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# Maximizing Cardiovascular Event Reduction by Expanding and Intensifying the Targets

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**H**ypertension is a leading risk factor for death and disability-associated life years in the United States.<sup>1</sup> The US prevalence of hypertension using a conventional definition of hypertension, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, is at epidemic proportions and continues to increase alongside the prevalence of modifiable lifestyle factors for high blood pressure, such as physical inactivity, high-sodium diets, obesity, tobacco use, and alcohol use.<sup>2</sup> Despite our tremendous scientific understanding of the cardiovascular risk factors that predispose to adverse health outcomes, pinpointing the blood pressure for optimal risk reduction continues to evolve and be debated. Although it has been well established that a linear relationship exists between elevations in systolic blood pressures  $>110$  to  $115$  mmHg and cardiovascular events in every age group,<sup>3</sup> most blood pressure guidelines have focused on blood pressure-lowering treatment in those patients meeting conventional hypertension definitions. National and international blood pressure awareness, treatment, and control campaigns have been aimed exclusively at patients with blood pressure  $\geq 140/90$  mmHg. By targeting such patients, where it was commonly perceived that the majority of cardiovascular events were occurring, it was hoped that the majority of preventable cardiovascular events could be most effectively addressed. Yet taking a more expansive view beyond which patients are at highest risk to one that accounts for which patients constitute the majority of cardiovascular events, a different perspective emerges. For the entire population,  $\approx 450\,000$  Americans die each year from cardiovascular diseases secondary to chronic elevations in systolic blood pressure  $>110$  to  $115$  mmHg, with many cardiovascular events occurring in individuals with blood pressures above optimal but below conventional hypertension definition.<sup>1,4</sup>

The recent landmark SPRINT (Systolic Blood Pressure Intervention Trial) provided strong evidence that the undertreatment of high blood pressure for patients with high cardiovascular risk increases rates of death and cardiovascular events.<sup>5</sup> A meta-analysis of published trials demonstrates that achieving systolic blood pressures between  $120$  and  $124$  mmHg compared with  $125$  and  $129$  mmHg results in lower cardiovascular events and mortality.<sup>6</sup> The conventional definition of the stages of hypertension are nebulous when population health and personalized risk reduction are considered based on the recent evidence that lower targets are beneficial for certain patients. When pooled, the clinical trial evidence suggests that, in appropriately selected patients, blood pressures goals must be lower and treatment more intensive than prior guidelines recommended.

Making the case that the conventional definitions of hypertension may not adequately encompass the population having events and that undertreatment of blood pressure is a significant public health burden, Tajeu and colleagues<sup>7-9</sup>

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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pooled individuals from 3 longstanding US cohorts—the REGARDS study (Reasons for Geographic and Racial Differences in Stroke) the MESA (Multi-Ethnic Study of Atherosclerosis), and the JHS (Jackson Heart Study), recruited between 2000 and 2007—to describe the risk of cardiovascular events for individuals without hypertension and those with “controlled hypertension” based on current guidelines. With >7 years of follow-up, 63.0% incident cardiovascular events occurred in individuals with blood pressures <140/90 mmHg. These findings held for individuals younger and older than 65 years of age, men and women, and across all race and ethnic groups studied. The authors observe that 19.5% of cohort participants would have met SPRINT eligibility, providing an opportunity for additional risk reduction. Furthermore, only 33.2% of participants who meet eligibility based on the current statin guideline recommendations were receiving 1, highlighting an added prospect for population-based risk reduction.

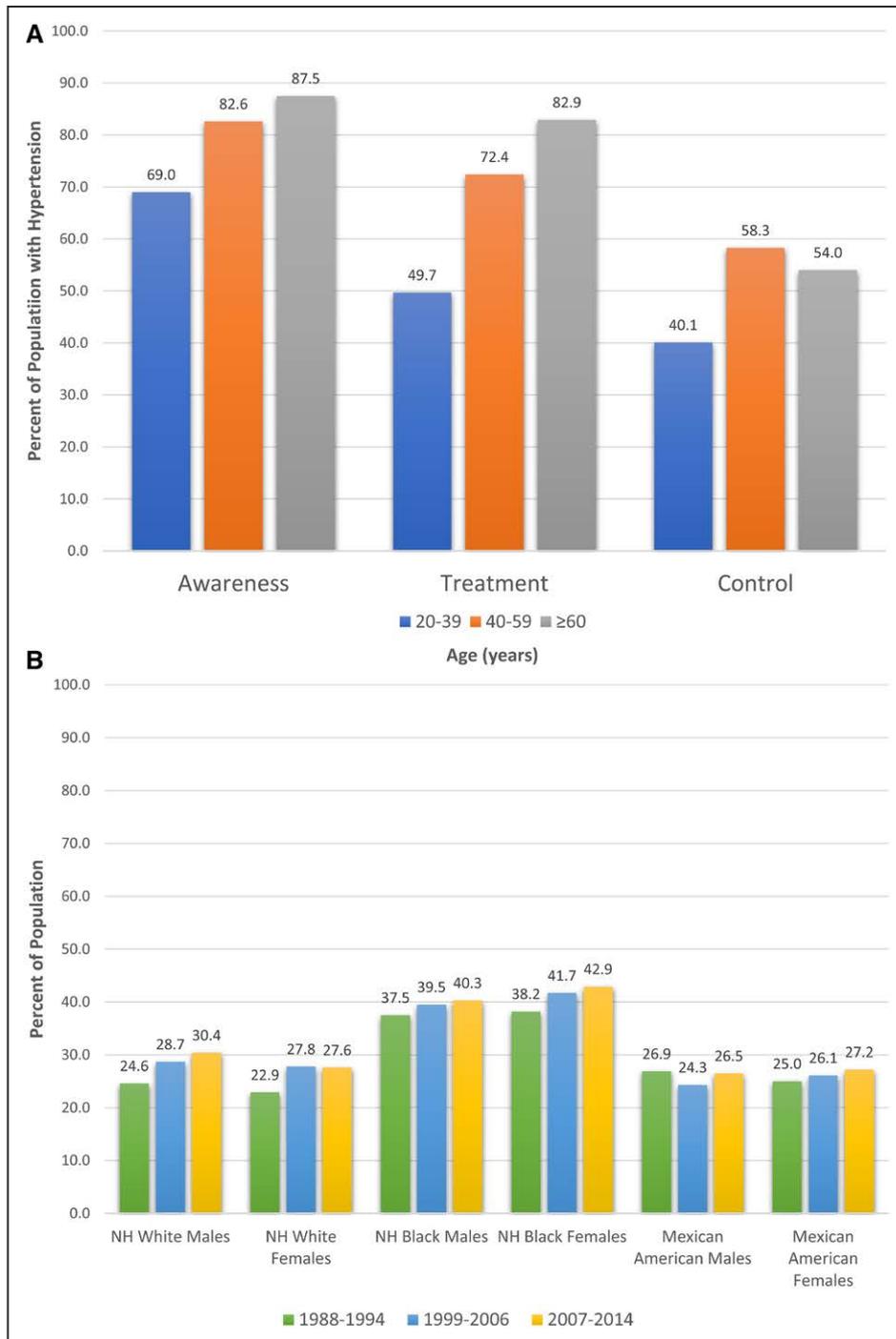
Globally, preventable cardiovascular disease is the leading cause of death, and over the last 50 years progress has been inconsistent. For the United States, some of the largest gaps in care are with respect to hypertension awareness and management. Of US participants with blood pressures  $\geq$ 140/90 mmHg,  $\approx$ 15% to 20% were unaware of their diagnosis, 25% to 30% receive no treatment, and only 50% to 55% of those with hypertension have it controlled (defined as <140/90 mmHg) (Figure A).<sup>10</sup> Although these rates have slowly improved over recent decades, they are far from maximizing reductions in preventable cardiovascular death and events. Further, as illustrated in the study by Tajeu and colleagues,<sup>7–9</sup> a much larger population is at risk, with blood pressures <140/90 mmHg but above optimal. Nationally, adherence to guidelines must be improved and expanded for patients with unquestionable elevations in blood pressure, targeting patients at risk and lowering blood pressure treatment targets to SPRINT-defined levels for select populations along with use of other effective cardiovascular risk reductions strategies in eligible individuals.

In this pooled cohort study, patients with blood pressure  $\geq$ 140/90 mmHg had an observed event rate that was 2.25 times the rate of cardiovascular events as those with blood pressure <140/90 mmHg. The event rate for patients not taking any antihypertensive medication compared with those who were was nearly 3 times greater.<sup>7</sup> Whether event rates in this pooled cohort study would be nationally representative is an issue that may limit the extrapolation of certain findings. The REGARDS study oversampled blacks from the US “stroke buckle” and “belt,” the MESA oversampled minorities in primarily urban environments, and the JHS recruited blacks from Mississippi. These populations and regions have among the highest rates of cardiovascular diseases. In the United States, disparities in hypertension

awareness, access to care, and treatment with respect to race/ethnicity and socioeconomic status are some of the most profound reported (Figure B). When cardiovascular disparities are visualized through the social determinants lens, vulnerable low-income and minority populations have the highest rates of cardiovascular risk factors and incident disease.<sup>11</sup> Although redefining treatment targets for high blood pressure management is of vital importance, the greater challenge is identifying the population-based policies and healthcare system approaches that improve hypertension treatment and cardiovascular risk-reduction efforts.

Unfortunately, the speed with which US guidelines have responded to evidence for lower hypertension targets is still ticking.<sup>8</sup> Both Canada and Australia have made recommendations using lower targets for patients meeting SPRINT inclusion criteria. Although many medical providers have integrated the practical SPRINT-directed protocols into daily practice, the uptake of the latest evidence is likely far below desired levels. Given the knowledge that we have with respect to cardiovascular disease risk modification, the lack of appropriate treatment for blood pressure levels and low-density lipoprotein-cholesterol levels above optimal is a persistent public health burden costing nearly a half-million lives per year, with untold morbidity and economic expense. Both medical providers and patients should evaluate the seriousness of cardiovascular risk with the same diligence that automobile safety and seat belt compliance received after successful public health efforts through the implementation of population-based interventions and policies that transformed routine public behaviors.<sup>12</sup> In the case of seat belt usage, rates of adherence went from 14% in the early 1980s to >97% in certain states.<sup>13,14</sup> The potential cost-effective interventions that are known to reduce the incidence of cardiovascular death, heart failure, myocardial infarction, and stroke remain underutilized for millions of US citizens.

Although traditionally patients have been reassured that they do not have hypertension at levels <140/90 mmHg or their hypertension was adequately controlled <140/90 mmHg, the current study highlights that the vast majority of cardiovascular events in the modern era are among individuals below that blood pressure threshold. Treating only the poorly controlled hypertensive patient intensively is akin to not seeing the forest for the trees. Ample opportunity remains to effectively reduce event rates through either identifying patients that would benefit from SPRINT-targeted blood pressure levels or the receipt of a statin based on the guidelines for arteriosclerotic cardiovascular disease risk reduction. The clinical effectiveness of intensive blood pressure management and statin therapy is far more reasonable and cost-effective than many other strategies commonly recommended for primary prevention. Further research on the benefits and limits of more aggres-



**Figure. National awareness, treatment, and control of high blood pressure.**

**A**, Extent of awareness, treatment, and control of high blood pressure by age (NHANES 2007–2012).<sup>10</sup> **B**, Age-adjusted prevalence trends for high blood pressure in adults  $\geq 20$  years of age by race/ethnicity, sex, and survey year (NHANES 1988–1994, 1999–2006, and 2007–2014).<sup>10</sup> Hypertension is defined as systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg if the subject said “yes” to taking antihypertensive medication or was told on 2 occasions that he or she had hypertension. NH indicates non-Hispanic; and NHANES, National Health and Nutrition Examination Survey. \*The category of Mexican Americans was consistently collected in all NHANES years, but the combined category of Hispanics was only used starting in 2007. Consequently, for long-term trend data, the category Mexican American is used.

sive hypertension management of additional populations is required to address shortcomings in the literature. In trying to achieve improved population health and reduce

preventable cardiovascular events anything short of 95% adherence with the known strategies of atherosclerotic risk reduction for all eligible should not be accepted.

## DISCLOSURES

Dr Fonarow has conducted research at the National Institutes of Health and has provided consulting for Amgen, Janssen, Medtronic, Novartis, and St Jude Medical. The other author reports no conflicts of interest.

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## FOOTNOTES

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