the field of cardio-obstetrics may provide an important avenue for developing and implementing these interventions [77], and guidelines surrounding incorporation during cardiology fellowship training are emerging [141, 142]. Virtual interventions incorporating telemedicine, which have been extensively developed recently in the setting of the COVID-19 pandemic, have also been shown to reduce disparities in Black, preeclamptic women by increasing access to care [97].

The refinement of contemporary risk calculators to better predict ASCVD risk in women from racial/ethnic minority backgrounds is another crucial step to improving their outcomes. Alternatively, we recommend using more accurate methods of risk assessment in those of indeterminate or intermediate risk, such as coronary artery calcium [143] or precision medicine [144], to better guide treatment of minority women. Additionally, it is important to consider the genetic heterogeneity of ethnic groups which are often studied collectively as a race. For example, self-identified Blacks have up to 99% European ancestry, and in Hispanics, African ancestry varies from 3% in Mexican Americans to 16% in Puerto Ricans [145]. This reiterates the heterogeneity within race/ethnicity, and how individual genomic information is far more valuable in predicting treatment outcomes or classifying risk than the current system using racial and ethnic classifications. The rise of precision medicine, including subpopulation-specific pharmacokinetics and pharmacogenomics of drugs, will likely further our understanding of the value of race, ethnicity, and ancestry in prescribing therapies and formulating management strategies for minority women [146].

Conclusion

Given the growing racial/ethnic diversity in the USA and known gender and racial/ethnic disparities in CV care, women, especially those from racial/ethnic minority backgrounds, deserve further targeted interventions and increased attention in research. With the COVID-19 pandemic highlighting healthcare disparities among minorities and the structural racism endemic we are facing, increasing workforce diversity in cardiology is crucial to improving CV care. Poor delineation and representation of these groups in major CV trials impede appropriate understanding and treatment of minority women and need to be addressed by increasing cultural competency of research staff and ensuring diversity among trial investigators. Population data reveal disproportionate CV risk in woman and racial/ethnic minority individuals, including higher rates of many traditional and female-specific risk factors. Bridging gaps in access to care through telemedicine, incorporation of female-specific risk in trial demographic data, are measures that can address the disparities in differential risk. Persistent disparities in CV outcomes, especially among NH Black women, remain largely unaddressed. Strategies to improve their outcomes start with representation, in trial enrollment, in clinical care, and among investigators. Additional areas for improvement include understanding biases, knowledge/care gaps, creating community-based and virtual interventions, and refining risk calculators to improve cardiac care among this growing population.

Compliance with Ethical Standards

Conflict of Interest

Fatima Rodriguez was funded by a career development award from the National Heart, Lung, and Blood Institute (K01 HL 144607) and the American Heart Association/Robert Wood Johnson Harold Amos Medical Faculty

Development Program. Sujana Balla declares that she has no conflict of interest. Sofia Elena Gomez declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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