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EDITORIAL

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Strategies for prevention of cardiovascular disease in adults with hypertension

A recent editorial in The Lancet, entitled "Is the concept of hypertension as a disease unhelpful?", raises questions regarding the optimal approach to prevention of blood pressure (BP)-related cardiovascular disease (CVD).[1] Initially, the editorial called attention to the fact that awareness, treatment, and control of hypertension (systolic BP [SBP] ≥140 mm Hg, diastolic BP [DBP] ≥90 mm Hg or treatment with antihypertensive drug therapy) is inadequate worldwide but especially so in middle- and low-income countries. This was based on two reports published in the same issue.[2,3] While disturbing, the findings in these two articles are not surprising. Previous reports, based on representative samples, have reported a high and increasing prevalence of elevated BP and hypertension worldwide,[4,5] and inadequate awareness, treatment, and control of hypertension, especially in low- and middle-income countries where Mills et al[4] estimated that only 7.7% of adults with hypertension were being treated and controlled to a systolic BP < 140 mm in 2010. Recognizing differences in methods and timeline, the 10.3% estimate of awareness, treatment, and control in low- and middle-income countries by Geldsetzer et al is similar.

The editorial goes on to ask the question "So, is the concept of hypertension as a disease with defined, albeit changing thresholds actually unhelpful?" The debate as to whether CVD risk reduction is best achieved by a focus on pre-existing (underlying) CVD risk, high levels of individual CVD risk factors, including high BP, or both is not new.[6] The Lancet editorial cites a retrospective analysis by Herrett et al which modeled the potential effect of the four following BP-lowering strategies on burden of CVD: Treatment based on (a) a BP threshold (SBP/DBP ≥ 140/90 mm Hg), (b) the 2011 National Institute for Health and Care Excellence (NICE) guideline combination of CVD risk and BP thresholds, (c) the 2019 NICE guideline combination of CVD risk and BP thresholds, which employs a lower threshold for estimated CVD risk compared to the 2011 guideline, and (d) a CVD risk estimation threshold.[7] The percentages of adults eligible for treatment, associated rate of CVD per 1000 patient-years of observation, and expected number of CVD events that would be prevented during slightly more than 4 years in the United Kingdom were 22.2%, 15.2%, and 271 963 using the 2011 NICE guideline thresholds, 26.8%, 14.9%, and 327 429 using the 2019 NICE guideline thresholds, 39.4%, 11.4%, and 301 523 using the BP threshold, and 29.3%, 16.9%, and 322 921 using the CVD risk estimation threshold. In summary, each approach was predicted to be beneficial with CVD risk estimation (alone) being identified as the best approach to CVD prevention, with a slight advantage compared to use of the BP (alone) threshold approach (BP-lowering treating for approximately 25% fewer adults but 7% more CVD events prevented) and a greater advantage compared to the two NICE treatment approaches.

While interesting, the findings in the Herrett et al report should be interpreted with considerable caution. First, the estimates were based on a retrospective observational analysis not a randomized trial comparison. Second, they are specific to the thresholds employed and should not be extrapolated to the expected treatment benefits with use of other guideline recommendations, which employ different BP and/or CVD risk estimation thresholds.[8-11] Third, the study assumes complete and equal implementation of the four strategies. There is considerable evidence that guideline recommendations are only partially implemented in practice. This is particularly the case for recommendations to employ CVD or ASCVD risk estimation. Survey data suggest that the majority of clinicians in the United States, even cardiologists, do not even report use of CVD risk estimating tools in practice, despite the fact that CVD risk estimation is a central component for US CVD prevention recommendations.[12] A similar lack of CVD risk estimation has also been noted in other countries.[13-16] Fourth, the Harrett et al paper is based on a relatively short period of follow-up (median of 4.3 years) whereas treatment of hypertension is a lifelong strategy. BP reduction in adults with hypertension who are unlikely to have a CVD event in the short term may still be prudent and beneficial, especially in younger adults who typically have a high lifetime risk of ASCVD.[8] Finally, strategies that focus entirely on BP reduction in those who are already at high CVD risk will result in effective absolute CVD risk reduction but are likely to be accompanied by high residual risk in those who are treated.[17]

Most English language BP guidelines recommend BP-lowering decisions that are based on a combination of high BP and elevated risk for CVD.[8-11] In the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) BP guideline, CVD risk estimation was recommended in all adults with high BP but there was acceptance of high CVD risk (estimated 10-year atherosclerotic CVD [ASCVD] event ≥10%) in all US adults with clinical CVD, the vast majority of adults with hypertension and either chronic kidney disease, diabetes or age ≥65 years, and in most adults with stage 2 hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg).[18-21] Explicit estimation of ASCVD was recommended for adults with stage 1 hypertension (SBP 80-89 mm Hg or DBP 80-89 mm Hg), a BP category where addition of antihypertensive drug therapy to nonpharmacological therapy was only recommended in the approximately 30% of US

adults with high ASCVD risk. Recognizing the challenges associated with implementation of guideline recommendations, the ACC/AHA BP guideline writing committee employed (only) two categories of ASCVD risk and chose the same ASCVD risk predicting instrument as that which is recommended for management of lipid abnormalities and aspirin decision-making in the United States.[22] This risk estimating tool is being integrated into electronic health records, minimizing clinician burden which is identified as the principal barrier to use of CVD risk estimation in practice.[12] The writing committee also chose to use (only) two categories of hypertension (stage 1 and stage2). It was felt that use of two categories for stratification of hypertension and ASCVD would provide sufficient information for treatment decision-making and would be easier than use of more complex classification systems in clinical practice settings.

The Lancet editorial misrepresents BP guideline recommendations, suggesting that both the 2017 ACC/AHA and the 2018 ESC/ESH guideline documents focus their treatment recommendations entirely on BP thresholds and treat hypertension as a disease. In fact, both documents identify BP as a CVD risk factor, not a disease state, and use categories of BP as well as CVD/ASCVD risk as a practical means for decision-making in clinical practice. The two guidelines employ distinct BP categories and separate risk estimation instruments that have been validated in the populations for whom the guidelines were written. Despite these differences, both guidelines are based on strategies that are more similar than different.[23] Treatment recommendations in the Canadian and Australian hypertension guideline documents are also based on a combination of BP levels and underlying CVD risk.[10,11]

Use of underlying CVD risk estimation (in combination with level of BP) is more complicated in countries where risk estimating instruments have not been validated. It is well known that instruments which are valid in a specific population[24] may not be as useful in other population settings.[25] In addition, laboratory variables such as the lipid values that are used in the ACC/AHA pooled cohort and ESC/ESH SCORE risk assessment equations may not be available, particularly in low- and middle-income countries. In such settings, advocating use of CVD risk estimation is likely to be a counterproductive distraction rather than a benefit. Recommendations for treatment decision-making in a population must be crafted in the context of existing awareness, treatment, and control of hypertension, the prevailing health care structure and workforce, socio-economic status, culture, and availability of a sustainable supply of affordable antihypertensive medications. In many countries, adults with high levels of BP are unaware of their condition and are almost certainly at high CVD risk. For example, awareness at the SBP/DBP level of ≥140/90 mm Hg is less than 20% in most sub-Saharan African countries and globally is less than 40% for adults living in low-and middle-income countries.[4] Many are likely to have SBP levels that exceed 150 or even 160 mm Hg—levels at which CVD risk is likely to be very high. In this context, population-wide identification and control of high BP is a more practical and achievable goal than prevention strategies based on CVD risk estimation. Population-based control of hypertension has a strong evidence base for efficacy and represents an affordable strategy that can substantially improve population health. Now more than ever before is the time to collaborate and leverage the resources needed to detect, treat, and control hypertension globally.

CONFLICT OF INTEREST

None for Drs. Whelton, Lackland, Parati, Ram or Zhang. Dr Campbell was a paid consultant to the Novartis Foundation (2016-2017) to support their program to improve hypertension control in low- to middle-income countries which includes travel support for site visits and a contract to develop a survey, provided paid consultative advice on accurate BP assessment to Midway Corporation (2017), and is an unpaid member of World Action on Salt and Health (WASH). Dr Weber has received research/consultant fees from AbbVie and Bristol Myers Smith, and honoraria from ReCor Medical, Medtronic, Johnson & Johnson, Ablative Solutions, Boston Scientific, Omron, Sanofi, and Astellas.

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Paul K. Whelton[1]
Norm R. C. Campbell[2]
Daniel T. Lackland[3]
Gianfranco Parati[4,5]
C. Venkata S. Ram[6,7]
Michael A. Weber[8]
Xin-Hua Zhang[9]

[1]*Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA*
[2]*Department of Medicine, University of Calgary, Calgary, AB, Canada*
[3]*Department of Neurology, Medical University of South Carolina, Charleston, SC, USA*
[4]*Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy*
[5]*Department of Cardiovascular, Neural and Metabolic Sciences, Instituto Auxologico Italiano, IRCCS, Milan, Italy*
[6]*Texas Blood Pressure Institute, University of Texas Southwestern Medical School, Dallas, TX, USA*
[7]*Apollo Institute for Blood Pressure Management, Apollo Hospitals and Apollo Medical College, Hyderabad, India*
[8]*Department of Medicine, Downstate College of Medicine of the State University of New York, New York, NY, USA*
[9]*Beijing Hypertension Institute, Beijing, China*

Correspondence
Paul K. Whelton, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Room 2015, New Orleans, LA 70112, USA.
Email: pkwhelton@gmail.com

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