

## Editorials

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### The 2017 American College of Cardiology/ American Heart Association Clinical Practice Guideline for Blood Pressure: Implications for India

Globally, raised blood pressure is a leading modifiable risk factor for cardiovascular disease. In India, the rates of raised systolic blood pressure (SBP) have increased substantially since 1990, making it the fourth leading risk factor contributing to death and disability.<sup>1</sup> The Global Burden of Disease 2015 Study estimates mean age-standardized SBP among Indian men and women to be 126.6 mmHg (95% uncertainty interval [UI] 126.3–126.9) and 125.8 mmHg (95% UI 125.4–126.1), respectively.<sup>2</sup> This translates into an estimated 1 million (95% UI 0.9–1.1) deaths attributable to SBP  $\geq$ 140 mmHg in India in 2015. The 2017 American College of Cardiology/American Heart Association (ACC/AHA) clinical practice guideline for prevention, detection, evaluation and management of high blood pressure has led to changes in: (i) the definition and method of diagnosis of hypertension; (ii) the recommended threshold for initiation of pharmacotherapy; and (iii) the treatment target.<sup>3</sup> We discuss the implications of implementing these three changes in the Indian health system.

First, the 2017 ACC/AHA clinical practice guideline lowers the threshold for the diagnosis of hypertension by 10 mmHg compared with previous international guidelines.<sup>3</sup> The revised categories of blood pressure are: normal (<120/<80 mmHg); elevated (120–129/<80 mmHg); stage 1 hypertension (130–139/80–89 mmHg) and stage 2 hypertension ( $\geq$ 140/ $\geq$ 90 mmHg). This new classification is based on high-quality evidence showing a log-linear association between higher blood pressure and higher risk of cardiovascular disease.<sup>4</sup> The lower threshold for the diagnosis of hypertension will substantially increase the number of Indian adults diagnosed with hypertension. Using nationally representative data from 2018, the crude prevalence of hypertension in India using the threshold of 140/90 mmHg was 25.3% (95% CI 25.0–25.6), or 193 (95% CI 191–196) million Indian adults.<sup>5,6</sup> Data from the USA suggest a 40% increase in the number of individuals diagnosed with hypertension using the 2017 definition compared with previous definitions. A similar increase in India based on data from the USA would lead to an estimated prevalence of 35.4% (95% CI 35.0–35.8) or 271 (95% CI 268–274) million Indian adults with hypertension.<sup>7</sup> Among the 78 million newly diagnosed adults, approximately one-third or 24 million would be recommended for pharmacological treatment based on the USA estimates and risk-based treatment promulgated by the 2017 guideline. This increase will disproportionately affect states with a higher age-adjusted prevalence of hypertension such as Kerala, Himachal Pradesh and Punjab.<sup>5</sup> The remaining 54 million would be recommended for behavioural interventions, including reducing dietary sodium and alcohol consumption, increasing dietary potassium intake, weight loss and increasing physical activity.

However, the potential for over-diagnosis of hypertension seems greater in India than in the USA because clinic-based blood pressures are typically higher than home or ambulatory blood pressure measurements. The 2017 ACC/AHA guideline recommends confirmation of the diagnosis of hypertension with home or ambulatory blood pressure monitoring, but these are rarely performed and often not feasible to implement for most Indians. Lowering the threshold for the diagnosis of hypertension by 10 mmHg and the

subsequent possibility of over-diagnosis bears the higher risk for patients who do not have ready access to medical care in remote regions of the country.

Second, the 2017 ACC/AHA clinical practice guideline recommends initiation of pharmacotherapy for patients who have stage 1 hypertension ( $\geq 130/\geq 80$  mmHg) or higher in the setting of clinical cardiovascular disease or predicted 10-year atherosclerotic CVD (ASCVD) risk of 10% or higher. Blood pressure lowering medication is recommended for all patients with stage 2 hypertension ( $\geq 140/\geq 90$  mmHg) regardless of underlying ASCVD risk.<sup>3</sup> A 2014 meta-analysis of >50 000 individuals showed that blood pressure lowering pharmacotherapy led to a similar degree of cardiovascular risk reduction across all levels of baseline cardiovascular risk.<sup>8</sup> The greatest absolute risk reduction of cardiovascular events was observed in individuals with the greatest baseline cardiovascular risk, supporting the use of a risk-based approach to blood pressure treatment.

This risk-based approach parallels the 2013 ACC/AHA blood cholesterol guidelines and represents a substantial shift in the management of hypertension.<sup>9</sup> Implementing risk-based hypertension management in India is challenging given the dearth of validated risk prediction models for Indians as well as the limited clinical effectiveness of implementing risk prediction models.<sup>10</sup> Nevertheless, a risk-based approach targeting patients with the greatest baseline cardiovascular risk represents a more cost-effective blood pressure control strategy for health systems in low- and middle-income countries.<sup>11</sup> Using multivariable risk to identify individuals eligible for pharmacotherapy revives the argument for multivariable risk-reducing treatment through fixed-dose combination, or polypill, therapy of at least one blood pressure lowering drug and one lipid-lowering drug.<sup>12</sup> While the role of a polypill in secondary prevention of atherosclerosis is clear, the utility in primary prevention is still under evaluation through ongoing randomized clinical trials.<sup>13</sup>

Third, the 2017 ACC/AHA clinical practice guideline recommends a lower blood pressure target ( $<130/<80$  mmHg) in patients eligible for pharmacological treatment compared with previous targets ( $<140/<90$  mmHg). This recommendation was informed by the Systolic Blood Pressure Intervention Trial (SPRINT), which randomized 9361 high-risk participants to intensive treatment targeting an SBP  $<120$  mmHg compared with standard treatment targeting an SBP  $<140$  mmHg. The intensive treatment group, which recorded a 14.8 mmHg lower mean SBP, experienced a 25% relative risk reduction in the primary composite outcome of cardiovascular disease events over a median follow-up of 3.26 years (1.65% per year in intensive group v. 2.19% per year in the standard group; hazard ratio [HR] 0.75 [95% CI 0.64–0.89]) compared to the standard treatment group.<sup>14</sup> Participants in the intensive treatment group in SPRINT experienced a 38% lower relative risk of heart failure and 27% lower relative risk of all-cause mortality compared to participants in the standard treatment group. These compelling data provide evidence of benefit for lower SBP targets for higher risk patients with hypertension.

In contrast to SPRINT, the Heart Outcomes Prevention Evaluation (HOPE)-3 trial enrolled participants with intermediate risk of cardiovascular disease (based on a predicted ASCVD risk ~1% per year). The HOPE-3 trial showed that treatment with candesartan plus hydrochlorothiazide lowered SBP by 6 mmHg but did not result in a significant reduction in major cardiovascular disease events over a mean follow-up of 5.6 years.<sup>15</sup> However, the pre-specified subgroup with the highest (SBP  $>143.5$  mmHg, mean [SD] 154.1 [8.9] mmHg) experienced lower rates of cardiovascular events (HR 0.73 [95% CI 0.56–0.94]) compared to placebo. Data from both SPRINT and HOPE-3 suggest that the benefits of lowering blood pressure are greatest in individuals with highest baseline cardiovascular risk and highest baseline blood pressure. Health system interventions targeting individuals at highest risk will perhaps be the most beneficial, particularly for resource-constrained health systems based on diminishing returns among individuals with lower cardiovascular risk.

The implications of the 2017 ACC/AHA clinical practice guideline for blood pressure are varied in India based on state-level differences in the burden of disease and capacity of the health system. The 2017 launch of the India Hypertension Management Initiative (IHMI) by the Ministry of Health and Family Welfare, in collaboration with the Resolve To Save Lives Initiative, highlights the priority of high blood pressure control at a national level.<sup>16</sup> The IHMI aims to improve health system control of high blood pressure by standardizing simplified management plans, ensuring a consistent supply of high-quality medications, task-shifting distribution of medications to health workers at the community level, and focusing on treatment adherence at the patient level. Data collected from streamlined monitoring systems will be used to improve management of hypertension

starting from the primary health centres. The rationale for this approach is based on the substantial increase in hypertension control from 44% to 80% between 2001 and 2009 in the Kaiser Permanente Northern California health system through implementation of a large-scale hypertension programme. This programme included a comprehensive hypertension registry, sharing of performance metrics, evidence-based guidelines and visits by medical-assistants for blood pressure measurement.<sup>17</sup> The IHMI initiative provides a platform in India to implement and evaluate components of the 2017 ACC/AHA clinical practice guideline that are most relevant to India's health system at a national and subnational level. This initiative can help bridge the gap between guidelines developed in high-income countries and pragmatic implementation in low- and middle-income countries.<sup>18</sup> One limitation of this initiative is the focus on the public sector given a large majority of healthcare is provided by the private sector in most states. Furthermore, there is a need for integration of management of hypertension and diabetes given the immense dual burden of disease in India.

The 2017 ACC/AHA clinical practice guideline for blood pressure represents a major shift in recommendations for diagnosis, treatment initiation and targets for hypertension. The guidelines may be appropriate for specific clinical contexts in India; however, the broader public health system needs to evolve to mitigate raised blood pressure throughout the country where individuals may not have easy access to healthcare. This evolution must address the spectrum from prevention to treatment of complications of hypertension for optimal control of this key risk factor. National- and state-level burden of disease, availability of resources and priorities of the health system will influence India's adaptation, contextualization and implementation of this guideline to reduce the burden of cardiovascular disease in India.

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