

# Analyzing cardiovascular treatment guidelines application to women and minority populations

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Garth Graham<sup>1,2</sup>, Yang-Yu Karen Xiao<sup>1</sup>,  
Terry Taylor<sup>3</sup> and Amber Boehm<sup>3</sup>

## Abstract

Despite nearly 30 years of treatment guidelines for cardiovascular diseases and risk factors and a parallel growth in the understanding of cardiovascular disease disparities by sex and race/ethnicity, such disparities persist. The goals of this review are to consider the possible role of three factors: the one-size-fits-all approach of most treatment guidelines, adoption of guideline-recommended treatments in clinical practice, and patient adherence to recommended practice, especially the relationship between adherence and patient perceptions. Guideline authors repeatedly call for more inclusion of women and minorities in the clinical trials that make guidelines possible, but despite challenges, guidelines are largely effective when implemented, as shown by a wealth of post hoc analyses. However, the data also suggest that one-size-fits-all treatment guidelines are not sufficiently generalizable and there is evidence of a distinct lag time between definitive clinical evidence and its widespread implementation. Patient perspectives may also play both a direct and indirect role in adherence to treatments. What emerges from the literature is an important continuing need for increased inclusion of women and minority subgroups in clinical trials to allow analyses that can provide evidence for differential treatments when needed. Increased effort is needed to implement definitive clinical improvements more rapidly. Patient input and feedback may also help inform clinical practice and clinical research with a better understanding of how to enhance patient adherence, but evidence for this is lacking for the groups most affected by disparities.

## Keywords

Adherence, cardiovascular disease disparities, patient perceptions, racial/ethnic minorities, treatment guidelines

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## Introduction

Despite remarkable advances in treatment and outcomes and updated treatment guidelines, cardiovascular disease (CVD) continues to be a leading cause of illness and death. Atherosclerotic CVD (coronary heart disease, cardiovascular death, myocardial infarction (MI), and stroke) is the leading cause of morbidity and mortality in the Western world.<sup>1</sup>

Almost as persistent as CVD itself are the disparities in risk factors, comorbidities and symptoms, treatments, and outcomes experienced by women and racial/ethnic minorities compared to White men. Recent data continue to document some of these disparities in the treatment of acute myocardial infarction (AMI) for women<sup>2</sup> and more generally by sex and racial/ethnic subpopulations.<sup>3</sup> For example, women present with more risk factors such as diabetes are

less likely to receive guideline treatments and have higher mortality rates for MI than men.

Table 1 summarizes some disparities in CVD prevalence, incidence, and outcomes, based on the American Heart Association's (AHA) 2016 statistical update.<sup>4</sup> The overall CVD death rate among Black males is 32% greater than among non-Hispanic White males, and the death rate among Black females exceeds by 34% than among non-Hispanic

<sup>1</sup>School of Medicine, University of Connecticut, Farmington, CT, USA

<sup>2</sup>Aetna Foundation, Hartford, CT, USA

<sup>3</sup>Palladian Partners, Silver Spring, MD, USA

### Corresponding author:

Garth Graham, Aetna Foundation, Hartford, CT 06510, USA.

Email: gnsgraham@gmail.com



**Table 1.** Summary of current US gender and minority disparities in CVD.<sup>4</sup>

## Cardiovascular diseases

- 11.1% of non-Hispanic White adults aged  $\geq 18$  years have cardiovascular diseases (CVD), including 5.6% with coronary heart disease (CHD); 10.3% of Black adults have CVD (5.5% with CHD); 7.8% of Hispanics have CVD (4.9% with CHD); 6.0% of Asian Americans have CVD (3.3% with CHD); 13.7% of American Indians/Alaska Natives have CVD (6.0% with CHD); and 19.1% of Native Hawaiians/Pacific Islanders have CVD (6.9% with CHD).
- The overall death rate due to CVD among US adults is 222.9 per 100,000; 269.8 for males and 184.8 for females. For males: 270.6 per 100,000 for non-Hispanic Whites, 197.4 for Hispanics, and 356.7 for non-Hispanic Blacks. For females: 183.8 per 100,000 for non-Hispanic Whites, 136.4 for Hispanics, and 246.6 for non-Hispanic Blacks.
- CVD is the number 1 cause of death for US females aged  $\geq 65$  years.
- Total CHD prevalence in US adults  $\geq 20$  years is 6.2%; 7.6% in men and 5.0% in women.
- CHD prevalence in non-Hispanic Whites is 7.8% for men and 4.6% for women, compared to 7.2% for non-Hispanic Black men and 7.0% for women and 6.7% for Hispanic men and 5.9% for women.
- Estimated CHD prevalence is 3.3% among Asian Americans  $\geq 18$  years and 6.0% among American Indians/Alaska Natives  $\geq 18$  years.
- Overall CHD death rate is 102.6 per 100,000: 141.8 in non-Hispanic White males, 155.1 in non-Hispanic Black males, and 104.7 in Hispanic males; the rate for non-Hispanic White females is 75.0, 94.7 in non-Hispanic Black females, and 61.3 in Hispanic females.
- Overall prevalence of myocardial infarction (MI) in US adults aged  $\geq 20$  years is 2.8%; 4.0% for men and 1.8% for women: in non-Hispanic Whites, 4.1% for men and 1.8% for women; 3.4% for non-Hispanic Black men and 2.2% for women; and 3.5% for Hispanic men and 1.7% for women.
- Average age at first MI is 65.1 years for men and 72.0 years for women.
- The average age-adjusted rates per 1000 for first MI are 5.3 for Black men, 3.3 for White men, 3.6 for Black women, and 1.9 for White women.
- Within 5 years of first MI at ages  $\geq 45$  years, 36% of men and 47% of women will die; at ages 45–64 years, the rates are 11% of non-Hispanic White men, 17% of White women, 16% of non-Hispanic Black men, and 28% of Black women.
- At ages  $\geq 45$  years, 16% of men and 22% of women with first MI will have heart failure within 5 years; at ages 45–64 years, the rates are 6% of non-Hispanic White men and 10% of White women; 13% of non-Hispanic Black men and 25% of Black women.
- Median survival time after first MI for adults  $\geq 45$  years is 8.4 years for White men, 5.6 years for White women, 7.0 years for Black men, and 5.5 years for Black women.
- An estimated 5.7 million Americans aged  $\geq 20$  years had heart failure in 2012.
- At ages  $< 75$  years, heart failure incidence is higher in Blacks than in Whites.
- Heart failure below age 50 years is more common in Blacks than in Whites.
- At age 40, the lifetime risk of heart failure without antecedent MI is 1 in 9 for men and 1 in 6 for women.
- Lifetime risk for heart failure for people with blood pressure  $> 160/90$  mmHg is double that for people with blood pressure  $< 140/90$  mmHg.
- Age-adjusted annual hospitalized heart failure incidence was 15.7 per 1000 for Black men, 13.3 per 1000 for Black women, 12.3 per 1000 for White men, and 9.9 per 1000 for White women.
- Overall any-mention death rates for heart failure in 2013 were 84 per 100,000: in males, 101.9 for non-Hispanic Whites, 105.4 for non-Hispanic Blacks, 48.2 for Asians or Pacific Islanders, 99.2 for American Indians/Alaska Natives, and 63.8 for Hispanics. In females, 75.0 for non-Hispanic Whites, 80.3 for non-Hispanic Blacks, 33.1 for Asians or Pacific Islanders, 73.0 for American Indians/Alaska Natives, and 47.7 for Hispanics.

White females. Yet from 2014 to 2060, the Black population in the United States is expected to grow by 42%, while the non-Hispanic White population is expected to shrink by 8.2%.<sup>5</sup> The urgency of learning how to reduce and eliminate CVD health disparities cannot be overstated; the costs to both the affected populations and the overall economy can only increase otherwise.

Even with enormous effort, resources, and research to improve CVD treatments, to better understand the extent of disparities, and to devise interventions to reduce or eliminate them, cardiovascular health disparities persist. Why? By no means do we propose to answer this question definitively, but we will review the nature of modern treatment guidelines as well as their efficacy and implementation. We will also explore patient perceptions of risk and disease understanding and examine intervention efficacy by sex, race, and ethnicity to ask whether patient perceptions help explain why disparities persist.

## CVD guidelines

### *Guidelines are often one-size-fits-all*

Despite the wealth of knowledge available about CVD disparities, typical CVD treatment guidelines may be viewed as a one-size-fits-all document. The reasons for that are multifactorial. For some conditions, there may not be sufficient difference between groups of people to treat them differently. In other cases, hypothetical differences may exist, making more individualized guidelines desirable, but evidence for the efficacy of differential treatment is lacking. The numbers enrolled in clinical trials from some groups and subgroups are often too small to support the analyses needed to provide such evidence.

Examples of notable, relevantly used guidelines that fit this description include the 2012 guideline for the diagnosis and management of patients with stable ischemic heart disease,<sup>6</sup>

from the American College of Cardiology Foundation (ACCF), the AHA, and other organizations; the 2013 guideline for the management of ST-elevation myocardial infarction (STEMI),<sup>7</sup> produced by the ACCF/AHA Task Force on Practice Guidelines; the 2015 focused update on primary percutaneous coronary intervention (PCI) for patients with STEMI;<sup>8</sup> the 2014 AHA/American College of Cardiology (ACC) guideline for the management of patients with non-ST-elevation acute coronary syndromes,<sup>9</sup> which include unstable angina and non-ST-elevation myocardial infarction (NSTEMI); and the 2013 guideline for the management of heart failure, by the ACCF/AHA Task Force on Practice Guidelines.<sup>10</sup> These all contain comprehensive recommendations on the diagnosis and treatment of the relevant conditions. Only the last includes a recommendation specific to African Americans (a combination of hydralazine and isosorbide dinitrate is recommended for African American patients with New York Heart Association class III–IV heart failure receiving optimal angiotensin-converting enzyme (ACE) inhibitor/ $\beta$ -blocker therapy, unless contraindicated). Table 2 provides a listing of the guidelines included in this review.

### Exceptions

On the contrary, the 2013 guideline on the assessment of cardiovascular risk<sup>15</sup> from the ACC/AHA Task Force on Practice Guidelines recommends use of a new race- and sex-specific pooled cohort algorithm to predict 10-year risk in non-Hispanic White and non-Hispanic Black patients aged 40–79 years. It allows use of the sex-specific equations for non-Hispanic Whites to estimate risk for patients from other populations, but calls for further research to develop similar equations applicable to other ethnic groups.

In the guidelines for the management of high blood pressure in Black patients, Flack et al.<sup>12</sup> lower the minimum recommended target blood pressure level for Black patients at lowest risk, emphasize effective multidrug regimens, and de-emphasize monotherapy.

Women too have received some specific recommendations. For example, Mosca et al.<sup>13</sup> make a wide range of preventive recommendations for women. These guidelines contain data concerning the epidemiology/incidence of CVD in women from racial/ethnic minorities. In the “Guidelines for the prevention of stroke in women,” Bushnell et al.<sup>14</sup> describe research gaps and discuss the risk of stroke in women related to pregnancy, preeclampsia, oral contraceptives, menopause, and hormone replacement therapy, as well as other risk factors more common in women. The guidelines nonetheless contain no recommendations specific to racial or ethnic minority women, although the authors comment in passing that stroke burden is higher in both Blacks and Hispanics.

### Are one-size-fits-all guidelines adequate?

Although guidelines are beginning to mention the disease burden faced specifically by women and minorities, they do

not provide recommendations on providing care to these populations. However, certain CVDs disproportionately affect some subgroups, suggesting that a more tailored approach is needed when considering whether the same guidelines are appropriate for everyone.

The 2014 revised guideline for the management of high blood pressure in adults<sup>16</sup> has recently been challenged because it raised the target for treated systolic blood pressure for patients aged 60 years or older to <150 mmHg from <140 mmHg, as previously recommended in the Seventh Report of the Joint National Committee.<sup>11</sup> In response, Krakoff et al.<sup>17</sup> drew attention to the likelihood that this new target would be a major threat to the health of this older group, especially to Blacks with hypertension, and would put women at disproportionate risk because there are more women in this demographic. See also the recent discussion of this issue in Balfour et al.<sup>18</sup>

Another direct challenge comes from a study of the “East Asian Paradox.” Jeong<sup>19</sup> showed compelling evidence that East Asians are at increased risk for bleeding, especially intracranial hemorrhage, when treated according to current guidelines for anti-platelet therapy following primary PCI. The study concluded that dedicated guidelines for antithrombotic therapy are needed for East Asians.

Current treatment guidelines represent an earnest effort to create recommendations based on the most complete and best evidence available, but the guideline authors are the first to point to gaps in knowledge. Research to fill these gaps is essential to make treatment recommendations more specific to minority racial and ethnic groups, but much available evidence is not from clinical trials and is not suitable to support treatment guidelines.

A recent scientific statement by Mehta et al.<sup>20</sup> offers a comprehensive review of AMI in women with some discussion of racial and ethnic disparities. Palaniappan et al.<sup>21</sup> reviewed existing research on CVD disparities among subgroups of Asian Americans. Frank et al.<sup>22</sup> looked at differential patterns of type of dyslipidemia in subgroups of Asian Americans, Hispanics, and Blacks. They found not only that most minority subgroups had higher prevalence of dyslipidemia than non-Hispanic Whites but also that the distribution of types of dyslipidemia (high low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol, high triglycerides) varied among subgroups.

Jose et al.<sup>23</sup> examined heart disease and stroke mortality rates in the six largest subgroups of Asian Americans, reviewing the death records of more than 10 million Americans. They found higher proportional mortality from ischemic heart disease among Asian Indian men and women and Filipino men, and every Asian American subgroup examined had higher proportionate mortality from hypertensive heart disease and cerebrovascular disease compared to non-Hispanic Whites. Jose and colleagues specifically called for more research to help “create public health policy, and to offer appropriate clinical guidelines.”

**Table 2.** Summary of clinical practice guidelines included in this review.

Title	Organization	Year of publication
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report <sup>11</sup>	NHLBI	2003
Management of high blood pressure in Blacks <sup>12</sup>	ISHIB	2010
Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update <sup>13</sup>	AHA	2011
2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease <sup>6</sup>	ACCF/AHA/ACP/ AATS/PCNA/SCAI/STS	2012
2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction <sup>7</sup>	ACCF/AHA	2013
2013 ACCF/AHA guideline for the management of heart failure <sup>10</sup>	ACCF/AHA	2013
2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes <sup>9</sup>	AHA/ACC	2014
Guidelines for the prevention of stroke in women <sup>14</sup>	AHA/ASA	2014
2013 ACC/AHA guideline on the assessment of cardiovascular risk <sup>15</sup>	ACC/AHA	2014
2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction <sup>8</sup>	ACC/AHA/SCAI	2016

AATS: American Association for Thoracic Surgery; ACC: American College of Cardiology; ACCF: American College of Cardiology Foundation; ACP: American College of Physicians; AHA: American Heart Association; ASA: American Stroke Association; ISHIB: International Society on Hypertension in Blacks; NHLBI: National Heart, Lung, and Blood Institute; PCNA: Preventive Cardiovascular Nurses Association; SCAI: Society for Cardiovascular Angiography and Interventions; STS: Society of Thoracic Surgeons.

Hutchinson and Shin<sup>24</sup> found large disparities both in risk factors for CVD and in CVD itself among American Indians and Alaska Natives. They likewise call for more research to understand the causes of these health disparities and to find treatments to overcome them.

The results presented here indicate that CVD treatment guidelines are not always sufficiently generalizable to meet the needs of all subpopulations. This finding underscores the calls for more inclusive clinical trials often included in their work by guideline authors.

## Guideline implementation

### *Are guidelines effectively implemented?*

Effective implementation of guidelines is also a challenge. Mehta et al.<sup>20</sup> concluded that women are under-treated in terms of guideline-based recommendations and are often not adherent to those recommendations. This is not a new or novel observation. In 1998, Frolkis et al.<sup>25</sup> examined compliance with the National Cholesterol Education Program (NCEP-ATPII) guidelines for screening for cardiovascular risk factors and treating hyperlipidemia among physicians treating high-risk patients in a coronary care unit. The investigators found significant under-screening of these high-risk patients, and one-third to one-half of eligible patients were left untreated.

In 2004, Smaha<sup>26</sup> reported on the AHA's Get With the Guidelines program, a hospital-based quality control program initiated largely to remedy noncompliance with evidence-based best practices. Smaha found, for example, that compliance with AMI treatment guidelines for the use of

$\beta$ -blockers was only 49.5%, and even smoking-cessation advice, which is not only relatively easy to provide but also basically free to patients, was given only 41.9% of the time.

There is also evidence that it simply takes time for practitioners to adopt recommended treatments. Putera et al.<sup>27</sup> looked at the uptake of recommended therapies based on current and historical ACC/AHA guidelines for patients with STEMI and unstable angina/NSTEMI. The time from pivotal clinical trial publication to inclusion in guidelines was a median 2 years, with a median 7 years from guideline publication to 70% uptake in clinical practice and 14 years to 90% uptake. This lag perhaps helps explain the persistence of CVD morbidity, mortality, and disparities in the face of evidence-based therapies.

### *Are treatment guidelines effective when followed?*

Data from the AHA Get With the Guidelines program indicate that when treatment guidelines are followed, many health and outcome disparities disappear, although some treatment disparities persist. For example, Klein et al.<sup>28</sup> studied heart failure in 99,841 patients at 247 hospitals, with women accounting for 50% of admissions. Women were less likely than men to have their ejection fraction measured, to be treated with anticoagulation for atrial fibrillation, or to receive implantable cardioverter-defibrillators. In-hospital mortality was low and was similar in men and women, but women tended to have longer hospital stays and were more likely to be discharged to long-term care.

Cavender et al.<sup>29</sup> examined data from 7445 patients in 137 hospitals undergoing primary PCI as treatment for STEMI between 2006 and 2009. The median door-to-balloon time

fell over the course of the study from 82 to 68 min, with decreases seen across sexes and races/ethnicities. The authors found no difference in the proportion of Whites, African Americans, and Hispanics achieving door-to-balloon time  $\leq 90$  min, and the proportions of patients of all races/ethnicities/sexes achieving door-to-balloon time  $\leq 90$  min increased significantly over the study period. African American males had slightly lower odds of door-to-balloon time  $\leq 90$  min than White males, but the investigators found no significant difference in in-hospital mortality by race or ethnicity.

Li et al.<sup>30</sup> looked at data from 49,358 coronary artery disease patients aged  $\geq 65$  years, admitted to 366 hospitals from 2003 to 2009. They found a significant interaction between sex and quality of care, with women having significantly higher odds of mortality if they received suboptimal care. This disparity disappeared with optimal care. Black patients had significantly higher odds of mortality than White patients, and this disparity persisted regardless of quality of care.

Among older ( $\geq 65$  years) coronary artery disease patients studied by O'Brien et al.,<sup>31</sup> 67.9% (24,367 of 35,903) were discharged on statins, with 4488 receiving high-intensity statins. The investigators found that patients discharged on statins were slightly younger, more likely to be White, and less likely to be female. Nonetheless, regardless of sex or race, patients discharged on statins had significantly lower hazards for mortality and major adverse cardiovascular events, but not for readmission. High-intensity statin use was not associated with lower mortality, major adverse cardiovascular events, or readmission.

In a recent study of Asian Americans with heart failure, Qian et al.<sup>32</sup> analyzed data from 153,023 heart failure patients (3774 (2.5%) Asian Americans) treated in 356 US centers. After adjusting for patient-level factors and hospital characteristics, they found that Asian Americans were less likely to receive an aldosterone antagonist at discharge but more likely to have a follow-up visit within 7 days and to be discharged to home. There were no racial differences in in-hospital mortality or length of hospital stay exceeding 4 days. These investigators also found no race/sex interactions except that Asian American women were significantly more likely to be discharged to home than non-Hispanic White women.

These data suggest that guidelines are not always implemented, which is partially explained by the long lag time between publication and uptake, but when a real effort is made to adhere to evidence-based treatment guidelines, some disparities in measurable outcomes disappear. At the same time, the data also tell another story in which some outcomes disparities linger despite equal quality of care by guideline standards. Again, this suggests that one-size-fits-all CVD treatment guidelines are not always sufficiently generalizable to meet the needs of all subpopulations.

## Patient perceptions

### *Do patient perceptions help explain why cardiovascular health disparities persist?*

In their comprehensive review of evidence on the presentation, pathophysiology, treatment, and outcomes of women with AMI, Mehta et al.<sup>20</sup> point to excess mortality in female patients, which they consider “multifactorial”: Research is incomplete, with women making up only about 20% of patients enrolled in clinical trials that might help to close knowledge gaps; women are under-treated with guideline-based recommendation treatments; and women’s adherence to evidence-based recommendations is sub-optimal.

In the absence of similarly up-to-date, comprehensive, and granular reviews of evidence for other conditions among women or ethnic/racial minority patients, it seems reasonable to suspect that the persistence of CVD disparities among these groups also has a multifactorial basis and that patient nonadherence is more widespread and could play a role in CVD disparities among these groups. A recent Cochrane Review of studies on medication adherence reported that patients who are prescribed self-administered medications take only about half their prescribed doses and often stop taking medications entirely.<sup>33</sup>

If adherence to treatments can lead to better clinical outcomes, why don’t patients take their medications? Do they not perceive the seriousness of their risks or their disease? Do they not believe the medication is effective? Do perceptions vary by sex or race/ethnicity?

A recent scientific statement from the AHA stressed the importance of seeking and measuring patient-reported health status to assess the extent to which interventions are “improving patients’ health and experience with health care.”<sup>34</sup> The authors define patient-reported health status as “the impact of disease(s) and medical treatments on function and well-being as reported by the patient.” Not only are health status surveys a direct assessment of patients’ perceptions, but they also independently predict objective health outcomes such as mortality, cardiovascular events, hospitalization, and cost of care, and they have demonstrated associations such as the correlation between patient-reported physical function limitations and exercise treadmill testing. Self-reported health status could serve as a key measure of cardiovascular health in clinical research, clinical practice, and surveillance.

Here, we review some recent studies on patient-reported perceptions of their own health, the seriousness of CVD and their risks, and their healthcare providers and how these perceptions might affect their adherence to treatment.

### *Patients’ perspectives on disease*

Women aged  $< 55$  years have twice the risk of dying while hospitalized for AMI than men of the same age. Lichtman et al.<sup>35</sup> interviewed women aged 30–55 years while they were hospitalized with AMI to explore their decision-making

process in seeking medical care. They found that women's symptoms varied both in nature and in duration; women often attributed their symptoms to something other than cardiac causes; women allowed other priorities, such as family and work responsibilities, to compete with their decision to seek acute care; and they perceived the healthcare system to be unresponsive and did not routinely access primary care, partially because of previous bad experiences. The investigators emphasized the need for targeted interventions aimed at encouraging prompt patient presentation and facilitating timely and accurate AMI diagnosis in younger women. These findings expand on those of Mosca et al.,<sup>36</sup> whose ongoing surveys of women's knowledge about their risk of CVD show increasing awareness, but with further need for improvement; only 56% of women identified CVD as the leading cause of death in women. These investigators also found a continuing significant gap in awareness among racial/ethnic minority women.

Investigators in the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study looked at 3501 AMI patients (2349 women, 1152 men) between the ages of 18 and 55 years in 127 US and Spanish hospitals.<sup>37</sup> The investigators collected information on five potentially modifiable risk factors: diabetes mellitus, dyslipidemia, hypertension, obesity, and current smoking. Only 56% of study participants considered themselves at risk for heart disease prior to their index AMI. Women in the study had a risk factor burden similar to or greater than that of the men, but women were 11% less likely to have been told by a healthcare provider they were at risk for heart disease and 16% less likely to have discussed heart disease and ways to lower their risk.

Although mortality due to AMI has declined with better therapies, prior to Medicare Part D as many as 50% of Medicare recipients were nonadherent to statins, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) therapies, and  $\beta$ -blockers. To determine whether gender and racial/ethnic disparities continue in adherence to these medications, Lauffenburger et al.<sup>38</sup> studied Medicare claims in a 2007–2009 cohort of 85,017 individuals alive 30 days after an index AMI. These investigators found no significant differences in adherence by race/ethnicity at 30 days, but women were less likely than men to take ACEI/ARB or  $\beta$ -blockers. At 12 months, compared to White men, Black and Hispanic women were the least likely to be adherent, followed by White, Asian, and other women, and Black and Hispanic men. The investigators conclude that even after the introduction of Medicare Part D, gender and racial/ethnic gaps still exist in adherence to evidence-based secondary preventive therapies.

In their study of patient perception of risk for diabetes or heart attack, Fukuoka et al.<sup>39</sup> used surveys to explore perception of risk among 904 Californians, mean age 44.3 years, 64.3% female, with over-sampling for Koreans, Filipinos, and Latinos. The investigators found that 46.5% of the

participants thought they had a greater likelihood than others to develop diabetes, but only 14.3% believed they had a greater likelihood than others to have a heart attack. Although Korean and Filipino Americans perceived themselves at highest risk for diabetes, predictors of perception of risk for heart attack included only family history of early heart attack, high blood pressure, and high body mass index. Neither race/ethnicity nor sex influenced perception of risk for heart attack.

In their study of 197 Black patients presenting in the emergency department with chronic hypertension (>140/90 mmHg at presentation) at hospitals in Detroit, Michigan; Ifakara, Tanzania; and Kingston, Jamaica. Purakal et al.<sup>40</sup> explored perceived causes, symptoms, and consequences of chronic hypertension among a group of racially similar patients with widely divergent cultural backgrounds. At all three sites, recognition that chronic hypertension is a disease was low, most patients associated high blood pressure with symptoms such as headache, and more than one-third of patients believed hypertension could be cured. This study found poor overall understanding of hypertension as controllable but not curable, with substantial variation by location in patient-perceived causes of hypertension. For example, in Tanzania, few patients saw high salt or diet as causative, but they overemphasized stress. These results suggest that perceptions could not only influence risky behaviors (such as eating a high-salt diet) but also that a single racial category of "Black" could obscure real and important cultural differences in perception.

Chamberlain et al.<sup>41</sup> examined the relationship of self-reported physical functioning and self-rated general health with healthcare usage and skilled nursing facility admission in 417 heart failure patients, mean age 73.3 years, 43% female, with average follow-up of 2.1 years. Patients with low self-reported physical functioning had a 50% increased risk of both hospitalizations and emergency department visits compared to patients with moderate-to-high physical function. Patients with low self-reported general health had a 70% increased risk of hospitalizations and emergency department visits compared to those reporting good-to-excellent general health. After adjusting for confounders, the investigators found a similar but non-significant association between self-reported physical functioning/general health and skilled nursing facility admission, but not with outpatient office visits. These results suggest that self-reported measures of health status can predict hospitalizations and emergency department visits in heart failure patients.

Winham and Jones<sup>42</sup> explored knowledge about CVD among 172 young African American men and women (aged 18–26 years) using a questionnaire adapted from the AHA's national surveys. Only 16% of study respondents recognized heart disease as the leading cause of death, and only 39.5% disagreed with a statement that they were at low risk for heart attack or stroke. Knowledge of causes of heart disease and of ways to prevent or reduce the risk of heart disease was high. The investigators found no significant differences

between men and women in knowledge of the warning signs of heart attack, but more men than women knew that low estrogen (24% vs 21%) and menopause (18% vs 15%) were risk factors for women, although more women than men knew that heart disease is the leading cause of death among women. Knowledge of some aspects of CVD was high in this group, but the investigators suggest that knowledge of specific risk factors and warning signs of heart attack in women could be increased.

### *Patients' perspectives on physicians*

Mounting evidence suggests that the quality of physician–patient interaction can affect patient trust, satisfaction, and perception of partnership. In a study of the association between physician communication behaviors and patient trust and of the effect of patient race and race concordance with the physician, Martin et al.<sup>43</sup> examined the interactions between 227 Black and White hypertension patients and the 39 physicians who treated them. There were no differences by patient's race in the number of biomedical or psychosocial statements by physicians, but Black patients received significantly fewer rapport-building statements from physicians and more rapid physician speech, had shorter visits, and their physicians were more verbally dominant. Black patients were significantly less likely to have high trust in their physicians. Positive physician affect was significantly associated with higher patient trust in the entire sample, but among Black patients, the odds of high trust increased significantly with each unit of positive physician affect score. No communication process variable achieved significant association with high trust, but longer visits, higher physician verbal dominance, and patient-centered talk tended to increase the odds of high trust. Although not addressed in this study, these results raise the question of whether increased trust in one's physician increases the likelihood of adherence to prescribed medications and recommended behavioral changes intended to improve hypertension.

The quality of patient–provider communication may directly affect patient adherence to treatment. Zullig et al.<sup>44</sup> studied the perception of provider communication in a racially diverse group of adherent and nonadherent post-MI patients and asked whether the association of having unanswered questions with nonadherence varied by patients' race. Overall, among the 405 patients in their sample, 232 (57.3%) were adherent, but only 63 of 140 (45%) minority patients were adherent. Satisfaction with provider communication was fairly high, but among adherent patients, 79% never left their doctor's office with unanswered questions, compared to 67% of nonadherent patients. Among adherent patients, 78% reported having things well explained by their physicians, compared to 65% of nonadherent patients. The investigators found no significant differences in satisfaction with provider communication by race to help explain the greater nonadherence among non-White patients.

In another attempt to look at ways patient perceptions might affect health disparities, Dolezsar et al.<sup>45</sup> systematically reviewed the literature on hypertension and perceived discrimination, analyzing 44 studies with a total of 32,651 subjects, 62.2% Black. They found a small but significant relationship between perceived racial discrimination and hypertension, stronger among older participants, males, Blacks, those with lower educational attainment, those who were hypertensive, and those with a physician diagnosis of hypertension. The strongest association was between perceived discrimination and nighttime ambulatory blood pressure, especially among Blacks.

### *Changing patient perspectives*

Patients' perceptions of their disease and their relationships with their physicians may be potential targets for improving medication adherence, but changing patient perspectives may be difficult. A recent pilot randomized controlled trial of an intervention to improve medication adherence in CVD patients discharged with antihypertensive medication<sup>46</sup> found no improvement in adherence at 1 year, but adherent patients, regardless of whether they were in the control or intervention group, had significantly lower rates of both readmission and mortality at 1 year than nonadherent patients.

Rimando<sup>47</sup> studied patient-perceived barriers and facilitators of hypertension management among underserved African Americans (average age 62 years, range 55–75 years) attending a hypertension clinic in the southeastern United States. Patient-reported barriers to managing hypertension included inadequate income to pay for medications, missing appointments at the clinic, lack of motivation to exercise, and fear of pain or injury from exercising. Facilitators of managing their hypertension included gaining knowledge of hypertension by attending the clinic, improving quality of life by losing weight, and finding cues to action such as learning they had hypertension or being motivated by family members. Most had no prior education on hypertension from their physicians and did not know the consequences of hypertension before attending the clinic.

In a study of 723 African American and White patients and 205 White and African American providers in 119 primary care clinics, Schoenthaler et al.<sup>48</sup> examined the associations between patient–physician racial concordance and blood pressure control and the effects of patient trust on medication adherence. In this sample, 637 patients (88%) were in racially concordant relationships with their providers. White patients in racially concordant relationships with their providers were significantly more likely to report better adherence than African American patients in racially discordant relationships, but there was little difference in adherence among African American patients regardless of their concordant/discordant relationships. However, increased patient trust was associated with significantly better adherence. These data show no association between racial/ethnic concordance and

blood pressure control, but patients' trust in their physicians was associated with medication adherence and blood pressure control.

These studies provide evidence that patient perceptions influence their adherence to guideline treatments, but do not necessarily link treatment adherence to patients' perceptions of their health-related quality of life. The data suggest that other aspects of patients' perceptions, such as physician trust and understanding of disease and risk, may have a more direct effect on patient compliance.

## Limitations

This review has two important limitations. First, it is not a comprehensive review of CVD guidelines. The guidelines chosen (hypertension, CVD prevention in women, MI, heart failure, and stroke) were chosen specifically because of their pertinence to the primary prevalent CVD disparities seen in women and by race/ethnicity. We have made no attempt to review or reiterate the specific treatments found in these guidelines because disparities (and differences) are not solely in treatments, but also in symptoms, presentation, and short- and long-term outcomes. The interested reader is referred to the guidelines themselves for review of specific treatments. The question this review asks is whether the modern, one-size-fits-all CVD guideline is adequate, when implemented, to address CVD disparities. This is also not a comprehensive review of the literature on adherence to treatment guidelines. We instead have looked at large-scale attempts to implement evidence-based guidelines and to assess the impact of doing so. This review is intended to be understood at the population level, not at the individual patient level, where there can be large variability.

## Future perspectives and conclusion

This review has looked at possible reasons for the persistence of racial/ethnic and gender CVD disparities in the age of one-size-fits-all treatment guidelines. The guidelines themselves do not explain the persistence of disparities; the evidence suggests that despite their one-size-fits-all nature, guidelines can eliminate many clinically significant disparities when they are actually put into practice.

Can guidelines be made better, more precise, and aimed more specifically at certain populations or sub-populations? They probably can, but guidelines must be based on the best existing evidence. Recent reviewers like Mehta et al.<sup>20</sup> can still point out that despite the many CVD disparities seen in women (e.g. within a year of AMI, 26% of women die compared to 19% of men), they remain underrepresented in clinical trials, making up only about 20% of CVD clinical trial participants. If the guidelines need to recommend different treatments for women to end such disparities, clinical researchers must find those better interventions and produce evidence that they work. The same holds true for racial and

ethnic minority populations. Guideline authors repeatedly call for more inclusion of women and minorities in clinical trials to make the guidelines more generalizable. One-size-fits-all guidelines may be the best guidelines possible given the existing evidence, but clinical CVD researchers should strive to find ways to make their trials more inclusive.

This review has demonstrated that even if treatment guidelines are based on the best existing evidence of treatment efficacy, there is room for better strategies and more specificity.

This review also asked whether one-size-fits-all guidelines work when implemented. The overwhelming evidence supports their effectiveness. The guidelines' effectiveness is seen across all groups and populations as deaths and hospitalizations due to CVD plummet, but it is also seen in specific racial/ethnic groups and among women. The recurring pattern seems to be of continued small but significant treatment disparities that are largely not important clinically, with a convergence of clinical outcomes. A good example was the finding by Cavender et al.<sup>29</sup> that African American males had slightly lower odds of door-to-balloon times  $\leq 90$  min, but no significant difference in in-hospital mortality. Some important exceptions to this pattern exist, however. For example, Li et al.<sup>30</sup> found that excess mortality in Black patients persisted regardless of quality of care. And Jeong<sup>19</sup> found that East Asians are at increased risk for bleeding even if they are treated according to current guidelines for anti-platelet therapy following PCI.

One important barrier to the implementation of guidelines seems to be time itself. Putera et al.<sup>27</sup> found a median 16 years from pivotal clinical trial and 14 years from guideline publication to 90% uptake. Time has been a key barrier to guideline implementation.

We also conclude that patient perceptions can facilitate or impede patient willingness to seek and accept treatment in a timely way and to comply with medications once prescribed. Physicians can be involved in educating their patients about both the risks they face and the consequences of treating or not treating their disease. Clinicians may also be able to enrich their understanding of their patients' conditions by measuring patients' self-perceived health status as part of clinical care.

The data reviewed here suggest that patients' perceptions of their health, their risks, their disease, their physicians, and even of discrimination against them can have both direct and indirect effects on their health and their willingness to participate in treatment. Nonetheless, more research is needed to determine whether routine use of validated CVD health status surveys, as suggested by Rumsfeld et al.,<sup>34</sup> would have a real impact in the populations most affected by CVD disparities.

Decades of work by numerous associations have helped minimize the CVD disparities among different US populations. However, differences persist despite these efforts. Here, we have identified a few key factors that may alleviate



these continuing disparities. These include tailored guidelines for women and minorities, efficient implementation of those guidelines, and patient adherence to treatment, based on improved patient perspectives. Identifying strategies to improve these and other areas will help us focus our efforts to continue shrinking CVD disparities.

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