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REVIEW

WILEY

Seven-action approaches for the management of hypertension in Asia – The HOPE Asia network

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Abstract

Asia is a large continent and there is significant diversity between countries and regions. Over the last 30 years, absolute blood pressure (BP) levels in Asia have increased to a greater extent than those in other regions. In diverse Asia-Pacific populations, for choosing an Asia-specific approach to hypertension management is important to prevent target organ damage and cardiovascular diseases. In this consensus document of HOPE Asia Network, we introduce seven action approaches for management of hypertension in Asia.

1 | WHY IS AN ASIA-SPECIFIC APPROACH NEEDED?

Asia is a large continent and, along with Asia-specific features of hypertension, there is also significant diversity between countries and regions within the continent.[1,2] Over the last 30 years, absolute blood pressure (BP) levels in Asia have increased to a greater extent than those in other regions, such that these are amongst the highest in the world.[1] In addition, the proportion of individuals with hypertension who achieve BP control is relatively low in Asian countries/regions compared with the US, Canada and Europe.[3,4] Again, statistics for Asia are notable for their heterogeneity, with large variations in rates of hypertension awareness, treatment and control throughout the continent.[4–6] Potential explanation for this may be differences in genetic background, diet, lifestyle, and sociodemographic factors in the region,[7] where there are various factors that contribute to the development of hypertension and cardiovascular disease.[8]

In most Asian countries, common risk factors for hypertension include obesity, sedentary lifestyles, alcohol intake, higher socioeconomic status, high salt intake, diabetes mellitus, and smoking. Lower social class is also a risk factor for hypertension in Japan (and the Asia-Pacific countries of Australia, and New Zealand), while continued high smoking rates are an issue in China and several other Asian countries.[9]

Another important reason for choosing an Asia-specific approach to hypertension management is the differential impact of hypertension on target organ damage in diverse Asia-Pacific populations. The association between BP and cardiovascular disease has been shown to be stronger in East Asian individuals compared with those from Australia or New Zealand.[10] There was also higher prevalence of hypertension in stroke patients from South Asia compared with China in a population-based analysis.[11]

2 | CURRENT BP CONTROL STATUS IN ASIA

The Hypertension Cardiovascular Outcome Prevention and Evidence in Asia (HOPE Asia) Network's Asia BP@Home study investigated BP control status in eleven Asian countries/regions.[5] It was the first study of home BP control status to utilize the same home BP monitoring (HBPM) device and measurement protocol for all patients and study centers.[5] Overall, 53.6% of medicated patients with hypertension were well controlled for morning home systolic BP (SBP; < 130 mmHg – the 2017 AHA/ACC threshold[12]). However, there were marked differences in home BP control status between countries/regions; these were highest in the Philippines, Korea, Japan, Pakistan, Thailand, and Taiwan, and lowest in China and Indonesia.[5]

In a subanalysis of the Asia BP@Home study, both office and home heart rates in patients from South Asia were higher than those in other Asian countries (by ≥5 beats/min), even after controlling for demographics and beta-blocker use.[13] Given what is known about the impact of heart rate on heart disease, our findings suggest a possible benefit of regionally tailored clinical strategies for cardiovascular disease prevention, such as the use of beta-blockers.

TABLE 1 HOPE Asia Network: Seven action approaches for the management of hypertension in Asia

1	Strict reduction of sodium intake
2	Strict BP control
3	Home BP-guided management
4	Reducing morning home BP as the first target and nighttime BP as the second target for high-risk patients
5	Choice of preferred antihypertensive agents
6	Widespread screening to improve awareness
7	Use of telemedicine strategies

Abbreviation: BP, blood pressure.

Comparing the ambulatory BP monitoring (ABPM) data from Japan and Thailand also shows significant between country differences in the BP profile.[14] Even when office BP was comparable, a non-dipper/riser pattern of nighttime BP was more common in patients from Thailand, while morning BP surge was higher in those from Japan. Furthermore, even within the same county, there were rural and urban disparities in BP control status in Asia, partly due to the differences in the uptake of a western diet and lifestyle.[14]

3 | THE HOPE ASIA NETWORK

The HOPE Asia Network was set up to improve the management of hypertension in Asia with the goal of achieving "zero" cardiovascular events in the region.[15] Asian evidence and guidelines have been discussed by Network members to reach consensus on key topics such as target BP level, practical application of HBPM and ABPM, salt intake and preferred antihypertensive medications, among others, resulting in the publication of a number of consensus documents and Asia-specific recommendations that cover nearly all major topics relating to the management of hypertension.[15–20] These documents should contribute to optimizing individual and population-based hypertension management strategies in Asian countries/regions.[20]

The HOPE Asia Network model is an excellent example of how interpretation, modification, and dissemination of international best practices at a regional level, in collaboration with local hypertension societies, can be used to benefit specific populations. The HOPE Asia Network was officially established in June 2018 and includes experts from twelve countries/regions across Asia. It is endorsed by the World Hypertension League, and is an affiliated organization of the International Society of Hypertension.[15]

Hypertension management, and mitigation of the negative cardiovascular effects of hypertension, is being addressed by local hypertension societies in Asia. There are several strategies likely to be effective in managing hypertension in Asia based on the local characteristics of the disease. Widespread salt restriction and population-level implementation of HBPM are key approaches. These, and an additional five strategies focusing on the Asia-specific management of hypertension, are detailed below (Table 1 and Figure 1).

4 | THE HOPE ASIA NETWORK: SEVEN ACTION APPROACHES FOR HYPERTENSION MANAGEMENT IN ASIA

4.1 | Strict reduction of sodium intake

High salt intake compared with other populations[21] and a genetic predisposition to salt sensitivity[22] are likely to be key factors that drive hypertension and the BP profile in the Asian region. Salt intake in Asia exceeds that recommended by the World Health Organization (WHO; < 5 g/day).[23] For example, the average salt intake for adults is 15.3 g/day in Vietnam, 12–14 g/day in China, 11.6 g/day in Korea, 10.4 g/day in Japan, 10.8 g/day in Thailand, and 7.2 g/day in Malaysia.[24,25]

Data from studies involving 49 countries demonstrated that there is a U-shape relationship between salt consumption and cardiovascular events.[26] In patients with hypertension, sodium intake of > 6 g/day is associated with higher risk of cardiovascular disease and death.[26] In addition, a nationwide study conducted in Japan showed that higher household salt intake was associated with long-term all-cause and cardiovascular mortality.[27]

In 2017, WHO designated "sodium intake reduction" as a "best buy" to avoid premature deaths and reduce the economic impact of noncommunicable diseases in low- and middle-income countries.[28] Most successful programs include multi-component strategies.

One simple and effective way to reduce salt intake is the complete or partial substitution of sodium chloride with potassium chloride. There is a good body of evidence, including that from the Salt Substitute and Stroke Study (SSaSS) study conducted in China and a study in rural India, showing the beneficial effects of reducing salt intake on BP and cardiovascular disease event rates.[29,30] Furthermore, a digital therapeutic strategy designed to facilitate lifestyle modifications, including salt restriction and body weight reduction, successfully reduced home and ambulatory BP in patients with hypertension.[31]

There are also many national-level programs in Asia designed to reduce population salt intake. These include the Chinese government's "Healthy Lifestyle for All" program (as part of China's health development agenda),[32] and a series of effective salt reduction programs that were created and implemented nationwide by Action on Salt China (ASC), a unit funded by National Institute of Health Research.[32] In addition, significant reduction in sodium intake in both children and adults was achieved through the School-based Education Program to Reduce Salt Intake in Children and Their Families (School-EduSalt).[33] In 2005, the Japanese Society of Hypertension (JSH) set up a Salt Reduction Committee to promote the reduction of population salt consumption, and in 2019 JSH announced the "Tokyo Declaration in Promotion of Salt Reduction," which included six strategies to achieve a target salt intake of < 6 g/day.[34] This was followed by The Okinawa Declaration on the unity of hypertension societies in Asian countries and regions to overcome hypertension and hypertension-related diseases, which was announced in 2021.[6]

The National Health and Nutrition Survey of Japan provides an indication of the impact of these programs. The data showed that sodium

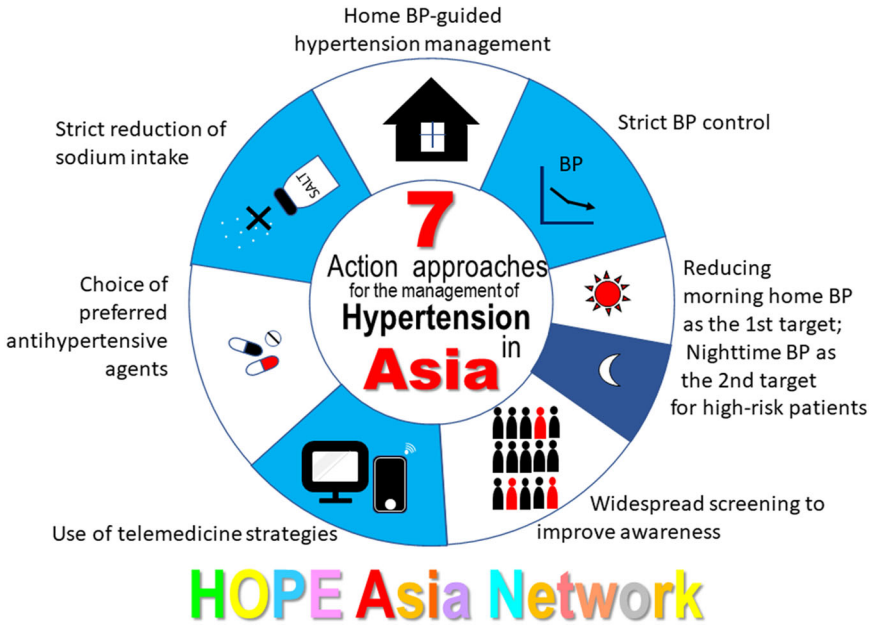

FIGURE 1 Seven action approaches for the management of hypertension in Asia – The HOPE Asia Network

intake gradually decreased between 2005 and 2018, from 12.4 to 11.0 g/day in men and from 10.7 to 9.3 g/day in women. In addition, the number of men with hypertension being treated with antihypertensives increased from 53.5% in 2000 to 66.9% in 2016, and the average SBP in these patients decreased from 147.1 to 140.2 mmHg.[35] In parallel with the improvement in BP control, there was a 17.5% decrease in stroke deaths (from 132 529 in 2000 to 109 320 in 2016).

A higher urinary sodium-to-potassium (Na/K) ratio has been reported to be associated with high BP and subsequent cardiovascular events.[36] A urinary Na/K molar ratio of < 1 may be a useful indicator for adherence to the WHO-recommended levels of sodium.[37]

Another important determinant of salt sensitivity is obesity, and Asian individuals can develop hypertension even when there is only a small increase in the body mass index (BMI).[38] In addition, the risk of prehypertension and hypertension develops at a lower BMI threshold than in Westerners (25 vs 30 kg/m^2).[38] Thus, body weight control, especially in younger and middle-aged adults, is important for Asians.

4.2 | Strict BP control

Previous studies have shown that the slope of the association between BP and cardiovascular events is steeper in Asians than Westerners.[39] Data from the recent STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) trial, conducted in China, showed that strict BP control (SBP 110–130 mmHg) was superior to standard BP control (SBP 130–150 mmHg) for preventing cardiovascular events.[40] The findings of this study are relevant for hypertension management in Asia,[41–43] and suggest that elderly Asians would benefit from strict BP control to reduce cardiovascular risk.

A recent Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) meta-analysis, which includes data from the Systolic Blood Pressure Intervention Trial (SPRINT), has been released.[44] The results showed that a 5-mmHg reduction in office SBP reduced the risk of total cardiovascular disease by 10%, the risk of stroke and heart failure by 13%, and the risk of coronary artery disease by 8%.[44] In addition, these benefits of BP lowering were seen in individuals aged up to 85 years.[45] In the STEP study, a 5-mmHg reduction in office SBP was associated with an 18% reduction in total cardiovascular disease risk, a 23% reduction in the risk of stroke and coronary artery disease, and a 58% reduction in heart failure risk. These findings showing greater reductions in cardiovascular risk in the STEP study than in SPRINT and the BPLTTC (Table 2), suggest that strict BP control is probably more effective for cardiovascular disease prevention in Asians than in Westerners.

4.3 | Home BP-guided hypertension management

Individuals with masked hypertension or poorly controlled hypertension are at increased risk of target organ damage and cardiovascular disease.[19,38,46] Masked hypertension is more prevalent in Asia than in Western countries due to higher rates of abnormal patterns of BP variability, including exaggerated early morning BP surge and non-dipper/riser phenotypes of nocturnal BP.[47]

Three prospective observational studies conducted in Asia (Ohasama, J-HOP [Japan Morning Surge Home Blood Pressure], and HONEST [Home blood pressure measurement with Olmesartan Naive patients to Establish Standard Target blood pressure]) showed that morning hypertension detected using HBPM is associated with a higher risk of cardiovascular disease, regardless of office BP.[48] In addition to the average home BP, day-to-day variability in home BP is associated with cardiovascular disease risk, especially in those with increased arterial stiffness.[49–52] A recent analysis of data from the

TABLE 2 Estimated cardiovascular risk reduction in the STEP and SPRINT studies, and the BPLTTC meta-analysis

	Percentage reduction associated with a 5-mmHg reduction in office SBP				
			BPLTTC		
	STEP	SPRINT	Total	Age 65–74 years	Age 75–84 years
Outcomes					
Stroke	−23	−4	−13	−10	−8
CAD	−23	−11	−8	−7	−9
HF	−58	−15	−13	−14	−18
CVD[a]	−18	−11	−10	−9	−9

Abbreviations: BPLTTC, Blood Pressure Lowering Treatment Trialists' Collaboration; CAD, coronary artery disease (myocardial infarction/acute coronary syndrome); CVD, cardiovascular disease; HF, heart failure; SPRINT, Systolic Blood Pressure Intervention Trial; STEP, Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients.

[a]Definition of CVD are as follows: STEP: a composite of stroke (ischemic or hemorrhagic), acute coronary syndrome (acute myocardial infarction and hospitalization for unstable angina), acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes. SPRINT: a composite of myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes. BPLTTC: a composite of fatal or non-fatal stroke, fatal or non-fatal myocardial infarction or ischemic heart disease, or heart failure causing death or requiring admission to hospital.

J-HOP study demonstrated that greater morning-evening difference in home SBP (especially ≥20 mmHg),[53] and peak home SBP over 14 days were associated with cardiovascular disease.[54]

Thus, identifying and treating masked hypertension phenotypes seems particularly important for cardiovascular risk reduction in Asian populations. This can be facilitated by the use of HBPM. However, current usage of this important tool varies across Asia.[16] Although HBPM devices are practical to use and affordable, but in the real world they are usually ignored even many patients got one of their own. Therefore, strategies are needed to improve HBPM usage, and there are local guidelines to increase utilization and support the correct usage of HBPM in Asia.[19,55] Region-wide differences in hypertension prevalence, control, and management practices in Asia highlight the importance of information sharing to facilitate best practices while taking relevant regional aspects into account.

Development of HBPM devices capable of measuring nocturnal BP along with other information and communication technology-based strategies are key developments in the widespread implementation of anticipation medicine strategies to detect and prevent cardiovascular events in patients with hypertension.[38]

4.4 | Reducing morning home BP as the first target and nighttime BP as the second target for high-risk patients

Reducing morning home BP and nighttime BP are actionable targets that could help to improve BP control in the Asian region. Morning BP just before antihypertensive dosing is important because this is when the BP-lowering effects of the previous morning's dose are at their lowest. Morning BP surge is greater in Japanese versus Western patients with hypertension.[56]

Based on data obtained using wearable BP monitoring devices, morning SBP measured in accordance with guideline recommendations was most closely associated with left ventricular mass measured using cardiac magnetic resonance imaging in medicated patients with hypertension.[57] In addition, in the J-HOP Study, high morning SBP measured by using HBPM (especially SBP ≥135 mmHg) was stronger predictor of stroke than evening BP measured just before going to bed.[49] For high-risk patients with a history of stroke or diabetes, the pathological SBP threshold is lower, at about 125 mmHg.[58,59]

Another important feature of hypertension in Asian populations is high nighttime BP, which is commonly associated with high salt sensitivity and salt intake. Nocturnal hypertension, including isolated nocturnal hypertension with well-controlled office and/or morning BP, is a risk factor for organ damage and cardiovascular disease even.[60–63] Nocturnal hypertension is often found in high-risk patients with comorbidities such as diabetes, chronic kidney disease and sleep apnea.[64,65] Furthermore, high nighttime BP, especially the riser pattern of nocturnal BP, is a risk factor for the development of heart failure,[64,66] and partly explains the higher B-type natriuretic peptide seen in hypertensive patients.[67] Another important consideration is sleep duration, which should be ≥6 hours, with control of nighttime BP, to reduce the risk of cardiovascular disease.[68]

In cases where the patient's BP is uncertain or labile, or where there is nonadherence to HBPM, 24-hour ABPM is recommended for confirming the level of BP control.[18] Nocturnal HBPM devices are also clinically available.[60,63] In addition, wrist-type nocturnal HBPM devices that cause less sleep disturbance have now been validated and are available for use in clinical practice.[69,70] Thus, both ABPM and nocturnal HBPM are useful to detect nocturnal hypertension, especially in high-risk patients.[71–73]

Seasonal changes in BP and vascular properties, especially home BP control status in relation to room temperature also need to be considered.[74–82] Morning BP increases to a greater extent in the winter (colder temperatures) and is associated with organ damage, while nighttime BP is increased in the summer (warmer temperatures).[81] Compared with evening home BP, morning home BP might be a better

predictor of winter-onset cardiovascular events,[83] and the winter morning BP surge partly explains the increased risk of cardiovascular events in the winter.[84] Therefore, BP surges during winter should be an important target of a home BP-guided approach to hypertension management.

4.5 | Choice of preferred antihypertensive agents

Preferred antihypertensive agents for Asian patients with hypertension are calcium channel blockers (CCBs, which have a sodium-independent BP-lowering effect),[85] renin-angiotensin system (RAS) inhibitors, and sodium-excreting agents (eg, diuretics). For strict BP control without decreasing drug adherence, single-pill combinations are preferred, where feasible.

CCBs are the most popular antihypertensive drugs in Asia. They have powerful dose-dependent and salt intake-independent BP-lowering effects and reduce BP variability, making them ideally suited as first-line therapy in Asian populations.[85] In addition, sodium-excreting drugs such as diuretics should be effective in Asians, who have high salt intake and salt sensitivity. Lower serum potassium levels are also seen in patients from some of Asian countries, meaning that thiazide-like diuretics excrete potassium. Mineralocorticoid receptor (MR) blockers reduce potassium excrete and hence increase serum potassium, and the recently developed selective MR blocker, esaxerenone, has been shown to reduce nighttime and morning BP, and decrease levels of N-terminal pro B-type natriuretic peptide (NT-proBNP).[86–89] Other sodium-excerting drugs such as angiotensin receptor-neprilysin inhibitors (ARNI) and sodium-glucose co-transporter 2 (SGLT2) inhibitors, both of which are proven therapies for heart failure, are also effective in lowering BP.[90–97] SGLT2 inhibitors also decrease 24-hour BP in patients who have both diabetes and hypertension.[98–101]ARNI have recently been launched for the treatment of hypertension in Japan and China. The BP-lowering effects of ARNI are greater in Asians than in Westerners,[91,102] highlighting the potential of these agents in Asian populations. However, availability and cost of these drugs are main obstacles for general use.

4.6 | Widespread screening to improve awareness

Rates of hypertension awareness in some Asian countries/regions are low, meaning that strategies such as screening for hypertension in public places (eg, the workplace or COVID-19 vaccination centers), and self-measurement of BP using HBPM at home and/or at work might be useful.[103–105] As part of the May Measurement Month initiative, BP was measured in millions of people in several Asian countries/regions.[106] The prevalence of hypertension in screened populations was found to be 30.6% in East Asia and 47.8% in South-East Asia and Australasia; corresponding hypertension awareness rates were 59.0% and 66.5%.[106] Of patients with hypertension in Asia Pacific, only 16.8% to 28.6% were being treated with antihypertensive medication. Of those treated, more than one-third (33.4% in East Asia and 36.8% in South-East Asia and Australasia) had uncontrolled BP.[106] This reinforces the need for effective strategies to both diagnose and treat hypertension in the region.

4.7 | Use of telemedicine strategies

The COVID-19 pandemic has increased the use of telemedicine strategies and means that telemedicine has become an increasingly popular and important option in Asia to ensure patient and physician safety and facilitate infection control.[107–109] A wearable BP monitoring device has been developed and validated,[110] and there is also an ABPM technology platform to facilitate diagnostic and treatment decisions without the need for an office visit.[108] In addition, telemedicine represents a useful approach to help deliver effective care to patients with hypertension, regardless of their location, in terms of monitoring BP, improving uptake of lifestyle recommendations and increasing medication adherence, all of which help to optimize disease management.[111]

In the STEP trial, the study participants and physicians used the smartphone-based Hypertension Doctor App platform.[40] This app is designed to help patients adhere to antihypertensive medication and monitor BP using several modules, including a link with medication records and the antihypertensive treatment plan, graphic data of home BP during follow-up, interactive communications between patients and physicians, and cardiovascular health education. Digital hypertension management appears to contribute to sustained reductions in office and home BP, and has the potential to provide additional insights into disease pathophysiology and therapeutic targets, and contribute to personalized medicine strategies in hypertension.[112] Digital therapeutics is another area showing promise for the management of patients with hypertension. The recent randomized controlled HERB Digital Hypertension 1 (HERB DH1) pivotal study investigated the use of the HERB system, which facilitates individual lifestyle modifications on six guideline-recommended components (decrease salt intake, body weight control, regular exercise, better sleep, stress management, and moderating alcohol intake). The results showed significant reductions in both 24-hour ambulatory BP and morning home SBP in patients managed using the HERB system.[99]

Compared with specialist physicians, non-specialists are less likely to provide adequate guidance on lifestyle modifications,[113] possibly due to their uncertainty in understanding treatment guideline recommendations. In addition, there are significant gaps between physician and patient perspectives on hypertension management.[114] Compared with physicians, patients had a lower perception of the amount of education provided on hypertension management by their physicians. In addition to effective regular follow-up regarding lifestyle modifications, patient motivation by physicians is an important factor in improving implementation of lifestyle modifications and achieving effective hypertension management. Digital therapeutics provides a practical solution to bridge gaps in hypertension management.

5 | OTHER CONSIDERATIONS

5.1 | Renal denervation

Resistant hypertension, defined based on HBPM or ABPM, is a significant risk for cardiovascular disease, including heart failure.[115,116] Renal denervation (RDN) is an alternative approach to treatment for patients with resistant hypertension that has potential in Asian populations.[117–121] One of the benefits of RDN is a sustained reduction in BP, and this can be used as an adjunct or alternative to antihypertensive drug therapy and/or digital therapeutics-guided lifestyle modifications. The optimal approach for each patient will best be determined based on a shared decision-making process based on patient preference and evidence-based recommendations from their physician.

There is a growing body of clinical evidence to support decisions about whether to use RDN. In terms of evidence from Asia, the REnal denervation on Quality of 24-hour BP control by Ultrasound In REsistant hypertension (REQUIRE) trial did not find any difference between the RDN and sham control group in the primary endpoint of 24-hour SBP at 3-month follow-up after ultrasound RDN.[122] However, there were a number of potential reasons that contributed to these findings. For example, increased awareness of high BP may change adherence to medication or lifestyle modifications after randomization, especially in the control group. In the REQUIRE trial, the difference in home SBP was greater in the RDN versus control group at 1-month follow-up but this difference disappeared at 3 months due to a progressive reduction in BP in the sham group.

Data from a recent meta-analysis including data from nine sham-controlled trials, including the REQUIRE study, found that RDN significantly reduced 24-hour SBP by 3.3 mmHg, daytime SBP by 3.5 mmHg, nighttime SBP by 3.2 mmHg, and office SBP by 5.3 mmHg compared with control.[123] There were no significant differences in the 24-hour BP-lowering effects of RDN between patients who were versus were not receiving antihypertensive medication, or between radiofrequency and ultrasound RDN devices.[123] However, in certain cases whose BP could not be controlled in spite of receiving a huge amount of antihypertensive drugs, RDN can be considered.

5.2 | Perfect 24-hour BP control

Early achievement and maintenance of 24-hour BP control includes three components: strict lowering of 24-hour BP; maintaining the dipper pattern of nocturnal BP; and maintenance of optimal BP variability. These are essential to reduce and prevent hypertension-related target organ damage and associated diseases throughout the lifespan.[38] To facilitate the achievement of this goal, research and development of wearable BP monitoring devices is needed.[124] In the first study to compare BP values measured using a recently developed wrist-worn watch-type oscillometric BP monitoring (WBPM) device with those obtained using traditional ABPM, between-device differences in both office and out-of-office BP were acceptable.[110] In addition, BP measured using a wearable device has been shown to correlate with left ventricular mass.[57] The larger number of BP measurements provided by a wearable device could detect individual peak BP, and might add to the clinical value of these measurements, thus complementing guideline-recommended HBPM. "Cuff-less" approaches to BP monitoring are ideal, but this technology needs further evaluation for measurement of absolute BP before it can be used in clinical practice.

6 | PERSPECTIVES

The benefits of effective BP lowering are greater in Asians than in Westerners. Therefore, antihypertensive strategies and action plans that take into account Asian characteristics should be shared and developed within and across the different and heterogeneous countries/regions in Asia. We hope that these seven action approaches from the HOPE Asia Network contribute to achieving the goal of "zero" cardiovascular events in Asia.

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CONFLICTS OF INTEREST

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