
















# Comparison of guidelines for the management of hypertension: Similarities and differences between international and Asian countries; perspectives from HOPE-Asia Network

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#### Abstract

Guidelines on the management of hypertension have been developed by various professional bodies and institutions to primarily address the issues of diagnosis, treatment, and control in order to rationalize and improve the management of hypertension. Hypertension guidelines across the world have recently been updated following the new and controversial lower blood pressure threshold of  $\geq 130/80$  mmHg for the diagnosis of hypertension adopted by the Americans. While there are differences between the major as well as between the Asian national guidelines, there were also many similarities. This paper discusses and highlights the differences and similarities between the major international guidelines of the American College of Cardiology/American Heart Association, of the European Society of Cardiology/European Society of Hypertension, and of the International Society of Hypertension and also compares them with the Asian guidelines.

## 1 | BACKGROUND

Hypertension is the leading cause of cardiovascular (CV) mortality and morbidity worldwide with more than a billion people in the world living with hypertension.<sup>1,2</sup> It is of particular importance in Asia as more than half of the world's population with hypertension live in Asia and is expected to rise further as the population ages and with increasing obesity in the region.<sup>3,4</sup>

There is very little doubt in today's clinical practice that treatment of hypertension is very effective in reducing CV mortality and morbidity. However, there is a wide disparity in awareness, treatment, and control rates between the high-income and low- to middle-income countries many of which are in Asia.<sup>5,6</sup> Guidelines on the management of hypertension have been developed by various professional bodies and institutions to primarily address the issues of diagnosis, treatment, and control in order to rationalize and improve the management of hypertension. While initial guidelines were developed in the United States and Europe and used by many practitioners, many countries in Asia have more recently produced their own national guidelines. Hence, we aim to compare the different guidelines and highlight differences and similarities between them.

## 2 | CHRONOLOGY OF HYPERTENSION GUIDELINES

### 2.1 | US guidelines

The United States was the first to introduce guidelines on the management of hypertension in 1977 developed by the Joint National Committee (JNC) an organization established in 1972 through the

US National Institute of Health. Subsequently, updates were done periodically. In the JNC VII in 2003, instead of the previous classification of what was termed "normal" and "borderline" blood pressure (BP), the term pre-hypertension was introduced for the first time to replace these two categories of BP ie pre-hypertension for systolic BP between 120-139 mmHg or diastolic BP between 80-89 mmHg. This itself raised a lot of discussions then but surprisingly no further update or changes were forthcoming until 14 years later in November 2017 when instead of the JNC, it was the professional societies lead by the American Society of Cardiology, American Heart Association who were tasked with issuing an update to the JNC VII. As history tells us a major and in some ways controversial change in this 2017, guidelines were in the threshold for the diagnosis of hypertension where any BP  $\geq 130/80$  mmHg is deemed to receive a diagnosis of hypertension. Consequently, the target of control for most adults was also lowered to a BP of  $<130/80$  mmHg.<sup>7</sup>

### 2.2 | European guidelines

It was several years later in 2003 that the European Society of Hypertension (ESH) released their first guidelines on the management of hypertension. New updates were published in 2007, 2013, and the latest in August 2018. Unlike the US guidelines, the ESH in their latest update did not alter the threshold for the diagnosis of hypertension but instead retained it as a BP of  $\geq 140/90$  mmHg. However, their new recommended target BP for control of  $<130/80$  mmHg for most adults and for most of the associated clinical conditions like stroke and coronary artery disease was strangely lower than their diagnostic threshold.<sup>8</sup>

What was also a revolutionary departure from their previous guidelines was the ESH-ESC's recommendation for the use of combination drugs as initial therapy in patients with hypertension. This was in part driven by the new and more stringent BP target of <130/80 mmHg and also by the ample evidence that most patients need 2 or more drugs even to achieve the previous higher target of <140/90 mmHg.

The exceptions to combination therapy as initial therapy as recommended by the ESH-ESC are to consider use of monotherapy in low-risk grade 1 hypertension (systolic BP <150 mmHg), or in very old ( $\geq 80$  years) or frailer patients.

The AHA-ACC guidelines recommend initiation of combination therapy for those with stage 2 hypertension and an average BP >20/10 mmHg above their BP target. But because the United States' definition of stage 2 hypertension is a BP  $\geq 140/90$  mmHg, effectively this is similar to the ESC-ESH's recommendations of using combination therapy as initial therapy in patients with hypertension. For their stage 1 hypertension, that is BP 130–139/80–89 mmHg, monotherapy is recommended.

All other guidelines on the other hand continue to recommend monotherapy as initial therapy for patients with hypertension, except when the BP is  $\geq 160/100$  mmHg whence dual therapy can be considered as initial therapy.

### 2.3 | International guidelines

To improve the management of hypertension, the International Society of Hypertension (ISH) published in 2014 with the American Society of Hypertension Clinical Practice Guidelines for the Management of Hypertension in the Community. Subsequently, ISH developed and issued for the first time in 2020 a worldwide practice guidelines.<sup>9</sup> Recognizing that there are disparities of resources between high- and low- to middle-income countries, the ISH tailored recommendations as essential and optimal standards of care in a practical format that is easy-to-use particularly in low, but also in high resource settings by clinicians, but also nurses and community health workers, as appropriate.

The International Consortium on Health Outcome Measures (ICHOM) has also recommended standards of care in low- and middle-income countries which would be appropriate for use in South East and East Asia countries.<sup>10</sup>

### 2.4 | Asian guidelines

Low- and middle-income regions often follow guidelines from high-income regions closely, as their resources and health systems to develop and implement local guidelines remain challenging. However, more recently several countries in Asia particularly the low- to middle-income countries with large populations but low treatment and control rates have developed their own national guidelines. Except for a few countries like Cambodia, most South East Asian

countries do have their own national guidelines. Table 1 shows the year of their latest guidelines, and as can be seen, almost everyone except Singapore released an updated guideline after 2017, the year the latest US guidelines were released.<sup>11–27</sup>

## 3 | DIFFERENCES AND SIMILARITIES

Although guidelines were developed based on existing evidence and using the same evidence base, there were still differences in their recommendations particularly on the diagnostic BP threshold. There were also differences in the recommendations for the use of out-of-office BP measurements, the target BP for control and initiation of drug therapy, and use of combination therapy in particular the single pill combination. However, there were also many similarities. Below, we compare and discuss the differences and similarities from the angle of the diagnostic BP threshold, BP categories, recommendations for overall CV risk assessment, use of out-of-office BP measurements, initiation of anti-hypertensive therapy (for all adults, adults with increased CV risk, older adults and adults with specific indications), and the recommended target of BP control in the various groups.

## 4 | DIAGNOSTIC BP THRESHOLD FOR HYPERTENSION AND HYPERTENSION CATEGORIES

The US guidelines created a lot of controversies and discussions when they lowered the threshold for the diagnosis of hypertension to a systolic BP (SBP) of  $\geq 130$  mmHg and/or a diastolic BP (DBP)  $\geq 80$  mmHg in 2017.<sup>28</sup> However, almost all other guidelines following the release of the US guidelines including the ESH, ISH, and many of the Asian guidelines retained the diagnostic threshold of  $\geq 140/90$  mmHg (Table 1).<sup>11</sup>

Changes also occurred in the hypertension categories. The US guidelines no longer had a stage 3 hypertension group, only classifying a BP of between 130/80–140/90 as stage 1 and anything above 140/90 as stage 2 hypertension.

The ESH retained the 3 grades of hypertension, while for the Asians guidelines all except Korea retained 3 categories of hypertension (Table 1). Like the US guidelines, the ISH opted for 2 categories of hypertension only.

When it comes to what is deemed “normal” BP, the guidelines differed considerably. The United States because of the new lower diagnostic threshold for hypertension now considers a SBP of <120 and DBP of <80 mmHg as normal while many of the Asian guidelines considered these levels as optimal and SBP of 120–129 and/or DBP of 80–85 as “normal” The ESH on the other hand deemed SBP 120–129 and/or DBP <80 mmHg as normal while the ISH used SBP <130 and DBP <85 mmHg as “normal” BP (Table 1).

One of the reasons for the lower diagnostic BP threshold proposed by the United States was attributed to the available and

consistent epidemiological evidence as well as several meta-analyses which showed that a BP of between 130–139/80–90 mmHg already carries a 1.5–2 times the risk of coronary and stroke events compared to SBP below 120 mmHg. Because of this increased CV risk even at BP lower than the conventional hypertension BP threshold of  $\geq 140/90$  mmHg, it was felt to be important to identify those at increased risk so that preventive measures are in place early, especially as it is known BP rises with increasing age. The concern with adopting this lower BP threshold is that many more people will now be labeled as “hypertensive” which by itself carries its own psychological, economic, and social issues.

However, to be fair to the United States, they do not recommend that all such individuals with BP in the range 130–139/80–89 mmHg be treated pharmacologically but to implement lifestyle changes and only be given drugs if associated with atherosclerotic events or target organ damage or the overall CV risk is greater than 10%. In fact, although the prevalence of hypertension will be increased from 31.9% to 45% an increase of 13.7%, the extra number of people needing pharmacological agents is only increased by 1.9% from 34.3% to 36.2%.<sup>29</sup>

Perhaps another reason is because of the Systolic Blood Pressure Intervention Trial (SPRINT) study which showed that hypertensives treated more intensively to achieve a lower BP target of  $<120/80$  mmHg benefitted more reduction in CV mortality and morbidity than a BP of  $<140/90$  mmHg.<sup>30</sup> However, patients with SBPs of  $<143.5$  mmHg in the HOPE-3 study did not benefit from BP-lowering drugs compared to those with baseline SBP  $>143.5$  mmHg.<sup>31</sup> A further important point to note is that the HOPE-3 was a primary prevention trial of patients with intermediate CV risk while the SPRINT patients were of high CV risk highlighting that the treatment threshold and goal BP may be different for individuals with different CV risk.

## 5 | GLOBAL CV RISK ASSESSMENT

Although earlier JNC editions on management of hypertension did include statements about the increased risk of CV mortality and morbidity in hypertensive individuals with other CV risk factors like smoking, presence of diabetes, hyperlipidaemia, there were no recommendations about overall/global CV risk assessment until JNC VI in 1997 where a new table describing risk stratification were added. Basically, CV risk was stratified into 3 groups moving from lower to higher risk, where Group A were hypertensive patients with no other CV risk factors, no target organ damage or clinical CVD, Group B patients with at least 1 CV risk factor but no diabetes, or target organ damage or clinical CVD and Group C hypertensive patients with target organ damage or CVD and/or diabetes, with or without other CV risk factors were added. These groups stratified by risk served as a guide as to when to initiate anti-hypertensive therapy and that it not just based on the absolute BP reading alone but on the presence of absence of other CV risk factors.

In the latest US guidelines, a formal approach to stratify CV risk was introduced where it was recommended that an overall CV risk assessment be done and an absolute value of risk be assigned to certain patients. This was of particular importance in those without co-existing atherosclerotic CVD or diabetes, as their recommendation in this group of patients is that a BP between 130–139/80–89 mmHg and with a CV risk of 10% using the pooled Cohort risk calculator or greater should be treated pharmacologically.

The 2018 ESH guidelines stratified CV risk by categories of low, moderate, high, or very high risk factoring in the hypertension stages according to BP levels, presence of CV risk factors, hypertension-mediated organ damage (HMOD), or comorbidities.

Like the ESH, the ISH stratified CV risk by BP levels according to additional risk factors, HMOD, and previous CVD but has only 3 instead of 4 categories, that is, low, medium, or high.

Almost all the Asian guidelines also recommended performing an overall CV risk assessment (Table 1). Most Asian countries except for Thailand do not have their own country's risk prediction chart nor have they validated existing risk calculation tools. Hence, most guidelines did not specifically recommend the use of any CV risk assessment tools but adopt and recommend the risk categories recommended by ESH for overall CV risk assessment. While the Malaysian guidelines' risk stratification table differs slightly from the ESH's and is recommended for use, the Framingham General CVD prediction tool has been validated and found to work well especially as the background CV risk of Malaysia mirrors that at the height of the CV epidemic in the United States around the 1950s.<sup>32</sup>

While there are differences in the risk categories, on a clinical and practical level, most guidelines recommend drug therapy as soon as the CV risk is high and some like the Malaysia guidelines even at medium CV risk.

## 6 | USE OF OUT-OF-OFFICE BP MEASUREMENTS

The benefits of out-of-office BP measurements are well known. Besides being better predictors of CV mortality and morbidity than office BP, they are needed to identify white coat (WCH), masked and resistant hypertension as well as to monitor BP control. The use of HBPM has been shown to lead to lower BPs, better adherence, and patient satisfaction to non-use.

The use of out-of-office BP measurements, using ambulatory BP measurements (ABPM preferred) or home BP measurement (HBPM) to confirm the diagnosis of hypertension, was actually first recommended by the National Institute for Health and Clinical Excellence (NICE) of United Kingdom in 2011 and retained in their recent update in 2019. This created quite a lot of concern especially as many low- to middle-income countries in Asia do not have ABPM and not many patients have HBPM.<sup>5</sup> The rationale for recommending this was that many individuals found to have an elevated BP in the office/clinic may actually have a normal BP while out of the office/clinic, a situation called white coat hypertension. Identifying those

TABLE 1 BP categories United States, European, International, and Asian hypertension guidelines

BP category (mmHg)	AHA/ACC 2017	ESC/ESH 2018	ISH 2020	CHL 2018	HK 2018	India 2019	Indonesia 2019	JSH 2019
SBP <120 and DBP <80	Normal	Optimal	–	Normal	optimal	optimal	optimal	Normal
SBP: 120–129 and DBP <80	Elevated	–	–	–	–	–	–	High normal
SBP 120–129 and DBP 80–84		Normal	–	–	Normal	–	Normal	–
SBP 120–139 and DBP 80–89				High normal				
SBP <130 and/or DBP <85			Normal		–	Normal	–	–
SBP: 130–139 and (or) DBP: 80–89	Grade 1		–		–		–	Elevated
SBP 130–139 and/or DBP 85–89		High normal	High normal	–	High normal	High normal	High normal	–
SBP: 140–159 and (or) DBP: 90–99	Grade 2	Grade 1	Grade 1	Grade 1 (mild)	Grade 1	Stage 1	Grade 1	Grade 1
SBP: 160–179 and (or) DBP: 100–109	Grade 2	Grade 2	Grade 2	Grade 2 (moderate)	Grade 2	Stage 2	Grade 2	Grade 2
SBP ≥180 and/or DBP ≥110	Grade 2	Grade 3	Grade 2	Grade 3 (severe)	Grade 3	Stage 3	Grade 3	Grade 3
SBP ≥140 and DBP <90	NA	ISH	ISH	ISH	ISH	ISH	ISH	ISH
Cardiovascular risk assessment	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note: Abbreviations: AHA/ACC, American Heart Association/American College of Cardiology; BP, blood pressures; CHL, Chinese Hypertension League; DBP, diastolic BP; ESC/ESH, European Society of Cardiology/European Society of Hypertension; HK, Hong Kong; ISH, International Society of Hypertension; JSH, Japanese Society of Hypertension; KSH, Korean Society of Hypertension; SBP, systolic BP.

<sup>a</sup>Taiwan Focused update 2017.

<sup>b</sup>Use of Framingham general CV risk score recommended.

<sup>c</sup>Thai Cardiovascular Risk Score.

with WCH translates to cost savings and adverse effects for the individuals for unnecessary drug treatment.

Not all the recent guidelines subscribed to this recommendation as the diagnosis of hypertension is still based on office/clinic measurements although out-of-office BP measurements are encouraged to help in confirming the diagnosis. Furthermore, most Asian countries do not have their own HBPM consensus to guide practitioners on its appropriate use but Asian consensus and insights on the use of HBPM and ABPM have recently been published to aid practitioners in Asia in the interim.<sup>33–36</sup>

Although the United States lowered their diagnostic office BP threshold to ≥130/80 mmHg, their diagnostic for both home BP and day ABPM threshold is also ≥130/80 mmHg, and this is puzzling as it has been shown that home BP tend to be around 5 mmHg lower than office readings. However, the United States did lower their ABPM threshold for the 24 h and night by 5 mmHg. On the other hand, the

ESC/ESH, ISH, and Asian countries retained their previous thresholds for out-of-office BP levels. (Table 2).

While NICE recommends out-of-office BP measurements for confirming a diagnosis of hypertension, it does not recommend that titration of treatment to reach BP target be based on HBPM. This is primarily because there is very little or at least no good evidence yet that treating hypertension based on HBPM results in a better reduction in CV mortality or morbidity compared to using the conventional clinic BPs, which are backed up by numerous clinical outcome trials.

The latest US guidelines have also recommended wider use of out-of-office BP measurements and like NICE recommends it for confirming and titration of BP-lowering medication. ESH recommends out-of-office, measurements to confirm diagnosis but only when it is logistically and economically feasible. ISH recognizes that out-of-office BP measurements may not be feasible in most low- to- middle countries and have recommended out-of-office

KSH 2018	Malaysia 2018	Pakistan 2018	Philippines 2018	Singapore 2017	Taiwan 2015, 2017	Thailand 2019	Vietnam 2018
Normal	Optimal	Optimal	Normal	–	Normal	Optimal	Optimal
Elevated	–	–	–	–	–	–	–
–	Normal	Elevated	–	–	–	Normal	Normal
–	–	–	Elevated	–	Pre-HTN	–	–
Pre-HTN	–	–	–	Normal	–	–	–
–	At risk	Pre-HTN	–	High normal	–	High normal	High normal
Grade 1	Stage 1 (mild)	Stage 1	Stage 1	Grade 1	Stage 1	Stage 1	Grade 1
Grade 2	Stage 2 (moderate)	Stage 2	Stage 2	Grade 2	Stage 2	Stage 2	Grade 2
Grade 2	Stage 3 (severe)	Stage 3	Stage 2	Grade 3	Stage 3	Stage 3	Grade 3
ISH	ISH	ISH	ISH	ISH	ISH	ISH	ISH
Yes	Yes <sup>b</sup>	Yes	Yes	Yes	Yes	Yes <sup>c</sup>	Yes

**TABLE 2** Thresholds for diagnosing hypertension based on clinic and out-of-office (home and ambulatory) blood pressures for United States, Europe, and Asia

	ACC/AHA	ESC/ESH	ISH	Asia
Clinic	130/80	140/90	140/90	140/90
Home	130/80	135/85	135/85	135/85
ABPM				
Daytime	130/80	135/85	135/85	135/85
Nighttime	110/65	120/70	120/70	120/70
24-h average	125/75	130/80	130/80	130/80

Note: Abbreviations: ABPM, ambulatory blood pressure measurements; ACC/AHA, American College of Cardiology/American Heart Association; ESC/ESH, European Society of Cardiology/European Society of Hypertension; ISH, International Society of Hypertension.

measurements as optimal and not essential. In general, all the Asian guidelines have in their latest guidelines recommended wider use of out-of-office BP measurements and to confirm diagnosis if feasible.

However, while all the guidelines do recommend and encourage the use of HBPM, the recommendation except for Japan is still to use office/clinic BPs to titrate medication while HBPM acts as a complement to management. In Japan, anti-hypertensive treatment based on home BP is strongly recommended (Recommendation Grade 1 Evidence Level B).<sup>17</sup>

## 7 | INITIATION AND CHOICE OF ANTI-HYPERTENSIVE MEDICATIONS

There is universal agreement across all the guidelines that anti-hypertensive drugs be given if the BP is  $\geq 160/90$  mmHg regardless

of the CV risk. In such instances, a combination of 2 agents can be initiated except in those  $\geq 75$  years old. There is also agreement among almost all guidelines, except the United States and Hong Kong guidelines, that for BPs between 140–159/90–99 mmHg treatment with pharmacological agents should be based not on the BP alone but on the overall CV risk as well. (Table 3) For these guidelines, the recommendation for those with this level of BP and with medium or higher risk, anti-hypertensive agents are recommended. In contrast, the AHA/ACC recommends anti-hypertensive drugs for those with a BP  $\geq 140/90$  mmHg without considering the overall CV risk. Because Hong Kong does not factor in CV risk, indication for treatment is to start when BP is  $\geq 160/100$  mmHg and only to start treatment for those with BP 140–159/90–99 mmHg when lifestyle modifications fail after a period of 6 months.

For the US guidelines, the recommendation is that all BPs  $\geq 140/90$  mmHg (i.e. their stage 2) should be treated with BP-lowering medication. For those with BP between 130–139/80–89 (their stage 1), the recommendation is that anti-hypertensive medication should be prescribed if there is any atherosclerotic CVD or the overall CV risk is  $\geq 10\%$ .<sup>28</sup> On the other hand, the European and Asian guidelines recommend pharmacological agents in individuals with a BP between 130–139/80–89 mmHg only if their CV risk was high or very high.

The ESH differ somewhat in their recommendation of initial therapy, where a combination of 2 drugs are recommended except for those with low-risk stage 1 hypertension (BP 140–159/90–99 mmHg) or in the very old ( $\geq 80$  years) or frailer patients.<sup>8</sup>

In terms of choice of first-line anti-hypertensive drugs, the United States recommends calcium channel blockers (CCB), diuretics (DU), angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin

receptor blocker (ARB) omitting  $\beta$ -blockers (BB). The ESC/ESH on the other hand recommends all 5 classes including BB as possible first-line drugs. ISH, recognizing limited resources in low- to middle-income countries, recommends any class of drugs that is available as long as they are evidence-based in relation to morbidity/mortality prevention and benefiting the population being treated. Like the United States, in general the Asian countries' recommendation for first-line monotherapy includes DU, CCB, ACE-I ARB except for China, Indonesia, India, Korea, Singapore, and Thailand which also recommend BB as first line as well (Table 3).

For special groups of hypertensive patients, for example, hypertension and coronary artery disease, hypertension and stroke, again there is universal agreement about the class of anti-hypertensives. In general, most of these patients require at least 2 drugs as their BP target is also lower, and almost all the combinations include an ACE-I or ARB with a CCB or DU Japan recommends for adults  $< 75$  years and in special groups, a lower clinic BP target of  $< 130/80$  mmHg and home BP  $< 125/75$  mmHg while for those  $\geq 75$  years old, a higher target of clinic BP  $< 140/90$  and home BP  $< 135/85$  mmHg is recommended (Table 3).

## 8 | BP TARGET FOR CONTROL

The United States recommends the lower BP target of  $< 130/80$  mmHg as they use BP  $\geq 130/80$  mmHg for the definition of hypertension. This target applies to all groups of hypertensive patients regardless of their CV risk (Table 4).

Although the ESH guidelines retained the diagnostic threshold as BP  $\geq 140/90$  mmHg, their target for all groups of hypertensives

TABLE 3 Initiation and choice of anti-hypertension drugs

Indications	AHA/ACC	ESC/ESH	ISH	Asian guidelines	
				High income	
				Hong Kong	Japan
BP $\geq 130/80$ mmHg	Treat if ASCVD+ve or CV risk $\geq 10\%$	Consider treat in very high risk with CVD especially CAD	Consider treat if ACVD+ve or DM, or CKD or HMOD	Treat if ASCVD+ve or DM or CKD, CAD	Treat if high risk and LSC insufficient after 1 month
BP 140–159/90–99	Drug treatment	Immediate treatment in high or very high with CVD, CKD or HMOD	Immediate treatment in high risk or with CVD or CKD or DM or HMOD	Consider start if LSC insufficient after 6 months or if HMOD present	Low/moderate risk treat if LSC insufficient after 1 month High risk immediate drug treatment
BP $\geq 160/110$ mmHg	Drug treatment	Immediate drug treatment	Immediate treatment in all patients		Immediate drug treatment
1st line drug	DU, CCB ACE-I, ARB	DU, CCB ACE-I, ARB, BB	Any of DU, CCB ACE-I, ARB, BB if available	DU, CCB ACE-I, ARB	DU, CCB ACE-I, ARB

Note: Abbreviations: AHA/ACC, American Heart Association/American College of Cardiology; BP, blood pressures; ESC/ESH, European Society of Cardiology/European Society of Hypertension; HMOD, hypertension-mediated organ damage; ISH, International Society of Hypertension.

<sup>a</sup>China, Indonesia, Malaysia, Thailand.

<sup>b</sup>India, Pakistan, Philippines, Vietnam.

<65 years is surprising <130/80 mmHg but not going to SBP of <120 mmHg except in those with chronic kidney disease. In those  $\geq$ 65 years old, the target is 130–139/70–79 mmHg if tolerated. The ISH's recommended target is similar to ESH.

The guidelines have made very clear recommendations about drug choice for special groups (Table 4). The recommendations of drug choice for each special group are very similar, mostly recommending RAS blockers as the base and in combination with CCBs or diuretics or as clinically indicated, for example, in patients with coronary artery disease, it is universal a BB is also recommended besides the RAS blockers.

Most guidelines did not make any specific recommendation for individuals with metabolic syndrome and hypertension. The only exception is Taiwan who recommends ACE-I or ARB and not diuretics or  $\beta$ -blockers unless clearly indicated for other existing comorbidities (ref Taiwan GL 2015) and India who recommends an ACE-I or ARB. MS is very prevalent even in Asia and will increase with the epidemic of increasing obesity. Hence, it is important that future guidelines make specific commendations for such a situation.

For Asian countries, again all the countries except Japan recommend for patients with hypertension BP <140/90 as their target of control and lower targets of <130/80 mmHg if tolerated. Japan's like the United States' target is for <130/80 mmHg for all hypertensive patients including those in the special groups. Most of the Asian countries recommend the lower targets of <130/80 mmHg for the special group of patients with hypertension, with certain countries opting for the interim target of <140/90 (e.g. China), but going lower to <130/80 if tolerated. The classification of elderly to varies somewhat in the Asian countries but in

general the recommendation of target control is <140/90 mm for those under 75 years old and <150/90 mmHg for those 75 years or older.

Japan on the other hand recommends for adults <75 years a lower clinic BP target of <130/80 mmHg and home BP <125/75 mmHg, while for those  $\geq$ 75 years, a higher target of clinic BP <140/90 and home BP <135/85 mmHg is recommended but still 10 mmHg lower than other Asian countries (Table 4).

Of interest is the time frame to reach BP control. Studies have shown that early treatment can reduce left ventricular hypertrophy significantly within 6 months of treatment. Separation of stroke incidence can also be seen within 6 months of better BP lowering in clinical outcome trials. However, most guidelines except for China, Indonesia, Japan, Malaysia, and Pakistan do not clearly specify the time frame to reach control. (Table 4) Again, this aspect may need to be highlighted more in future guidelines.

## 9 | TARGET BP IN ELDERLY

While the diagnostic BP threshold for the elderly remains the same as that for younger individuals, that is,  $\geq$ 140/90 mmHg by all guidelines and  $\geq$ 130/80 mmHg by the US guidelines, the target BP for control in the elderly varies considerably between the guidelines and varies according to different ages used (Table 4).

This is in part due to the various definitions of elderly. As a consequence, the recommendations for treatment of hypertension in the elderly are complicated by these various definitions of "elderly" or "older" people used in randomized control trials where older was defined as >60 years in the earliest trials, then as 65, 70 and finally

Korea	Singapore	Taiwan	Upper middle income <sup>a</sup>	Lower middle income <sup>b</sup>
LSC or treat if ASCVD+ve or CAD DM or CKD	–	Treat if DM or CHD or CKD	Drug treatment if ASCVD+ve, DM, HMOD	Drug treatment if ASCVD+ve, DM, HMOD
Treat if RF $\geq$ 1, or DM or CVD or CKD or HMOD	Drug treatment	Drug treatment	Immediate drug treatment if very high risk, ASCVD+ve, DM or CKD	Immediate drug treatment if very high risk, ASCVD+ve, DM or CKD
Immediate drug treatment	Immediate treatment	Drug treatment	Immediate drug treatment	Immediate drug treatment
DU, CCB ACE-I, ARB, BB	DU, CCB ACE-I, ARB, BB	Depends on indication but all 5 classes can be used	DU, CCB ACE-I, ARB	DU, CCB ACE-I, ARB, BB except Pakistan: ACE-I, ARB, CCB



TABLE 4 Target for blood pressure control and recommended anti-hypertensive drugs in special groups

	AHA/ACC 2017	ESC/ESH 2018	ISH 2020	CHL 2018	HK 2018	India 2019	Indo 2019	Japan 2019
Target BP mmHg	<130/80	<sup>a</sup> SBP 130 DBP 70–79	<140/90 <sup>b</sup>	<140/90	<140/90 <sup>b</sup>	<130/80	<sup>a</sup> SBP ≤130 DBP 70–79 <sup>a</sup>	<130/80
HTN+CAD	<130/80	<sup>a</sup> SBP 130 DBP 70–79	<130/80	<140/90 <sup>b</sup>	NR	NR	<sup>a</sup> SBP ≤130 DBP 70–79	<130/80
HTN+CVA	<130/80	<sup>a</sup> SBP 130 DBP 70–79	<130/80	<140/90	NR	NR	<sup>a</sup> SBP ≤130 DBP 70–79	<130/80 HBPM <125/75
HTN+HF	<130/80	<sup>a</sup> SBP 130 DBP 70–79	<130/80 but not <120/70	<130/80	NR	<130/80	NR	SBP <130 DBP not <80
HTN+UA	<130/80	<130–139/70–79	<130/80	NR	NR	NR	NR	<130/80
HTN+CKD	<130/80	SBP <140 to 130 if tolerated DBP 70–79	<130/80	<sup>c</sup> UAE–ve <140/90 UAE+ve <130/80	V130/80	NR	SBP <140 to 130 if tolerated DBP 70–79	<130/80 Office HBPM <125/75
HTN+DM	<130/80	<sup>a</sup> SBP 130 DBP 70–79	<130/80	<130/80	<130/80	NR	<sup>a</sup> SBP ≤130 DBP 70–79	Office <130/80 HBPM <125/75
HTN+MS	NR	NR	NR	NR	NR	NR	NR	NR
HTN ≥65 years	<130/80 <sup>e</sup>	<sup>a</sup> 130–139/70–79	<140/80	<140/90	NR	130–140/80–90	SBP 130–139	<130/80
HTN ≥75 years					NR	130–140/80–90	SBP 130–139	<140/90 OBP <135/85 HBPM
HTN ≥80 years		<sup>a</sup> 130–139/70–79		<150/90	NR	130–140/80–90		
Drug choice in special groups								
HTN+CAD	BB RAS, CCB	RAS+BB /CCB or DU <sup>^</sup>	RAS CCB DU	BB CCB+ACE DU	ACE BB, CCB	BB	BB /CCB+ARB/DU or BB/DU+CCB or BB+DU	BB CCB
HTN+CVA	DU <sup>^</sup> RAS	RAS+CCB/DU <sup>^</sup> diuretic	RAS CCB DU	CCB RAS DU	ACE BB, CCB	CCB	NR	CCBs, RAS DU
HTN+HF	RAS BB DU MRA (non-DHP CCB)	RAS, BB and MRAs	RAS, BB and MRA	RAS BB MRA	ACE DU <sup>^</sup>	BB	RAS+DU +BB	RAS BB MRA+CCB DU
HTN+UA	RAS	RAS+CCB/DU <sup>^</sup>	RAS+CCB DU	RAS+CCB DU	ACE	RAS	NR	NR
HTN+CKD	RAS	RAS+CCB/DU <sup>^</sup>	RAS+CCB DU (Loop)	RAS+CCB/ DU	ACE	RAS ESRD α-B, central acting	RAS+CCB/DU	Protein+ve RAS Protein–ve RAS CCB DU <sup>^</sup>
HTN+DM	DU, RAS CCB	RAS+CCB/DU <sup>^c</sup>	RAS ± CCB/ DU	RAS+CCB DU			RAS+CCB/DU	Alb+ve RAS Alb–ve BB/ DU+CBB/ DU
HTN+MS	NR	NR	NR	NR	NR	RAS	NR	NR
HTN ≥65 year	DU CCB RAS						NR	
HTN ≥75 year	—	DU CCB RAS	DU CCB RAS	DU CCB RAS	CCB DU <sup>^</sup>	CCB DU	NR monotherapy	CCBs RAS DU <sup>^</sup>

Korea 2018	Msia 2018	Pakistan 2018	Philippines 2018	Singapore 2017	Taiwan 2015, 2017*	Thailand 2019	Vietnam 2018
<140/90	<140/90	≤140/90	<130/80	<140/90	<140/90	120–130/70–79	<130/80
<130/80	<130/80	<130/80	NR	NR	<130/80	120–130/70–79	<sup>a</sup> SBP 130 DBP 70–79
<130/80 lacunar stroke	<140/80 <130/80 lacunar stroke	<130/80	<130/80	Individualized	<140/90	120–130/70–79	<sup>a</sup> SBP 130 DBP 70–79
<130/80	<140/90	NR	NR	NR	NR	<130/80	<sup>a</sup> SBP 130 DBP 70–79
<130/80	Pro <1Gm <40/90 Pro >1Gm <130/80	NR	NR	<130/80	<120/NR	NR	<130–139/70–79
<sup>c</sup> UAE–ve <140/90 UAE+ve <130/80	<sup>d</sup> Pro <1G <140/90 Pro >1G <130/80	<130/80	<130/80	<140/90 If +DM <130/80	<sup>c</sup> UAE–ve <140/90 UAE+ve <130/80	120–130/70–79	SBP <140–130 if tolerated DBP 70–79
<140/85, complicated <130/80	<140/90. <130/80 high risk DM	<130/80	<130/80	<sup>c</sup> UAE–ve <140/80 UAE+ve <130/80	<130/80	120–130/70–79	<sup>a</sup> SBP 130 DBP 70–79
NR	NR	NR	NR	NR	NR	NR	NR
<140/90	<140/90	NR	NR	NR	<140/90	130–139/70–79	<sup>a</sup> SBP 130 DBP 70–79
		NR	NR			–	
	SBP <150	<150/90	<140/90	<150/90	<150/90	120–130/70–79	
BB CCB	BB RAS	BB, ACE	BB	BB, RAS	BB, RAS, CCB	BB RAS	RAS+BB CCB/DU <sup>^</sup>
DU, RAS or DU <sup>^</sup> +RAS	<140/90 <130/80 lacunar stroke	NR	RAS CCB, DU <sup>^</sup>	DU CCB RAS BB	RAS, DU <sup>^</sup> CCB	ACEIs+DU	RAS+CCB/DU <sup>^</sup> diuretic
BB RAS MRA	BB RAS MRA	DU BB RAS MRA	BB DU	RAS, DU, BB, MRA	DU <sup>^</sup> /loop DU BB RAS, MRA	RAS BB	RAS, BB and MRAs
NR	RAS+non-DHP CCB	NR	RAS CCB	RAS	RAS	RAS	RAS+CCB/DU <sup>^</sup>
RAS if albuminuria <sup>e</sup>	RAS+non-DHP CCB BP not to target DHP RAS	RAS	RAS DU <sup>^</sup> Non-DHP CCB	RAS	RAS loop DU	Any drug classes	RAS+CCB/DU <sup>^</sup>
		RAS	RAS DU CCB	RAS CCB	RAS Direct renin-Inhibitor	RAS CCB	DU, RAS CCB
RAS CCB BB DU+RAS	NR	NR	NR	NR	RAS	NR	NR
RAS CCB DU	DU CCBs	DU <sup>^</sup> CCB RAS	EAS, CCB, diuretic	CCB DU	NR	NR	DU CCB RAS

(Continues)

TABLE 4 (Continued)

	AHA/ACC 2017	ESC/ESH 2018	ISH 2020	CHL 2018	HK 2018	India 2019	Indo 2019	Japan 2019
HTN ≥80 year								
Time to reach control	NR	NR	NR	Yes	NR	No	Yes	Yes

Note: Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; Alb+ve, albuminuria present; Alb-ve, no albuminuria-; CCB, calcium channel blocker; DU, diuretic; DU<sup>^</sup>, thiazide-like diuretic; ESC/ESH, European Society of Cardiology/European Society of Hypertension; Hong K, Hong Kong; ISH, International Society of Hypertension; MRA, mineralocorticoid receptor antagonist; Msia, Malaysia; Non-DHP, non-dihydropyridine calcium channel blocker; NR, no recommendation; Protein+ve, proteinuria positive, Protein-ve proteinuria negative; RAS, renin-angiotensin system inhibitors [includes ACE (angiotensin-converting enzyme) and ARB (angiotensin receptor blocker).

<sup>\*</sup>Taiwan Focused update 2017.

<sup>a</sup>Recommends SBP 130 or lower if tolerated, but SBP not <120 and DBP 70–79.

<sup>b</sup><130/80 if tolerated.

<sup>c</sup>UAE-ve Albuminuria <30 mg/24 h, UAE+ve Albuminuria >30 mg/24 h.

<sup>d</sup>Pro Proteinuria <1Gm/24 h, Proteinuria >1Gm/24 h.

<sup>e</sup>For non-institutionalized ambulant community dwelling adults.

as 75 or 80 years. Furthermore, many clinical trials did not include patients older than 75 years, and if they did, it was patients who were already on anti-hypertensive treatment prior to entering into the study.

In their recommendations of treatment of hypertension in the elderly, the ESH categorizes the elderly as two separate groups, that is the “old” as those ≥65 years and “very old” as those aged ≥80 years. Drug therapy is recommended in the old and very old when the BP is ≥140/90 mmHg and ≥160/90 mmHg, respectively. However, although the BP treatment threshold is higher for the very old, the target BP is the same at 130–139/70–79 mmHg, if tolerated, for both the old and very old (Table 4).

The United States does not differentiate between the old and the very old, and their recommendation is a target of <130/80 mmHg, if tolerated, for anyone ≥65 years old.

The ISH like the Americans does not separate the elderly by different age groups but considers anyone aged ≥65 years as elderly. They are however more “conservative” than the Europeans and Americans as their BP target in anyone aged ≥65 years is higher at a BP of <140/80 mmHg.

Several of the Asian guidelines do differentiate between the “old” and the “very old” elderly but their recommended BP targets of <140/90 mmHg for the old and <150/90 mmHg for the very old are higher than that of the American and European's recommendation of <130/80 mmHg and 130–139/70–79 mmHg, respectively.

While several Asian guidelines do make recommendations of BP targets for those age ≥80 years, they actually did not make any specific recommendation for BP targets in those aged between 65–79 years. Presumably, their BP targets for those <80 years old would be the same as younger adults. On the other hand, several Asian guidelines while making recommendations of BP target for those aged ≥65 years do not make any specific recommendations in those

aged ≥80 years, perhaps implying that the target is the same as for those age 65–79 years (Table 4).

## 10 | CONCLUSION

In summary, the main differences between the guidelines are the new definition of hypertension where the United States is the only one recommending a lower diagnostic BP threshold of ≥130/80 mmHg. This leads to differences in treatment initiation and BP target of control. The main objective of the US guideline is to lower the burden of hypertension-related disease, and they are trying to do this by identifying at-risk individuals earlier with their lower BP levels for diagnosis of hypertension. On the other hand, the ESH and the Asian guidelines are more conservative and more focused on individuals and less on epidemiological issues. It would be interesting to see in the future which strategy will have a greater impact on the reduction of CV mortality and morbidity in a safe and cost-effective manner.

## CONFLICT OF INTEREST

S Hoshide has received research grants from Sanofi Co., Astellas Pharma Inc and Novartis Pharma KK. KK has received independent principal investigator-initiated research grants from Omron Healthcare Inc, Fukuda Denshi Inc, A&D Inc, Taisho Pharmaceutical Co. Inc, and Sanwa Kagaku Kenkyusho Co. Inc. YC Chia has received honorarium and sponsorship to attend conferences and seminars from Boehringer-Ingelheim, Pfizer, Omron, Servier and Xepa-Sol and an investigator-initiated research grant from Pfizer. CH Chen reports personal fees from Novartis, Sanofi, Daiichi Sankyo, SERVIER, Bayer, and Boehringer Ingelheim Pharmaceuticals, Inc. HM Cheng received speaker honorarium and sponsorship to attend conferences and CME seminars from Eli Lilly and AstraZeneca; Pfizer Inc; Bayer AG;

Korea 2018	Msia 2018	Pakistan 2018	Philippines 2018	Singapore 2017	Taiwan 2015, 2017*	Thailand 2019	Vietnam 2018
	DU RAS						
No	Yes	Yes	NR	NR	NR	NR	NR

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#### AUTHOR CONTRIBUTIONS

Yook-Chin Chia takes primary responsibility for this paper. Yook-Chin Chia wrote the manuscript. Yook-Chin Chia, Yuda Tura, Apichard Sukonthasarn, Yuqing Zhang, Jinho Shin, Hao-Min Cheng, Jam Chin Tay, Kelvin Tsoi, Saulat Siddique, Narsingh Verma, Peera Buranakitjaroen, Guru Prasad Sogunuru, Jennifer Nailes, Huynh Van Minh, Sungha Park, Boon Wee Teo, Chen-Huan Chen, Tzung-Dau Wang, Arieska Ann Soenarta, Satoshi Hoshide, Ji-Guang Wang and Kazoumi Kario contributed to the data about their own country. Yook-Chin Chia, Yuda Tura, Apichard Sukonthasarn, Yuqing Zhang, Jinho Shin, Hao-Min Cheng, Jam Chin Tay, Kelvin Tsoi, Saulat Siddique, Narsingh Verma, Peera Buranakitjaroen, Guru Prasad Sogunuru, Jennifer Nailes, Huynh Van Minh, Sungha Park, Boon Wee Teo, Chen-Huan Chen, Tzung-Dau Wang, Arieska Ann Soenarta, Satoshi Hoshide, Ji-Guang Wang and Kazoumi Kario read and approved the manuscript.

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