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Current status of adherence interventions in hypertension management in Asian countries: A report from the HOPE Asia Network

Jinho Shin MD[1] | Yook-Chin Chia MBBS, FRCP[2,3] | Ran Heo MD, PhD[1] | Kazuomi Kario MD, PhD[4] | Yuda Turana MD, PhD[5] | Chen-Huan Chen MD[6] | Satoshi Hoshide MD, PhD[4] | Takeshi Fujiwara MD, PhD[4] | Michiaki Nagai MD, PhD[7] | Saulat Siddique MBBS, MRCP, (UK), FRCP, (Lon)[8] | Jorge Sison MD[9] | Jam Chin Tay MBBS, FAMS[10] | Tzung-Dau Wang MD, PhD[11] | Sungha Park MD, PhD[12] | Guru Prasad Sogunuru MD, DM[13,14] | Huynh Van Minh MD, PhD[15] | Yan Li MD, PhD[16]

[1]Division of Cardiology, Department of Internal Medicine, Hanyang University Medical Center, Seoul, South Korea

[2]Department of Medical Sciences, School of Healthcare and Medical Sciences, Sunway University, Bandar Sunway, Malaysia

[3]Department of Primary Care Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

[4]Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, Tochigi, Japan

[5]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

[6]Institute of Public Health and Community Medicine Research Center, National Yang-Ming University School of Medicine, Taipei, Taiwan

[7]Department of Internal Medicine, General Medicine and Cardiology, Hiroshima City Asa Hospital, Hiroshima, Japan

[8]Punjab Medical Center, Lahore, Pakistan

[9]Cardiology Section, Department of Medicine, Medical Center Manila, Manila, Philippines

[10]Department of General Medicine, Tan Tock Seng Hospital, Singapore, Singapore

[11]Department of Internal Medicine, National Taiwan University College of Medicine, Taipei City, Taiwan

[12]Division of Cardiology Seoul, Cardiovascular Hospital, Yonsei Health System, Seoul, South Korea

[13]MIOT International Hospital Chennai, Chennai, India

[14]College of Medical Sciences Bharatpur, Kathmandu University, Dhulikhel, Nepal

[15]Department of Internal Medicine, University of Medicine and Pharmacy, Hue University, Hue City, Vietnam

[16]Department of Hypertension, The Shanghai Institute of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

Correspondence
Jinho Shin, Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, 222 Wangsimni-ro Sungdong-gu, Seoul,

Abstract

Adherence continues to be the major hurdle in hypertension management. Since the early 2000s, systematic approaches have been emphasized to tackle multi-dimensional issues specific for each regional setting. However, there is little data regarding implementation of adherence interventions in Asian countries. Eleven hypertension experts from eight Asian countries answered questionnaires regarding the use of adherence interventions according to 11 theoretical domain frameworks by Allemann et al. A four-point Likert scale: Often, Sometimes, Seldom, and Never used was administered. Responses to 97 items from 11 domains excluding three irrelevant items were

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04763, South Korea.
Email: jhs2003@hanyang.ac.kr

Kazuomi Kario, Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan.
Email: kkario@jichi.ac.jp

collected. "Often-used" interventions accounted for 5/9 for education, 1/8 for skills, 1/2 for social/professional role and identity, 1/1 for belief about capabilities, 0/3 for belief about consequences, 2/4 for intentions, 2/9 for memory, attention, and decision process, 11/20 for environmental context and resources, 0/2 for social influences, 0/2 for emotion, and 2/2 for behavioral regulation. Most of them are dependent on conventional resources. Most of "Never used" intervention were the adherence interventions related to multidisciplinary subspecialties or formal training for behavioral therapy. For adherence interventions recommended by 2018 ESC/ESH hypertension guidelines, only 1 in 7 patient level interventions was "Often used." In conclusion, conventional or physician level interventions such as education, counseling, and prescription have been well implemented but multidisciplinary interventions and patient or health system level interventions are in need of better implementation in Asian countries.

1 | INTRODUCTION

Hypertension is the most important controllable risk factor for cardiovascular events and mortality in the world.[1] There has been a progress in pharmacologic therapy to control blood pressure under the target level. Even in true resistant hypertension, the prevalence of refractory hypertension in response to maximal antihypertensive drug therapy has been reported to be low and around 5%.[2,3] However, in spite of efficacious, affordable, and available antihypertensive agents, overall control of hypertension in the general population is less than 60%, and this is seen even in developed countries.[4] With recent increase in the prevalence of hypertension in Asian countries due to Westernization, modernization, and urbanization, control of hypertension become a major public health challenge.[5] As shown in Table 1, in Asian countries, prevalence of hypertension varied widely from 20.8% in Taiwan to 50% in Pakistan. Awareness rate, treatment rate, and control rate among all hypertensives also ranged widely, from 30% to 73%, from 18% to 71%, and from 6% to 49.6%, respectively.[4,6,7] Even among subjects who were aware of their hypertension status, treatment and control rate also varied widely, from 60% to 96% and from 33% to 83%, respectively.[8–11] The level of adherence may be one of the reasons for this wide range of variation in the control rates among the different Asian countries.

Moreover, poor adherence or compliance in hypertension has been a major hurdle, not only for taking medicine but also failure to make lifestyle changes partly because of the asymptomatic nature of hypertension and the necessity of life-long treatment.[12] The report from the World Health Organization (WHO) as well as recent hypertension guidelines to address the adherence problem recommending systematic and patient-centered approaches has presented multi-dimensional challenges.[12] It is also unknown to what degree the guidelines for adherence has been implemented in real clinical practices in Asian countries.

There have been many attempts at interventions to improve adherence in hypertension management.[13] In general, there are five domains in adherence management suggested by the WHO: social- and economic-related factors, health system/healthcare team-related factors, therapy-related factors, condition-related factors, and patient-related factors.[12] In the 2018, European Society of Cardiology and European Society of Hypertension (ESC/ESH) hypertension guidelines for adherence interventions in hypertension management were categorized as physician level, patient level, drug treatment level, and health system level.[13] Even though there have been attempts to categorize adherence interventions, none has been widely accepted. Moreover, the conceptualization of some interventions spans cognitive and/or behavioral theories, which makes it difficult for a clinician to understand the quality or clinical standard behind the terminology.[13] Among several attempts to at categorize adherence interventions, the Theoretical Domain Framework (TDF) was developed to integrate the various behavioral change theories. It was also meant to simplify the evaluation of behavioral problems or to facilitate the intervention of behavioral problems such as adherence reporting of 14 domains: 1. knowledge, 2. skills, 3. social/professional role and identity (SPRI), 4. beliefs about capabilities, 5. optimism, 6. beliefs about consequences, 7. reinforcement, 8. intentions, 9. goals, 10. memory, attention and decision processes (MADP), 11. environmental context and resources (ECR), 12. social influences, 13. emotions, and 14. behavioral regulation.[14] Recently, Allemann et al. reviewed 103 interventions for 42 determinants (26 modifiable and 16 non-modifiable) and matched these interventions with 25 modifiable determinants generating 11 TDFs excluding three non-matched domains (optimism, reinforcement, and goal).[15] Hence, each intervention targets one of the modifiable determinants of adherence. This framework seems to be useful for a clinician to intuitively understand the concept of behavioral approaches and to develop an intervention in trials to investigate the effectiveness of adherence interventions.[15]

In this report, the authors carried out a survey using a questionnaire sorted by the 11 theoretical domains ("knowledge," "skills," "SPRI," "beliefs about capabilities," "beliefs about consequences," "intentions," "MADP," "ECR, "social influences," "emotions," and "behavioral regulation") of adherence interventions among hypertension experts in Asian countries participating in Hypertension

TABLE 1 Current status of hypertension management in Asian countries including treatment rate among patients with awareness and control rate in treated patients

		Among all hypertension subjects				
	Prevalence	Awareness rate	Treatment rate	Control rate	Treatment rate among patients with awareness	Control rate among the treated
China	28	47	41	15	87	38
India urban	33	42	38	25	90	66
Indonesia	34	37	30	25	81	83
Japan	42	65[a]	55	41	88	73
Korea	29	65	61	44	94	72
Malaysia[b]	35	38	31	12	83	37
Pakistan	50	30	18	6	60	33
Phillippines	28	91	56	20	62	36
Singapore[c]	24	74	71	50	96	70
Taiwan	21	72	64	39	89	61
Thailand	25	55	49	30	89	61
Vietnam	25	50	31	12	62	39

Note: All values in percent.

[a]Adopted from the reference[4];

[b]age 18 year or older;

[c]calculated from National survey data.[7]

Cardiovascular Outcome Prevention and Evidence in Asia (HOPE Asia) Network to investigate the current status of the availability of the adherence interventions as recommended in hypertension guidelines.

2 | METHODS AND MATERIALS

2.1 | Recruitment of expert panels

Recruitment of the expert panel was done by an e-mail announcements to 25 expert clinicians in hypertension from 12 countries in Asia who were participated in HOPE Asia Network. All of the panel members were informed of the matching interventions in the 11 TDF which corresponded with 26 modifiable determinants.[15]

Study protocol was submitted to Institutional Review Board (IRB) in Hanyang University Seoul Hospital (IRB File No. 2020-10-009) and "IRB review exemption" was acquired.

2.2 | Questionnaire for the current status of adherence interventions

Among the original 11 TDF domains, by excluding only three items in the ECR domain because of non-relevance in hypertension clinics, 97 items for 61 interventions were selected (20 items for 9 interventions in the "knowledge" domain, 8 items for 8 interventions in the "skills" domain, 5 items for 2 interventions in the "SPRI" domain, 1 item for 1 intervention in the "belief about capabilities" domain, 7 items for 3 interventions in the "belief about consequences" domain, 7 items for 4 interventions in the "intentions" domain, 16 items for 9 interventions in the MADP domain, 25 items for 19 interventions in the 4 subdomains (regimen, adverse events, integration and coordination of care, and financial aspects) for the "ECR" domain, 3 items for 2 interventions in the "social influences" domain, 2 items for 2 interventions in the "emotion" domain, and 3 items for 2 interventions in the "behavioral regulation" domain).

The key questions were "Are the following interventions on adherence regarding pharmacologic or non-pharmacologic management of hypertension used in your practice or in your country?" Panelists were supposed to choose one response among the four-point Likert scale of "Often," "Sometimes," "Seldom," or "Never." Responses on the availability of an adherence intervention in a country depended on the perception of the current status of the availability of adherence interventions in each country.

2.3 | Statistical analyses

The responses were represented by the mode among the Likert scale. For the Japanese data, the mode value among the four panelists was used to represent Japan. Because of the small number of respondents, the higher scale was chosen when it was of an adjacent bimodal distribution, and rounded median (4 for "Often," 3 for "Sometimes," 2 for "Seldom," and 1 for "Never") was chosen when multimodal values were more than one scale apart.

For testing the difference between the availability of adherence interventions in the clinic of the expert panel member and that in

each country, a dependent 2-group, exact Wilcoxon signed rank test was performed. The data were analyzed using R version 3.6.1 with the "coin" package. A p value of < .05 was considered to be statistically significant.

3 | RESULTS

3.1 | Panel members recruited

We recruited 11 expert clinicians in hypertension management from 8 countries/regions comprising one expert per country/region except for Japan where there were 4 experts: China (YL), Indonesia (YT), Japan (MN, TF, SH, and KK), Korea (JS), Malaysia (YCC), Pakistan (SS), the Philippines (JS), and Taiwan (CHC). The mean duration of career was 25 years (12 to 40). There were nine specialists in cardiology, one in neurology, and one in primary care internal medicine. The subspecialties consisted of six in hypertension, one in neurogeriatrics, one in interventional cardiology, one in echocardiology, and two in general cardiology. The modes of practice were public versus private (9 vs. 2), referral versus primary (9 vs. 2), and university versus non-university setting (8 vs. 3).

3.2 | Often-used adherence interventions

Among the 97 items for the 61 adherence interventions (Appendix Table S1), 26 items for 22 interventions (26.8%) were used often (Table 2). Often-used interventions were observed in 3/9 (33.3%) items of the knowledge domain, 1/8 of the skills domain, 3/5 of the SPRI domain, 1/1 of the beliefs about capabilities domain, none of (0/7) the belief about consequences domain, 4/7 of the intentions domain, 3/16 of the MADP domain, 16/25 of the ECR domain, none in the social influences and emotion domain, and 3/3 in the behavioral regulation domain. As shown in Figure 1, discussion and counseling about disease and health, discussion and counseling about treatment, and adequate labeling were "Often" used in the knowledge domain (Figure 1, panel A). Easy-to-use packaging was the only "Often" used intervention in the skill domain (Figure 1, panel B). Improvement of relationship and customer involvement, patient empowerment, counseling about lifestyle, and action plans were "Often" used interventions in SRI, beliefs about capabilities, and intention domains, respectively (Figure 1, panel C). Regimen with counseling and integration and coordination of care were the overall "Often" used subdomains in the ECR domain, and behavioral self-monitoring was also "Often" used (Figure 1, panel D).

3.3 | Never-used adherence interventions

Among the 97 items for 61 adherence interventions, 19 items for 14 interventions (14.4%) were never used (Table 3). Motivational interviewing was "Never" used in contrast with empowerment of patient, which was "Often" used. Recently developed reminder or cognitive tools were not adopted yet. Home visit, social support program, mass mailing, and internet-based support programs were not yet available or used.

3.4 | Adherence interventions recommended in the 2018 ESC/ESH hypertension guidelines

As shown in Table 4, among the 6 physician level recommendations in the 2018 ESC/ESH hypertension guidelines, 8 corresponding interventions, at least one for each recommendation, were "Often" used, but programmed learning, computer-aided counseling, and motivational interviewing were "Never" used. As for the seven patient level recommendations, self- monitoring of blood pressure was the only "Often" used intervention. The three corresponding interventions for group sessions, instruction combined with motivational strategies, and use of reminders were "Never" used. The others were "Sometimes" or "Seldom" used. For the two recommendations at drug treatment level, a drug regimen simplification or single-pill combination therapy was "Often" used but reminder packaging was "Never" used. For the five recommendations at health system level, the corresponding intervention for development of a monitoring system was "Never" used and for the others, there were no corresponding questionnaire responses.

3.5 | Perception of country level adherence intervention

Among the 9 panelists from 7 countries (except HS and CHC) summiting the perception about adherence intervention at the country level, four panelists perceived that institutional adherence interventions were better than country level interventions, and one panelist perceived that institutional adherence interventions were inferior to the country level interventions. Two panelists perceived that there were no significant differences (Table 5).

4 | DISCUSSION

Using the 97 items on the 61 adherence interventions categorized in 11 theoretical domain frameworks which were matched with 26 modifiable determinants of adherence, we surveyed the use of each intervention from the 11 panelists from eight countries in Asia. First of all, most of the "Often" used interventions were conventional and physician dependent approaches such as education, discussion, counseling, improving the relationship using patient-centeredness and doctor-patient co-operation, and empowerment of patients. For MADP domains, a conventional appointment was the only "Often" used reminder. Most of the physician level interventions recommended by the 2018 ESC/ESH hypertension guidelines were also "Often" used. In particular, recommendations for a regimen of antihypertensive drugs seem to have been very well implemented.

TABLE 2 Summary of "Often" used adherence interventions according to the 11 theoretical domain framework categories in Asian countries

Domains	Subdomains	Interventions
1. Knowledge		Education
		Provide medication charts/fact sheets
		Provide visual, verbal, written materials
		Adequate labeling about therapy
		Counsel, give advice about treatment
2. Skills		Easy-to-use packaging
3. Social/professional role and identity		Improve relationship, consumer involvement
		Encouraging doctor-patient co-operation
		Patient-centeredness
		Accurate recognition of the patient's problem by the health care provider
4. Belief about capabilities		Patient empowerment
5. Belief about consequences		Discuss
		Adherence
6. Intentions		Counseling about lifestyles
		Diet
		Exercise
		Smoking
		Action plans
7. Memory, attention, and decision process		Reminders
		Appointment
		Unit-of-use dispensing
		Feedback on medication use
8. Environmental context and resources	Regimen	Tailer treatment to daily habits
		Simplified dosing regimens
		Reduction the frequency of dosing
		Combination pills
		Changing medication formulation
	Adverse events	Counseling
		Safety
		Adverse events
	Integration and coordination of care	Collaborative care
		Reduced frequency of visits
		Liaison with general practitioner
		Pharmaceutical care services
		Medicines review
		Review illness history
		Care plan
		Multisystemic therapy
		Clarify responsibility for administration of therapy
		Increase the convenience of care
		Short waiting time
11. Behavioral regulation		Point-of-care testing
		Self-monitoring
		Treatment
		Symptoms

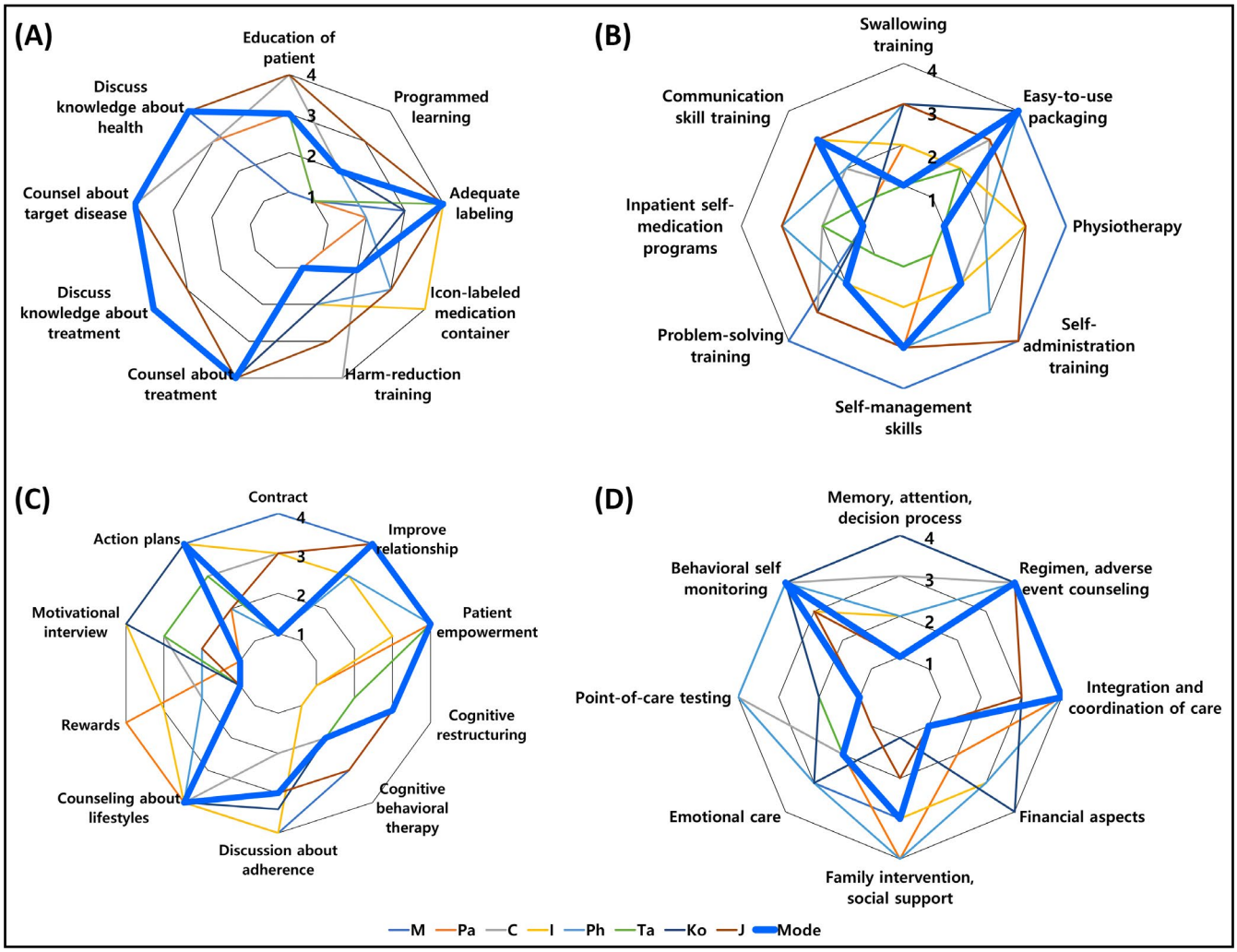

FIGURE 1 Responses to the questionnaire regarding the current use of adherence interventions according to the 11 theoretical domain frameworks in Asian expert panels. Bold line represents mode of the response. Panel A, use of adherence interventions in the patient Knowledge domain. Panel B, use of adherence interventions in the patient Skills domain. Panel C, use of adherence interventions in Social/professional role and identity, Belief about capabilities, and Belief about consequences, and Intentions domains. Panel D, use of adherence interventions in the Memory attention and decision process, Environmental context and resources, Social influences, Emotions, and Behavioral regulation domains. Scale: 1, never used; 2, seldom used; 3, sometimes used; 4, often used. M, Malaysia; Pa, Pakistan; C, China; I, Indonesia; Ph, Phillippines; Ta, Taiwan; Ko, Korea; J, Japan

On the other hand, newly introduced adherence interventions in need of more specialized facilities such as patient training or therapy, home visits, mass mailing, internet-based treatment support, and group programs were "Never" used. Financial or reward programs were also "Never" used interventions. In terms of the 2018 ESC/ESH guidelines, most of the patient level interventions did not seem to be implemented yet.

Even though the data were gathered through subjective perceptions about the country level adherence interventions, we may cautiously conclude that institute level interventions were assumed to be better in only four of seven countries. As shown in the results, the most "Often" used interventions in Asian countries are dependent on physician's capabilities. However, there are significant constraints on physician time and resources. Therefore, there might not in fact be a significant difference between expert and average physicians depending on the individual setting of each institute. For example, in some referral centers where the patient load was heavy, the physicians by himself may not be able to cope with the demand of adherence interventions, not because of a lack of capability but because of time constraints or non-availability of supporting staff or team, as shown in our study results. But, in general, quality of adherence intervention of the expert shown in this report should not be interpreted or generalized as those of general Asian doctors because attitudes or knowledge about adherence intervention may be different.

In the 2017 American College of Cardiology and American Heart Association (ACC/AHA) hypertension guidelines, a systematic team approach was graded as Class I recommendation with the level of evidence of A.[16] Because the recommendation of the ACC/AHA adherence interventions involved not only the conventional nurse or

TABLE 3 Summary of "Never" used adherence interventions according to the 11 theoretical domain framework categories in Asian countries

Domains	Subdomains	Interventions
1. Knowledge		Harm-reduction training
2. Skills		Swallowing training
		Physiotherapy
3. Social/professional role and identity		Contract
4. Intentions		Rewards
		Material or monetary
		Motivational interviewing
7. Memory, attention, and decision process		Reminders
		Postcard
		Mailing
		Prescription refill
		Telephone-linked computer system
		Mobile text messages
		Alarms
		Automated dispenser
		Reminder pill packaging
8. Environmental context and resources	Integration and coordination of care	Home visits
		Mass mailing
		Remote internet-based treatment support
	Financial aspects	Financial incentives
		Co-payments
9. Social influences		Social support
		(couple-focused) group programs

pharmacist but also other supporting staff such as the social worker, behavioral therapist, nutrition specialist, and physical therapist, the ACC/AHA guideline style team approaches and its implementation to improve adherence in Asian countries may be very challenging.

And in terms of behavioral aspects of adherence intervention, our results showed some discrepancy between "Often" used patient-centeredness and/or empowerment of patients and "Never" used motivational interviewing. Because these approaches are within the same spirit or principles, more formal education or training on the concept of motivational strategy or behavioral intervention would improve the quality of overall adherence interventions.[17,18]

There are studies reporting low adherence in Asian peoples or countries. In United States, the adherence was reported to be low in non-white races but these were associated with health literacy, socioeconomic status, co-payment system, and employment status.[19,20] In addition to the factors in the studies for immigrant Asian peoples, the self-efficacy, belief or knowledge about consequences, and self-perception of aging based on the health belief model (HBM) in Chinese studies,[21-24] health literacy in the elderly which would impact on the knowledge about complications in the Thailand study,[25] the choice of angiotensin converting enzyme inhibitor in the study done in Hongkong,[26] and employment status in a Korean study were associated with poor adherence to antihypertensive treatment in Asian Countries.[27]

When matching those determinants with corresponding TDFs, in addition to the conventional patient education, more personalized approaches considering health literacy and the age of the patient need to be developed. Moreover, the adherence interventions related to HBM reported in those Chinese studies are very closely related to those relatively newly introduced behavioral approaches such as patient empowerment, discussion about ambivalence to treatment as a part of motivational interviewing. The discrepancies of implementations among behavioral interventions with similar principles suggest that further studies about the details of behavioral interventions for further improvement are needed.

In the study by Cherry et al, Only 19% of physicians were confident about up-to-date in the most effective strategies for reducing treatment nonadherence among patients with hypertension and hyperlipidemia. fident, 17% confident, and only 2% very confident.[27] In this regards, American Society of Hypertension position paper about adherence emphasized the importance of providers developing skills to effectively communicate and counsel patients.[28,29] These include (1) providing clear, direct messages about the importance of adherence behaviors; (2) including patients in decisions regarding treatment goals and related strategies; and (3) incorporating behavioral strategies such as listening actively, tailoring strategies to each patient, anticipating and discussing potential barriers to adherence, and working with the patient to develop multi-dimensional strategies to overcome them.[29]

For those "Never" used adherence interventions such as better facility for patient training and tools of information technology, they are largely dependent on the team activities or multi-dimensional approaches. Therefore, the importance of all providers including each member of the team developing the skill to effectively communicate and counsel patients cannot be overemphasized. For a physician, it is still possible to develop those skill even when the team approaches are not available at the moment.

This report has some limitations. First, the perception about country level adherence intervention was subjective guessing. It needs more formal study in the future. Second, because of the TDF focus on the behavioral aspect of adherence intervention, health system level adherence interventions recommended by

TABLE 4 Level of Adherence interventions in Asian Countries based on the recommendations of the 2018 European hypertension guidelines

Adherence intervention recommended by 2018 ESC/ESH hypertension guidelines	Theoretical domain framework category	Adherence interventions	Level of Adherence Interventions[a]
Physician level			
Provide information on the risks of hypertension and the benefits of treatment, as well as agreeing a treatment strategy to achieve and maintain blood pressure	1. Knowledge	Counsel, give advice about treatment: benefits, importance, goal, mode of action	Often
Control using lifestyle measures and a single-pill-based treatment strategy when possible (information material, programmed learning, and computer-aided counseling)	1. Knowledge	Provide instruction: visual, verbal, written	Often
		Programmed learning	Seldom
		Computer-aided counseling	Not available
	6. Intentions	Counseling about lifestyle: diet, exercise, smoking	Often
	8. Environmental context and resources	Combination pills	Often
Empowerment of the patient	4. Beliefs about capabilities		Often
Feedback on behavioral and clinical improvements	6. Intentions	Motivational interviewing	Never
	7. Memory, attention, and decision process	Feedback on medication use	Often
Assessment and resolution of individual barriers to adherence	1. Knowledge	Counsel, give advice about treatment: medication adherence	Often
	2. Beliefs about consequences	Discuss: belief, barriers, ambivalence, adherence, stigma	Sometimes
Collaboration with other healthcare providers, especially nurses and pharmacists	8. Environmental context and resources	Collaborative care	Often
Patient level			
Self-monitoring of BP (including telemonitoring)	11. Behavioral regulation	Self-monitoring: treatment	Often
Group sessions	9. Social support	(couple-focused) group program	Never
Instruction combined with motivational strategies	6. Intentions	Motivational interviewing	Never
Self-management with simple patient-guided systems	2. Skills	Self-management skills	Sometimes
Use of reminders	7. Memory, attention, and decision process	Postcard, mailings, prescription refill, telephone-linked computer systems, mobile text messages, alarms	Never
Obtain family, social, or nurse support	9. Social support	Family intervention	Sometimes
Provision of drugs at worksite	8. Environmental context and resources	Provision of therapy at worksite	Seldom
Drug treatment level			
Simplification of the drug regimen favoring the use of single-pill combination therapy	8. Environmental context and resources	Regimen: simplify dosing regimen, combination pills	Often
Reminder packaging	7. Memory, attention, and decision process	Reminder pill packaging	Never
Health system level			
Supporting the development of monitoring systems (telephone follow-up, home visits, and telemonitoring of home BP)	8. Environmental context and resources	Integration and coordination of care: home visit, remote internet-based treatment support	Never

(Continues)

Table 4 (Continued)

Adherence intervention recommended by 2018 ESC/ESH hypertension guidelines	Theoretical domain framework category	Adherence interventions	Level of Adherence Interventions[a]
Financially supporting the collaboration between healthcare providers (e.g., pharmacists and nurses)	8. Environmental context and resources	No corresponding subdomain	Not available
Reimbursement of SPC pills	8. Environmental context and resources	No corresponding subdomain	Not available
Development of national databases, including prescription data, available for physicians and pharmacists	No corresponding domain or subdomain		Not available
Accessibility to drugs	No corresponding domain or subdomain		Not available

[a]Mode of the panelist responses.

TABLE 5 Perception about 61 adherence interventions at a country level compared to institutional level in Asia

Country	Level	Never	Seldom	Sometimes	Often	Z	Effect size	p^*
Malaysia	Institute	17	4	9	31			
	Country	39	16	6	0	6.2493	0.8001409	<.0001
Japan	Institute	13	9	23	16			
	Country	5	25	31	0	2.3831	0.3051247	.02
Pakistan	Institute	27	10	9	15			
	Country	25	22	10	4	3.3349	0.4269902	.0007
China	Institute	5	16	17	23			
	Country	1	13	23	24	−2.0678	−0.264755	.04629
Indonesia	Institute	9	13	17	22			
	Country	14	17	28	2	5.3248	0.6817708	<.0001
Philippines	Institute	3	17	23	18			
	Country	2	17	28	14	0.8665	0.110944	.5488
Korea	Institute	10	13	14	24			
	Country	6	23	13	19	0.82714	0.1059044	.3838

*p for effect of group.

the 2018 ESC/ESH hypertension guidelines were not available for our survey. Precise measure for health system level intervention needs be added to complement the scope of TDF for more comprehensive assessment. In this context, the comparison among the countries was not performed in this study even though the healthcare systems among countries vary widely. Thirdly, even though the information about TDF and the reference was shared among the panelist, there could be a difference among the depth of knowledge of each items for adherence intervention. To overcome this limitation, formal revision of TDF into a questionnaire tool with reliability testing is required.

In summary, in Asian countries, with the assessment of implementation of adherence intervention using the 11 TDFs, most experts showed good adherence with current hypertension guidelines in domains that can be covered by conventional resources including physicians, nurses, and pharmacists. However, for the concept of the behavioral aspect of adherence intervention needs, formal training or educational program at the individual level is needed. And newly introduced interventions, systematic team approaches, multidisciplinary specialty staff, and health system level intervention for improved adherence remain challenging in Asian countries.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

JSh designed questionnaire, leaded the survey, performed analyses, and wrote manuscript. KK conceived the project and leaded the project. YCC, YT, CHC, JSi, JSh, KK, MN, SH, TF, and YL submitted status report for each country. YCC, YT, SS, SP, RH, JCT, HVM, and TDW reviewed and revised manuscript.

ORCID

Jinho Shin https://orcid.org/0000-0001-6706-6504
Kazuomi Kario https://orcid.org/0000-0002-8251-4480
Yuda Turana https://orcid.org/0000-0003-4527-0285
Chen-Huan Chen https://orcid.org/0000-0002-9262-0287
Satoshi Hoshide https://orcid.org/0000-0001-7541-5751
Takeshi Fujiwara https://orcid.org/0000-0003-4151-2806
Michiaki Nagai https://orcid.org/0000-0002-3838-1369
Saulat Siddique https://orcid.org/0000-0003-1294-0430
Jam Chin Tay https://orcid.org/0000-0001-7657-4383
Tzung-Dau Wang https://orcid.org/0000-0002-7180-3607
Sungha Park https://orcid.org/0000-0001-5362-478X
Huynh Van Minh https://orcid.org/0000-0003-4273-4187
Yan Li https://orcid.org/0000-0002-5825-5968

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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