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EDITORIAL

Aiming higher in hopes to achieve lower: the European Society of Cardiology/European Society of Hypertension versus the American College of Cardiology/American Heart Association guidelines for diagnosis and management of hypertension

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The latest European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines for diagnosis and management of hypertension (HTN) [1], published in August 2018, have reignited the debate triggered by the preceding 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines [2]. The most salient features of these two guidelines, and their contrast to immediately preceding guidelines, are summarized in Table 1. To recapitulate, the most contentious changes in the ACC/AHA guidelines pertained to lower diagnostic cutoff, treatment threshold for drug therapy, as well as goal blood pressure (BP) in those who qualify for drug therapy. The diagnostic cutoff for HTN was lowered to 130/80 mmHg from 140/90 mmHg previously. Hence, patients with systolic BP (SBP) 130–139 mmHg, a highly prevalent category, are now classified as hypertensive as opposed to prehypertensive previously. However, drug-therapy threshold is dependent on global 10-year atherosclerotic cardiovascular disease (ASCVD) risk, using the ACC's pooled cohort equations (PCEs). Patients with ≥10% calculated risk were recommended drug therapy at ≥130/80 mmHg, and those with lower risk at ≥140/90 mmHg. Obviously, this creates a population of hypertensives who are not drug therapy candidates, i.e., those with SBP 130–139 mmHg and <10% ASCVD risk. The ESC/ESH has left the definition and classification of HTN unchanged, with the diagnostic threshold remaining at ≥140/90 mmHg. Consequently, the threshold for drug therapy, irrespective of ASCVD risk, remains 140/90 mmHg. As an exception, the ESC/ESH does recommend considering treating those with established coronary artery disease (CAD) at the lower threshold of 130/80 mmHg. Apart from diagnostic and treatment thresholds, the two guidelines are largely aligned in regards to treatment targets. The ACC recommends treating to <130/80 mmHg in those with >10% ASCVD risk, while "considering" similar targets in those at lower risk, and the ESC recommends treating to <140/90 mmHg as a primary objective, and further lowering to <130/80 mmHg if therapy is well tolerated.

Obviously, changes in diagnostic cutoff, treatment threshold, and target BP are enormously impactful to clinical practice. Seemingly small, the 10-mmHg gap in diagnostic cutoff between the two guidelines has major implications. By the ACC's own admission, the lower cutoff would increase HTN prevalence from ≈30% to almost half the adult US population. To put this in perspective, using the most recent National Health and Nutrition Examination Survey (NHANES) data, a 130/80 mmHg cutoff would add almost 15 million patients 45–75 years old in the US alone [3]. Though it has been argued that only a small minority of these additional "patients" would actually require drug therapy, the aforementioned NHANES data estimated an additional 7.5 million drug therapy candidates, and given the lower target BP, ≈14 million additional patients would require intensification of therapy. Hence, up to 7.5 million patients in the US would now be "hypertensive" without actually being candidates for drug therapy. Globally, the corresponding numbers for China are estimated at a daunting 82 million new hypertensives, 55 million new drug therapy candidates (hence 27 million hypertensives not requiring drug therapy), and 30 million requiring treatment

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Table 1 Comparing previous and current ACC/AHA and ESC/ESH guidelines for diagnosis of hypertension, treatment thresholds, and target BP

JNC-8 (2014)	ACC 2017	ESC 2013	ESC 2018
Diagnosis/classification (all BP is SBP/DBP and in mmHg)			
Normal: <120 /80 Pre-HTN: 120–139/80–89 Stage I: 140–159/90–99 Stage II: ≥160/100	Normal: <120/80 Elevated: 120–129/80 Stage I: 130–139/80–89 Stage II: ≥140/90	Normal: <130/85 High normal: 130–139/85–89 Grade 1: 140–159/90–99 Grade 2: 160–179/100–109 Grade 3: ≥180/110	Normal: <130/85 High normal: 130–139/85–89 Grade 1: 140–159/90–99 Grade 2: 160–179/100–109 Grade 3: ≥180/110
Treatment thresholds			
>60 years old: ≥150/90 <60 years old OR with comorbid conditions (CKD, DM): >140/90	Established CVD or 10-year ASCVD risk[a] >10%: SBP ≥ 130 or DBP ≥ 80 No CVD and 10-year ASCVD risk < 10%: SBP ≥ 140 or DBP ≥ 90 No age specific guidelines	High normal: No DRx Low-moderate risk grade 1 hypertension: DRx if persistent HTN after lifestyle intervention ≥80 year old: Drug therapy may be considered when SBP 140–159	Established CVD or 10-year ASCVD risk[b] >10% or HMOD: SBP ≥ 140 or DBP ≥ 90 10-year ASCVD risk < 5% and no HMOD: DRx if SBP ≥ 140 or DBP ≥ 90 despite lifestyle intervention SBP ≥ 130 or DBP ≥ 90: DRx may be considered in those with established CVD, especially CAD
Treatment targets			
>60 years old: <150/90 <60 years old or comorbid conditions (DM, CKD): <140/90	Clinical CVD or 10-year ASCVD risk > 10%: <130/80 No CVD and 10 year ASCVD risk < 10%: <130/80 may be reasonable	SBP < 140 in most 65–80 years old: SBP goal 140–150 >80 years old: SBP goal 140–150 if in good physical and mental condition DBP targets: <90 in all <85 in diabetics	SBP < 140 and DBP < 90 in all; ≤130/80 in most if well tolerated <65 years old: SBP target 120–129 65–80 years old: SBP target 130–139 >80 years old: SBP 130–139 if tolerated DBP target: <80 in all

ASCVD atherosclerotic cardiovascular disease, *DBP* diastolic blood pressure, *DM* diabetes mellitus, *DRx* drug therapy, *HTN* hypertension, *HMOD* hypertension mediated organ damage

[a]ASCVD risk as calculated using the ACC pooled cohorts equation (PCE)

[b]ASCVD risk as calculated using the Systematic COronary Risk Evaluation (SCORE) system

intensification [3]. Furthermore, almost 80% of people aged 65 years or more (an age group that usually earns a >10% ASCVD risk with the PCEs despite lack of any other cardiovascular risk factor will now be drug therapy candidates. The immense epidemiologic and economic impacts of these numbers, and the strain on public health policy, not to mention the psychological impact on individual patients has been extensively commented upon previously. In the US, carrying a diagnosis of HTN would have real impacts on an individual's health insurance costs, and in some instances, even employability, given that employer-sponsored health insurance is the most common source of health insurance in the US. It does seem like a hard sell to increase global burden of a disease by hundreds of millions of patients just to increase awareness, which by the way, can equally be achieved by calling these patients "pre-hypertensives" or "high-normal", as was previously recommended. Indeed, the American College of Physicians and the American Academy of Family Physicians refused to endorse the lower diagnostic threshold [4]. There is also the obvious concern regarding excessive and premature drug treatment either by over-enthusiastic physicians or at the insistence of anxious patients. Finally, given that rates of HTN control are well below 50% globally even per previous criteria [5], perhaps our energies and resources would be better spent on first improving those statistics. The ESC's stance of keeping diagnostic threshold unchanged, in our view, endorses these concerns.

Of note, the recommendation to treat those with an SBP 130–139 mmHg and high (≥10%) ASCVD risk stems largely from the SPRINT trial, which found that this population benefitted from reduced all-cause and cardiovascular mortality with BP lowering to <120 mmHg versus <140 mmHg [6]. However, SPRINT enrolled largely (≈90%) patients with preexisting HTN, with a baseline SBP of 139 mmHg (likely stage 2 hypertensive patients by ACC-2017 criteria) on a mean of 1.8 antihypertensive agents, and a very high mean Framingham ASCVD-risk score of 25%. The achieved SBPs were 121.4 and 136.2 mmHg in the intensive versus standard treatment groups, respectively, down from a baseline SBP of about 139 mmHg in both groups. However, SPRINT used unattended automated BP measurement, albeit somewhat inconsistently, which underestimates office SBP by up to 15 mmHg, suggesting that achieved SBP may in fact have been equivalent to conventional SBPs in the 130–140 and 140–150 mmHg range, in more versus less intensive treatment groups, respectively, down from a baseline of >150 mmHg. Hence,

the ACC recommendation to start drug therapy at an SBP of 130 mmHg, based almost solely on findings of SPRINT, do not seem entirely justified, and may very well have overshot the true evidence-based threshold. These caveats, plus findings of the larger, and perhaps more relevant HOPE-3 trial [7], gave the ESC/ESH pause in terms of lowering diagnostic and treatment thresholds. Recruiting largely normotensives (only 22% subjects were on baseline therapy) with intermediate ASCVD risk, baseline high-normal BP (mean SBP = 138 mmHg), and using more conventional BP measurement methods, HOPE-3 showed no reduction in CV events with further BP lowering. In addition, two recent meta-analyses, one coming after the ACC guidelines, showed a reduced risk of stroke but no other CV events in those with high-normal BP (SBP 120–139 mmHg) and >10% ASCVD risk [8], and a reduction in major CV events but not all-cause mortality in those with high-normal BP and previous CAD [9]. Hence the benefits of treating those with SBP 120–139 mmHg seem to be marginal at best and limited to those with very high risk. In our opinion, the ESC guidelines in this regard indeed seem to be better aligned to current evidence than the ACC.

Though admittedly, epidemiologic studies show a log-linear increase in CV risk starting from an SBP of 115 mmHg and a DBP of 75 mmHg, like most chronic illnesses, treatment of HTN follows the law of diminishing returns, with absolute benefits of BP lowering progressively decreasing with lower achieved BP [10]. Importantly, permanent discontinuation of antihypertensive therapy due to adverse events has been found to increase at lower SBP, with a steep increase at achieved SBP <130 mmHg, such that the modest additional benefits at these BP levels are significantly attenuated by harms of therapy discontinuation/noncompliance [11]. Therefore, any discussion of benefits of stringent goals in the 120–140 mmHg range is incomplete without considering the risks inherent to achieving these goals. In this regard too, the ESC guidelines take a more measured and individualized approach, recommending a target of <140/90 mmHg as first priority, and attempting further reductions only if patients tolerate it.

Besides these differences, the two guidelines agree on several aspects of diagnosis and management that have been generally lauded, including: (1) emphasis on accurate measurement technique, both in office and at home, (2) recognizing the importance of home and ambulatory BP measurements in the diagnosis of HTN, their role in detecting "masked" and "white-coat" HTN, (3) precisely defining corresponding values between office and out-of-office BP (ambulatory and home BP being lower than office BP), (4) global ASCVD risk assessment in making therapeutic decisions, as discussed above, (5) recognizing and recommending that most patients qualifying for drug therapy may be best treated initially with two agents, with combination thiazide/thiazide-like diuretic/CCB plus ACEI/ARB as the first choice in most patients, (6) encouraging use of single-pill combinations of two agents to improve adherence, and (6) considering functionality as opposed to chronological age when individualizing treatment goals in the elderly.

In conclusion, the American guidelines came out with bold new controversial recommendations, whilst the European guidelines were largely unaltered with no new headline grabbing changes and did not provoke the strong reactions following the American guidelines. The American guidelines were based purely on a single (albeit strong) study, while the European guideline writers felt that this single study was not sufficient to change guidelines, especially in presence of conflicting data that were not completely in line with this. It is very likely that when other regions and countries bring out their guidelines, they are more aligned with the pragmatic and practical European guidelines.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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