HYPERTENSION NEWS

March 2025

Childhood hypertension

Current challenges and how to improve care

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INTRODUCTION FROM THE PRESIDENT

GEORGE STERGIOU

President, International Society of Hypertension

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I am pleased to introduce the first edition of Hypertension News of 2025 – a time which marks almost 6 months since I took up the Presidency of the ISH. I cannot believe how fast this time has passed!

In this issue we place the spotlight on several important topics. We have articles looking at frailty and hypertension, some of the latest evidence around renal denervation, and the urgent need for diversity in hypertension research.

A particular highlight in this edition is the coverage of two recent large studies on blood pressure lowering – the ESPRIT and BPROAD trials – and the new evidence they provide on more intensive systolic blood pressure control.

Childhood and adolescence hypertension is also in focus, in a compelling article looking at the importance of optimising blood pressure screening and care in children and adolescents – a topic that deserves global attention.

Another theme in this edition is patient education in blood pressure management. One article looks at evidence around existing educational interventions, while another presents a patient education package currently in development. ISH is working on a project to improve patients' education.

We also wish to announce important news from ISH: our 2028 Scientific Meeting will be held in Europe, in collaboration with the European Society of Hypertension. We expect this partnership to be as fruitful and productive as our previous collaborations with our colleagues in Europe. Dates and location will be revealed in due course. Our upcoming conference, however, will be in Dubai in 2026. Save the dates of 22-25 October 2026!

I would like to say a heartfelt thank you to all contributors to this edition of Hypertension News. I have thoroughly enjoyed reading contributions as they came in – and I now hope you enjoy reading them too.

George Stergiou – president@ish-world.com

World Hypertension Day

World Hypertension Day is taking place on Saturday 17 May 2025.

Follow the ISH on our online platforms in the run up to the day, and share your activities with us: **comms@ish-world.com**.

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NEW PAPERS

Impact of frailty on antihypertensive treatment in older adults

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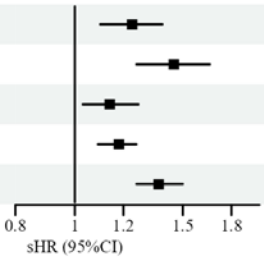
Frailty is a state in which the body becomes weaker and more vulnerable to health problems and disability. It happens gradually over time as the body's ability to recover and function across multiple physiological systems declines. This makes individuals more likely to experience various health issues and complications.[1] As a common syndrome that has been linked to hypertension,[2] frailty may influence the relationship between hypertension and adverse outcomes. Observational studies have demonstrated a contrasting association between systolic blood pressure (SBP) and adverse outcomes in frail and non-frail populations. While higher SBP is associated with an increased risk of adverse outcomes in non-frail individuals, evidence suggests that in frail populations, elevated SBP may be linked to lower mortality.[3, 4] This indicated that people who are frail may need different treatment approaches to manage their blood pressure (BP) effectively than non-frail individuals.[5] This has led to concerns about the potential efficacy of BP-lowering treatment in older adults who are frailer. As a result, three landmark trials have explored whether frailty affects the benefits of these treatments, but their findings have been inconsistent. Post hoc analyses of the Systolic Blood Pressure Intervention Trial (SPRINT) and the Hypertension in the Very Elderly Trial (HYVET) indicated that the frailty status of study participants did not influence the efficacy of BP-lowering treatment on cardiovascular outcomes.[6, 7] In contrast, the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial, which studied individuals with diabetes, found that BP-lowering medications were less effective in those who were frail.[8] Therefore, our study aimed to investigate the prospective association between baseline frailty and the risk of stroke, major cardiovascular events, and mortality in older adults with systolic hypertension. Secondly, we aimed to explore whether frailty status influenced the effectiveness of BP-lowering treatment on these outcomes, leveraging data from the landmark Systolic Hypertension in the Elderly Program (SHEP). The SHEP data are particularly valuable since it includes participants aged 60 and older, enabling us to examine how frailty affects individuals at different stages of aging, from early to late old age. Moreover, it provides crucial insights among individuals with higher baseline blood pressure levels compared to those in the HYVET and SPRINT studies.

In our study, we conducted a post hoc analysis of baseline and follow-up data from the SHEP trial – a seminal double-blind, randomized, placebo-controlled study.[9] This trial included 4,736 participants, all aged 60 or older, with a seated SBP ranging from 160 to 219 mmHg and a diastolic blood pressure (DBP) below 90 mmHg. The SHEP trial was originally designed to evaluate the effectiveness of antihypertensive treatment

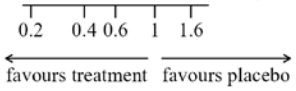
Outcome	No. of events (%)	sHR* (95%CI)	P-value
Stroke	259(5.52)	1.24(1.10-1.39)	<0.001
Heart failure	158(3.37)	1.45(1.26-1.66)	<0.001
Coronary heart disease	322(6.86)	1.14(1.03-1.27)	0.011
Cardiovascular disease	698(14.88)	1.18(1.09-1.26)	<0.001
All-cause Death†	446(9.50)	1.37(1.26-1.50)	<0.001



sHR for risks of outcome events associated with per SD higher in frailty index at baseline, adjusted for age, race, sex, education and treatment group.
† The risk of death is represented as the hazard ratio, as the results were obtained using the Cox proportional hazards regression model.
sHR: subdistribution hazard ratio; CI: confidence interval; TIA: transient ischemic attack; MI: myocardial infarction; HF: heart failure.

Figure 1. Association of baseline FI (per SD higher) with primary cardiovascular outcome and death

Outcome	Placebo*	Treatment*	sHR† (95% CI)	P for interaction
Stroke				0.420
Quarter 1	31(4.76)	16(2.48)	0.52(0.28-0.95)	
Quarter 2	41(7.14)	21(3.68)	0.50(0.30-0.86)	
Quarter 3	34(5.74)	31(5.28)	0.92(0.56-1.50)	
Quarter 4	51(9.59)	34(6.28)	0.63(0.40-0.96)	
Overall	157(6.68)	102(4.35)	0.63(0.49-0.81)	
Heart failure				0.101
Quarter 1	12(1.84)	11(1.71)	0.94(0.41-2.16)	
Quarter 2	18(3.13)	8(1.40)	0.41(0.18-0.95)	
Quarter 3	26(4.39)	15(2.55)	0.55(0.30-1.05)	
Quarter 4	48(9.02)	20(3.70)	0.37(0.22-0.63)	
Overall	104(4.43)	54(2.30)	0.49(0.36-0.69)	
Coronary heart disease				0.542
Quarter 1	35(5.38)	30(4.66)	0.88(0.54-1.44)	
Quarter 2	49(8.54)	33(5.78)	0.68(0.43-1.06)	
Quarter 3	46(7.77)	40(6.81)	0.88(0.57-1.35)	
Quarter 4	52(9.77)	37(6.84)	0.65(0.43-0.99)	
Overall	182(7.75)	140(5.97)	0.76(0.61-0.95)	
Cardiovascular disease				0.577
Quarter 1	85(13.06)	55(8.54)	0.64(0.45-0.90)	
Quarter 2	110(19.16)	66(11.56)	0.58(0.43-0.79)	
Quarter 3	97(16.38)	81(13.80)	0.84(0.62-1.12)	
Quarter 4	118(22.18)	86(15.90)	0.66(0.50-0.87)	
Overall	410(17.45)	288(12.29)	0.68(0.58-0.79)	
All-cause death‡				0.549
Quarter 1	36(5.53)	33(5.12)	0.95(0.59-1.51)	
Quarter 2	43(7.49)	43(7.53)	1.01(0.66-1.55)	
Quarter 3	72(12.16)	57(9.71)	0.77(0.54-1.09)	
Quarter 4	84(15.79)	78(14.41)	0.85(0.63-1.16)	
Overall	235(10.00)	211(9.00)	0.88(0.73-1.06)	



Quarter 1: FI ≤ 0.091; Quarter 2: 0.091 < FI ≤ 0.127; Quarter 3: 0.127 < FI ≤ 0.173; Quarter 4: FI > 0.173.
* Number of events and their percentage of treatment groups, according to FI groups.
† sHR for treatment effect on outcome events, adjusting for age, sex, race and education.
‡ The risk of all-cause death is represented as the hazard ratio, as the results were obtained using the Cox proportional regression hazards model.
sHR: subdistribution hazard ratio; CI: confidence interval; TIA: transient ischemic attack; MI: myocardial infarction; HF: heart failure.

Figure 2. Randomized treatment effect on cardiovascular outcomes and all-cause of death by quarters of FI

in reducing the risk of stroke among elderly individuals with isolated systolic hypertension. To investigate the association between frailty and clinical outcomes, as well as its impact on the effectiveness of BP-lowering treatment, we constructed a baseline frailty index (FI) comprising 55 health deficits to assess the frailty status of 4,692 participants in SHEP. The median FI was 0.127, with an interquartile interval of 0.091 to 0.173.

Our analysis revealed a significant positive association between higher baseline FI and the increased risk of future stroke. Specifically, for each standard deviation (SD) increase in baseline FI, we observed a 24% higher risk of stroke (Figure 1), with a subdistribution hazard ratio (sHR) of 1.24 (95% confidence interval (CI): 1.10–1.39), after adjusting for age, race, sex, education and treatment group. Similar associations were observed for heart failure (HF) (1.45; 1.26-1.66), coronary heart disease (CHD) (1.14; 1.03-1.27), and cardiovascular disease (CVD) (1.18; 1.09-1.26), after adjusting for the same covariates. A positive association was also found between baseline FI and the risk of all-cause death (HR, 1.37; 95% CI, 1.26-1.50). Importantly, consistent with post hoc analyses from the SPRINT, HYVET, we observed that the treatment's effectiveness in reducing adverse cardiovascular outcomes and mortality did not significantly differ across frailty groups (all P for interaction > 0.05, Figure 2). After adjusting for baseline FI, age, sex, race and education, randomized treatment was associated with a 37% reduction in the risk of future stroke (sHR, 0.63; 95% CI, 0.49-0.81). Similarly, the BP lowering treatment significantly lowered the risk of HF by 51% (0.49; 0.35-0.68), CHD by 24% (0.76; 0.61-0.94), and CVD by 33% (0.67; 0.58-0.78).

Our analysis of the SHEP trial shows that among older adults with higher BP, those who had higher levels of frailty had a higher risk of cardiovascular health problems. However, in these analyses, the benefits of BP control treatment were similar regardless of a person's level of frailty. These findings highlight the importance of considering a person's frailty when deciding on treatment plans and suggest that frailty assessments should be a routine part of healthcare. Our study utilized data from a multicenter, double-blind, placebo-controlled randomized clinical trial, which provides more robust results compared to observational studies. Nevertheless, because clinical trial participants may not fully represent the general population, more studies focused on highly frail individuals are needed to confirm these results.

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NEW PAPERS

Lowering of systolic blood pressure in patients with and without diabetes: The ESPRIT and BPROAD trials

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The treatment target range for pharmacological treatment of systolic blood pressure (SBP) in patients with hypertension is still a matter of controversy.[1,2] This is due to inconsistencies in results from randomized controlled trials (RCT) and their meta-analyses.[3] In this regard, the 2023 guidelines for the management of arterial hypertension from the European Society of Hypertension (ESH) aimed to address these challenges through a rigorous quality assessment of the available studies.[2] Accordingly, some available studies or meta-analyses, which supported a lower target BP range [4,5] had limited impact on the ESH recommendations due to methodological issues.[6] Against this background, the ESPRIT (Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing Risk of Vascular Events)[7] and BPROAD (Blood Pressure Control Target in Diabetes)[8] studies are two important RCTs providing valuable new data on the SBP target range in patients with hypertension.

Similar study design in the ESPRIT and BPROAD trials

The ESPRIT and BPROAD trials were multi-center, open-label, randomized controlled studies conducted in China, applying similar designs to investigate the benefit and harm of treatment targeting a SBP of less than 120 mm Hg compared to a target of 140 mmHg. While ESPRIT included a wide spectrum of the general hypertensive population at increased cardiovascular (CV) risk, including 38.7% of patients with type 2 diabetes mellitus (T2DM), BPROAD included exclusively patients with T2DM at increased CV risk. Nevertheless, the overall comparison of both studies as shown in **Table 1** reveals many similarities. The BPROAD is of particular importance, since the SBP target range of 120-129 mmHg that is recommended for most patients[1,2,9,10] is less strongly supported for patients with diabetes. The previous ACCORD trial failed to show a benefit of the intensive SBP target <120 mmHg[11] and a subsequent meta-analysis found an increased risk for CV death in response to BP lowering in people with T2DM and a SBP already <140 mmHg.[11,12]

Main Efficacy Outcomes

In ESPRIT, the mean achieved SBP during follow-up was 134.8 mmHg in the standard treatment group (mean number of antihypertensive medications 2.1) and 119.1 mmHg in the intensive group (mean number of antihypertensive medications used 2.8) resulting in a SBP difference of 15.7 mmHg (differences in mean number of antihypertensive drugs used 0.7).

In BPROAD, the mean achieved SBP one year after follow-up was 133.3 mmHg in the standard treatment group (mean number of

Table 1: Selected key features of the ESPRIT and BPROAD trials

	ESPRIT	BPROAD
Study design	Multi-center (116 hospitals or communities in China) open-label randomized controlled trial, assessor-blinded	Multi-center (145 clinical sites in China) open-label randomized controlled trial, assessor-blinded
Inclusion criteria	Age ≥50 years, SBP≥130 mmHg on 0 or up to 4 antihypertensive medications, prior CVD or at least 2 CV risk factors	Age ≥50 years, Diabetes, SBP≥140 mmHg on 0 medication or SBP≥130 mmHg up to 4 antihypertensive medications, increased CV risk (presence of CVD, subclinical CVD or at least 2 CV risk factors)
Exclusion criteria	Secondary hypertension, eGFR<45ml/ min1.73m2, symptomatic HF past 6 months, EF <35%	Type 1 diabetes, secondary hypertension, eGFR<30 ml/min1.73m2, proteinuria ≥1 g/d, albuminuria ≥600mg/d, symptomatic HF past 6 months, EF <35%
Participants		
Number	11,255	12,821
Ethnicity	Chinese	Chinese
Mean age, years	65	64
Women, %	41	45
SBP/DBP, mmHg	147/83	140/76
Antihypertensives, mean	1.7	1.4
BMI, kg/m2	26.3	26.7
eGFR, ml/min/1.73m2	83	89
Co-morbidities, %		
• CAD	28.9	Na
• Stroke	26.9	Na
• Diabetes	38.7	100
• History of CVD	na	23
Mean Follow-up	3.4 years	5 years
Primary outcome	Composite of MI, revascularisation, hospitalisa-tion for heart failure, stroke, or death from CV causes	Composite of nonfatal stroke, nonfatal myocardial infarction, treatment or hospitalization for heart failure, or death from CV causes
BP measurement and setting	Attended automatic office BP (Omron HBP-1100)	Attended automatic office BP (Omron HEM-907)
BP treatment strategy		Similar to the SPRINT trial
Funding/Sponsor	The Ministry of Science and Technology of China and Fuwai Hospital	National Key Research and Development Program from the Ministry of Science and Technology of China

antihypertensive medications used 1.3) and 121.6 mmHg in the intensive group (mean number of antihypertensive medications used 2.1) resulting in a SBP difference of 11.7 mmHg (differences in mean number of antihypertensive drugs used 0.8).

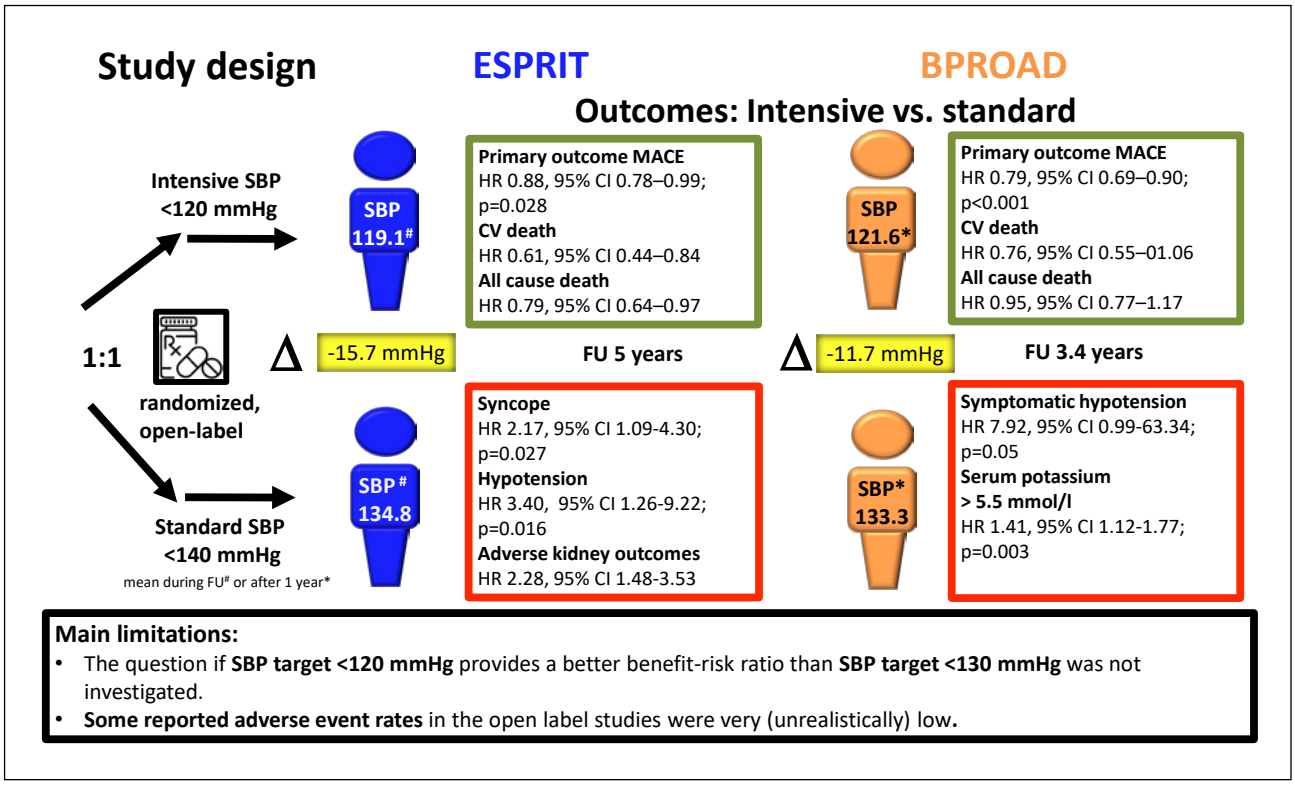
In ESPRIT, the intensive strategy resulted in lower rates of the primary MACE endpoint with a hazard ratio (HR) of 0.88, 95% confidence interval (CI) 0.78–0.99, p=0.028. CV mortality (HR 0.61, 95% CI 0.44–0.84) and all-cause mortality (HR 0.79, 95% CI 0.64–0.97) were also significantly reduced.

Intensive treatment in BPROAD also resulted in lower rates of the primary MACE endpoint (HR 0.79, 95% CI 0.69–0.90, p<0.001). CV mortality (HR 0.76, 95% CI 0.55–1.06) was numerically lower, but no reduction in all-cause mortality (HR 0.95, 95% CI 0.77–1.17) was observed (**Figure 1**).

Adverse events

Higher rates of adverse events were found in the intensive treatment groups of both studies, while the absolute event rates were low. Higher risks of

Figure 1



syncope (HR 2.17, p=0.027), hypotension (HR 3.40, p=0.016), and adverse kidney outcomes (HR 2.28, p<0.001) were observed in ESPRIT. Increased risks of symptomatic hypotension (HR 7.92, p=0.05) and hyperkalemia (serum potassium >5.5 mmol/litre, HR 1.41, p=0.003) were observed in BPROAD (**Figure 1**).

Discussion

Both trials reported significant cardiovascular benefits with intensive SBP control targeting a SBP < 120 mmHg compared to <140 mmHg. Thus, the evidence suggesting <140 mmHg as a suboptimal SBP target is mounting. Whether targeting a SBP <120 mmHg provides additional benefit as compared to a target of <130 mmHg, as suggested by guidelines,[1,2,10,13] is still an open question. The benefit of a SBP target <120 mmHg compared to <130 mmHg has not been assessed, and several trials aiming for <120 mmHg failed to achieve this ambitious goal, actually supporting the 120-129 mmHg target range.

Furthermore, adverse event rates were significantly more frequent in the intensive treatment group of both studies. Of note, adverse event rates were commonly based on clinical diagnosis, e.g. hypotension (17 vs 5 events in ESPRIT and 8 vs 1 events in BPROAD), with very low numbers compared to previous European and American trials. This raises some concerns regarding the validity of the safety assessment in these trials, which may underestimate potential harm in relation to clinical benefit. Lastly, it should not be dismissed, that both the ESPRIT and BPROAD trials exclusively enrolled Chinese participants, which means that the generalizability of their findings to other ethnic populations remains uncertain.

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MAY MEASURE MONTH®

May Measurement Month (MMM)

May Measurement Month (MMM) will run from 1 May to 31 July 2025.

This initiative, initiated in 2017 by the ISH, aims at improving awareness and control of high blood pressure around the world.

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RENAL DENERVATION

Renal denervation for hypertension in 2025: Where do we stand with this?

KONSTANTINOS TSIOUFIS

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The 2023 and 2024 guidelines for hypertension (HTN) management released by the European Society of Hypertension (ESH) and European Society of Cardiology (ESC) provided recommendations for use of Renal Denervation (RDN) as an additional therapeutic option (on top of lifestyle changes and appropriate combination therapy) in patients with resistant or uncontrolled HTN. (**Table 1**).

Both European guidelines highlight the importance of patient preference through a shared decision-making process taking into account that RDN is a safe (in terms of deterioration of renal function and development of new renal artery stenosis) and effective (in terms of reducing both office and ambulatory BP) procedure in a various spectrum of hypertensive phenotypes. Long-term follow-up data from the Global SYMPLICITY Registry, the SPYRAL HTN-ON MED trial and the RADIANCE-HTN SOLO trial indicate that the BP-lowering efficacy of RDN in patients with hypertension is sustained for at least up to three years, with a trend for continuous BP reduction over time. The so-called "Always on" effect of RDN on BP overcomes, at least partially, the critical issue of poor medication adherence that is mainly evident in hypertensive patients with uncontrolled or resistant HTN and a number of other comorbidities. For this reason, personally I think that in every hypertensive patient with difficult to control HTN (i.e. Resistant HTN) or with high cardiovascular risk due to other comorbidities (i.e. coronary artery disease, diabetes mellitus type II, atrial fibrillation, sleep apnea, heart failure etc.) we have to offer the

Table 1. ESH and ESC guidelines for the management of hypertension regarding use of RDN

RDN Recommendations by the 2023 ESH guidelines for HTN management	CoR	LoE
RDN can be considered as an additional treatment option in patients with resistant hypertension if eGFR is >40 ml/min/1.73 m2 who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	II	B
RDN can be considered as an additional treatment option in patients with true resistant hypertension if eGFR is >40 ml/min/1.73 m2.	II	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
RDN should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

RND Recommendations by the 2024 ESC guidelines for HTN management	Class	Level
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	B
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	A

possibility of RDN in parallel with the optimal pharmacological treatment. It is important to clarify that RDN is not an alternative to medication treatment, but it is a synergistic method that contributes to reduce the burden of uncontrolled HTN. On this topic, updated guidelines from the China Hypertension League plus a scientific statement from the American Heart Association, add further support to the above-mentioned European guidelines recommending RDN as the third pillar in hypertension management. This is in addition to local consensus statements supporting the safe and effective use of RDN in over 25 countries.

FDA approved two RDN systems in 2023, the Spyral catheter (provided by Medtronic) that uses radiofrequency energy to disrupt the renal fibers and the Paradise catheter (provided by RECOR) that uses intravascular ultrasound to modify the sympathetic tone. Currently, in the USA there is a long discussion on how and when Medicare will cover the RDN procedure for its beneficiaries. With recent approvals in China, Canada and India the Spyral catheter is now available in over 75 countries while over 30,000 patients worldwide have now been treated with the Symplicity renal denervation system, demonstrating its safety and efficacy.

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For the Paradise RDN system, apart from its approval in the USA by the FDA in 2023, it has been approved in all EU member states (CE Mark) since 2012. The system is also commercially distributed in several countries in the Persian Gulf region. China FDA, apart from the approval of the Symplicity catheter, has also approved another radiofrequency system, the Symap system. Real world data from Australia, Europe and Asia confirmed the safety and efficacy of RDN in hypertensive patients.

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RENAL DENERVATION

Renal denervation is durable: Insights from the Global Symplicity Clinical Program

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Hypertension remains a global health burden with 1 in 3 adults; equivalent to 1.6 billion people worldwide will have hypertension by 2025.[1] Lowering systolic blood pressure (BP) by 10 mmHg reduces the relative risk of major adverse cardiovascular events by 20%, irrespective of baseline BP or previous diagnoses of cardiovascular disease.[2,3] The evidence, consensus documents[4] and international guidelines (ESH and ESC)[5,6] now support catheter-based renal denervation (RDN) as an adjunctive technology in the hypertension care pathway. There is a robust evidence set, with sham-controlled trials[7,8] and registries[9] demonstrating the safety and blood pressure lowering efficacy in the short and long-term.

RDN has been shown to lower blood pressure (BP) in patients with HTN and pre-clinical research has shown that nerves do not functionally regrow.[10] Yet, questions remained regarding the sustained effect of RDN on blood pressure - whether they can be deemed truly durable. It is crucial to determine whether specific patient baseline characteristics are associated with BP reductions post-RDN, which will aid in refining the patient selection process.

To address these research questions, a pooled data set of RF RDN-treated patients derived from the entire Global Symplicity Clinical program were analyzed. A total of 4,156 patients, spanning from the SPYRAL First-in-Human, the Global Symplicity Registry (GSR) DEFINE, and a multitude of randomized controlled and sham-controlled trials including HTN-Japan, Symplicity HTN-3, and the SPYRAL HTN-OFF and ON MED studies were included. A multivariate, patient-level, mixed model was developed to assess two facets:

1. Long-term BP reductions following RDN.
2. Correlations between baseline patient characteristics and subsequent BP reductions.

How was it executed?

- BP measurements from each patient within the Global Symplicity Clinical program were analyzed using linear mixed models.
- Key fixed effects that were incorporated include baseline Systolic BP, the baseline number of antihypertensive (AH) medications, and AH medications over time.
- The results were refined and presented to show modeled SBP, adjusted for the effects of AH medications over time

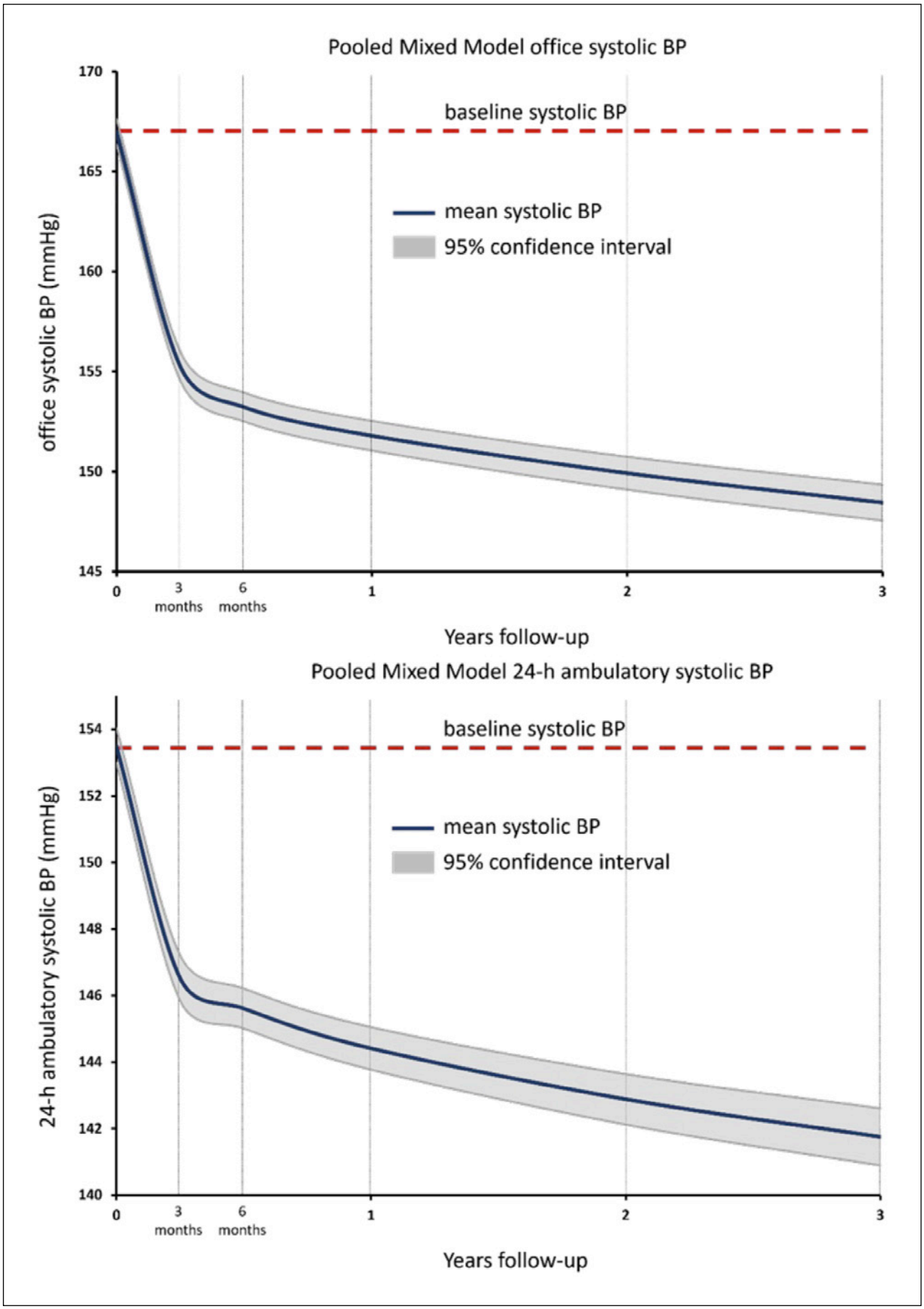
What were the Results?

- 4,156 patients treated showed a biphasic office systolic BP reduction over 3-years, illustrating a sharp reduction right after RF RDN through the initial 6 months, followed by a sustained, steady reduction thereafter through 3-years.
- Mixed model outcomes revealed that higher baseline systolic BP was correlated with heightened BP reductions during follow-up.

Importance and Implications

This mixed model analysis represents the most comprehensive analysis of RF RDN to date. The findings emphasize the durability of Symplicity RDN as a valuable adjunctive therapy alongside AH medications for treating patients suffering from uncontrolled HTN. In the study, high baseline SBP was the only parameter with moderate effect, while a few others that are associated with high sympathetic activity were weak.

Figure 1: Long term office and 24-hr ambulatory BP reduction through 3 years



Durability in clinical results, particularly for chronic conditions like hypertension, is crucial. Effective long-term hypertension management can significantly enhance patients' quality of life, reducing the risks of severe cardiovascular complications such as strokes, heart failure, and myocardial infarction.

In conclusion, the findings from the pooled analysis underscore the continued decrease in blood pressure over long-term follow up after RDN.

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Renal denervation: Bridging the gap in resistant hypertension management

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Renal denervation (RDN) represents a promising therapeutic strategy for managing resistant hypertension (R-HT), addressing the critical challenge of uncontrolled blood pressure in patients unresponsive to optimal pharmacological therapy. This review, based on findings from the Resistant Hypertension Working Group of the Argentine Hypertension Society, evaluates the awareness, perceptions, and acceptance of RDN among Argentine physicians.

High Awareness and Persistent Safety Concerns

A survey of 206 physicians, primarily cardiologists and internists, revealed a substantial level of awareness regarding RDN (83%), emphasizing the effectiveness of information dissemination. However, only 60% of respondents considered RDN safe, while 33% expressed uncertainty, and 7% regarded it as unsafe. These findings highlight the need for continued education and robust clinical evidence to address residual concerns about its safety profile.

Geographic disparities were evident, with 60% of participants based in Buenos Aires, suggesting that urban practitioners may have greater access to advancements in hypertension management compared to those in rural areas. Gender distribution was relatively balanced, with 41% female and 59% male respondents. (**Figure 1**)

Perceived Efficacy and Expanding Applications

The survey indicated that 58% of participants viewed RDN as a viable therapeutic option for R-HT, consistent with data from pivotal trials such as SPYRAL HTN-OFF MED and ON MED, which demonstrated significant reductions in blood pressure with RDN. Additionally, physicians identified emerging indications for RDN, including hypertension with atrial fibrillation (7.3%), obesity (7.8%), and ischemic cardiomyopathy (12%). These findings reflect growing interest in extending the scope of RDN beyond its primary indication.

Radiofrequency-based RDN was the preferred technique among respondents (66%), compared to ultrasound-based methods (25%). This discrepancy underscores the importance of enhancing awareness about evolving technologies in the field.

Bridging the Gap: Safety and Knowledge

Safety concerns remain a pivotal barrier to the broader adoption of RDN. Long-term studies, including the Global SYMPLICITY Registry and RADIANCE-HTN SOLO, have consistently

demonstrated the safety and efficacy of RDN, yet wider dissemination of these findings is critical to fostering physician confidence. Notably, respondents with greater familiarity with RDN expressed higher confidence in its safety and efficacy, reinforcing the value of targeted educational initiatives.

Clinical Practice Implications

This study draws attention to the importance of structured educational programs in bridging the gap between awareness and confidence in RDN. Shared decision-making, as recommended by the European Society of Hypertension, should be a cornerstone of integrating RDN into clinical practice. Patient-specific factors, including cardiovascular risk and hypertension-mediated organ damage, must be carefully evaluated when considering this intervention.

Enhanced training in patient selection and procedural execution, combined with collaborative efforts between healthcare providers and industry stakeholders, is essential for standardizing and optimizing outcomes.

Conclusion

RDN offers a valuable therapeutic alternative for patients with R-HT, particularly those unresponsive to pharmacological treatment. While awareness among Argentine physicians is high, lingering safety concerns and knowledge gaps mirror global trends. Addressing these barriers through comprehensive education, dissemination of robust safety data, and shared decision-making can facilitate the integration of RDN into routine clinical practice. As evidence continues to evolve, RDN has the potential to transform hypertension management and improve outcomes in this challenging patient population.

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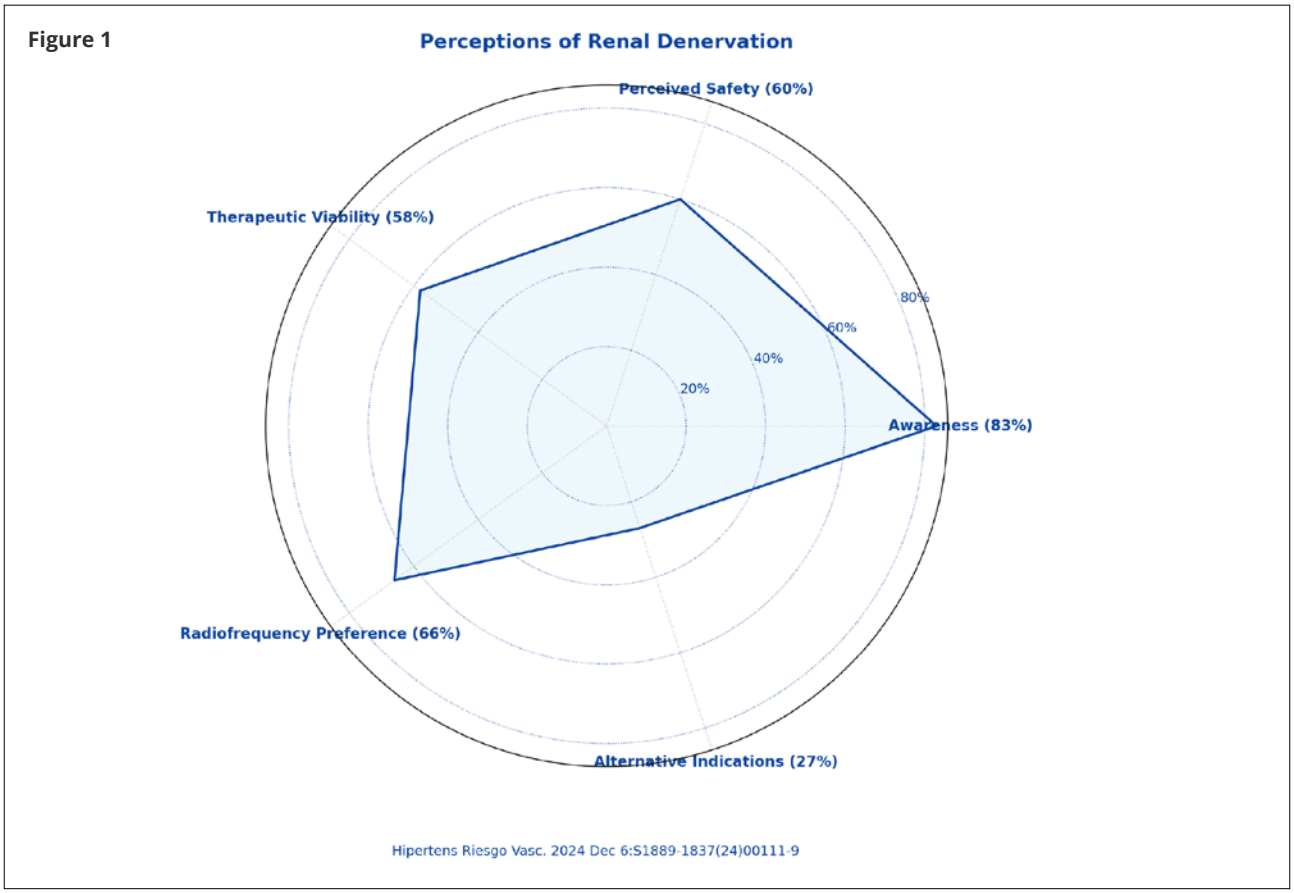
Figure 1



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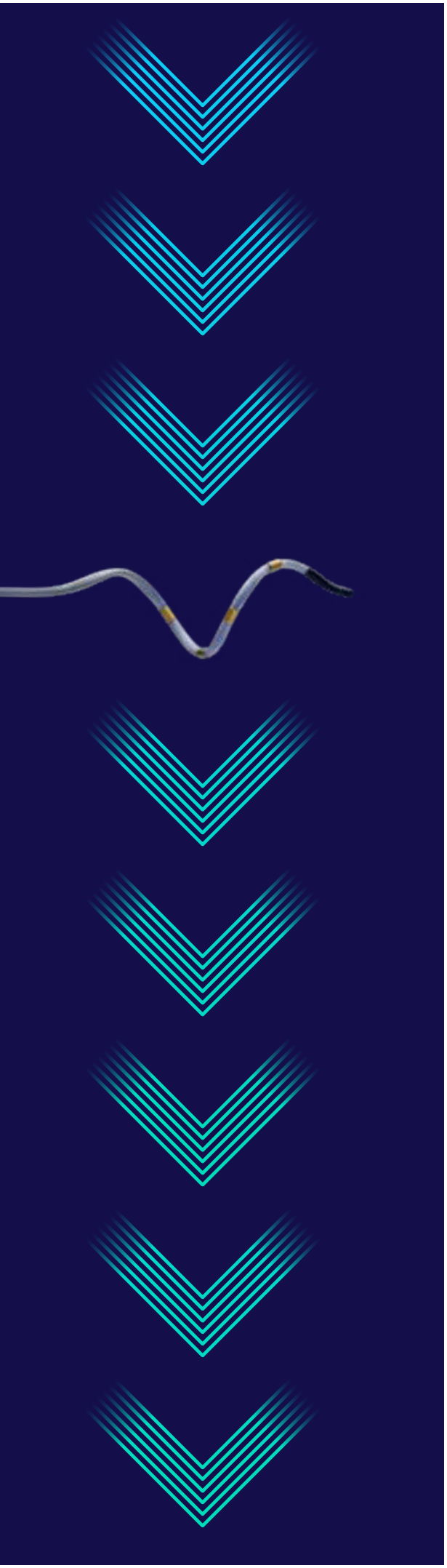

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PERSPECTIVES IN HYPERTENSION

New approaches and insights in the renin-angiotensin system

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The importance of the renin-angiotensin system (RAS) in blood pressure control is well established. In the traditional view, the RAS functions in an endocrine manner; that is, angiotensin II (Ang-II) is generated in the bloodstream to act on various peripheral organs. However, over the past decades, different organs have been identified as capable of generating Ang-II and responding to it locally. Conceptually, this means that, in addition to the endocrine RAS (where Ang-II acts as a hormone), there are local angiotensinergic systems operating in a paracrine, autocrine, and intracrine manner and independently of the circulating RAS.[1] The existence of the RAS operating locally in the central nervous system was established more than 50 years ago.[2] However, the enzymatic mechanisms that generate Ang-II in the brain have not been fully elucidated. Furthermore, the brain's ability to express renin, the rate-limiting enzyme of the RAS, has been a highly controversial topic due to several technical limitations that have prevented the detection of renin with high sensitivity, specificity, and specially with neuroanatomical precision.[3]

In our recently published study in *Hypertension*, we used more advanced in situ hybridization methods to demonstrate the presence and biological functionality of renin in the brainstem.[4] Surprisingly, renin was not detected in commonly studied regions within the field of hypertension research, which are in the majority associated with sympathetic drive, but rather in a region involved in vagal cardioinhibition. This renin-expressing nucleus, called the nucleus ambiguus, originates vagal projections to the cardiac ganglia and is involved in the parasympathetic regulation of the heart. Neuroanatomically, the nucleus ambiguus is strategically located dorsally to the rostral ventrolateral medulla, and communication between these two nuclei is believed to contribute to autonomic balance and cardiovascular function.[5]

To elucidate the physiological function of renin in the nucleus ambiguus, we developed a genetically modified mouse in which the renin gene's exon 1a was flanked and selectively removed from vagal neurons, but not from other cells. As expected, these mice did not express renin in the nucleus ambiguus, while circulating renin was paradoxically higher likely due to a compensatory response. Interestingly, the selective ablation of renin in the nucleus ambiguus led to a sexually dimorphic phenotype. That is, male mice lacking renin in cholinergic neurons exhibited suppression of vagal cardiac tone and a reduced baroreceptor reflex, whereas females showed increased parasympathetic tone and an exaggerated reflex response. To infer possible gene candidates mediating sex differences, we used bulk RNA sequencing from brain punches collected with the nucleus ambiguus. Interestingly, our data suggest the importance of the APJ gene, which encodes the apelin receptor and is known for its relevance in RAS regulation and blood pressure control, in sex-dependent phenotype in mice lacking renin in the nucleus ambiguus.[6]

Our current goal is to define the identity and the neural connectivity of renin-expressing neurons in the brainstem. To identify genes co-expressed with renin in the nucleus ambiguus, we performed 10x Genomics Xenium spatial transcriptomic profiling in brainstem sections collected from normotensive and hypertensive mice. Hypertension was induced by infusing deoxycorticosterone acetate and providing saline as a choice for drinking. Data collected from our first pilot study using

a 347 gene probe panel (including RAS genes) was presented at the 2024 ISH Conference in Cartagena. This experiment aimed to validate the method and confirm the presence of RAS genes, including renin, in the nucleus ambiguus using a completely different approach. Then, we also included brainstem sections from hypertensive mice to evaluate whether RAS genes could be dysregulated under pathological conditions. Finally, we compared transcriptomic differences in the nucleus ambiguus between males and females.

Our preliminary results indicate that Xenium profiling has superior sensitivity to detect low-expressed genes such as renin and G protein-coupled receptors in the brain compared to next-generation sequencing, which is limited by their sequencing depth. Then, we quantified and compared the number of transcripts in the nucleus ambiguus between normotensive and hypertensive males and females. First, we noticed that in the nucleus ambiguus, angiotensinogen expression increases in both males and females in hypertensive mice compared to normotensive control. However, several RAS components exhibited a sex-specific phenotype in response to hypertension. For instance, renin expression doubled in response to hypertension in males but was halved in females. Agtr1a, which codes for the angiotensin II type 1 receptor, was largely unchanged in males, but was decreased by 50% in females. Even still, some RAS components, such as angiotensin-converting enzyme (Ace), remained unaffected in hypertension regardless of sex. Notably, in female mice, induction of hypertension resulted in an approximately 4-fold increase in Agtr2 and Ace2, components of the anti-hypertensive axis of the RAS, suggesting compensatory mechanisms.

While this first assay confirms our recently published findings, future studies will include new high throughput panels (up to 5,000 genes) and secondary analyses to explore the transcriptomic profile, cell-to-cell interactions, and spatial organization of renin-expressing neurons in different physiological and pathophysiological states. The identification of differentially expressed genes will provide a starting point to elucidate a molecular mechanism underpinning the development of neurogenic hypertension.

The identification of cholinergic neurons capable of generating Ang-II in an unexpected brainstem nucleus linked to parasympathetic function raises several new questions and challenges. Can Ang-II be operating as a co-transmitter with acetylcholine? Can Ang-II modulate cholinergic neurotransmission? Looking ahead, we believe that the imbalance between the sympathetic and parasympathetic systems is a hallmark of various cardiovascular conditions, including hypertension, orthostatic hypotension, heart failure, and arrhythmias. While most studies on central RAS have focused on its role in blood pressure control via the sympathetic nervous system, the cholinergic system has been notably overlooked. The influence of renin on the cholinergic system could suggest new functions for RAS and, therefore, open up new possibilities for the use of RAS blockers in the treatment of conditions associated with parasympathetic nervous system dysfunction.

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PERSPECTIVES IN HYPERTENSION

Missed opportunities: Improving pediatric hypertension recognition and care

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Why hypertension in children and youth matters

Hypertension is a leading preventable cause of morbidity and death worldwide. Over the last three decades, the prevalence of hypertension has doubled globally, yet less than half of affected individuals are diagnosed, and even fewer receive adequate treatment.[1] This concern also extends to children and adolescents, where hypertension frequently begins but is often overlooked. Despite mounting evidence on the prevalence and long-term consequences of childhood hypertension, there remains a concerning lack of awareness among both healthcare providers and families. This poor recognition contributes to suboptimal screening practices and delays in diagnosis, increasing the risk of cardiovascular and kidney complications in early adulthood. Early detection and effective management of pediatric hypertension are crucial to mitigating these risks and reducing the burden of disease across the lifespan.

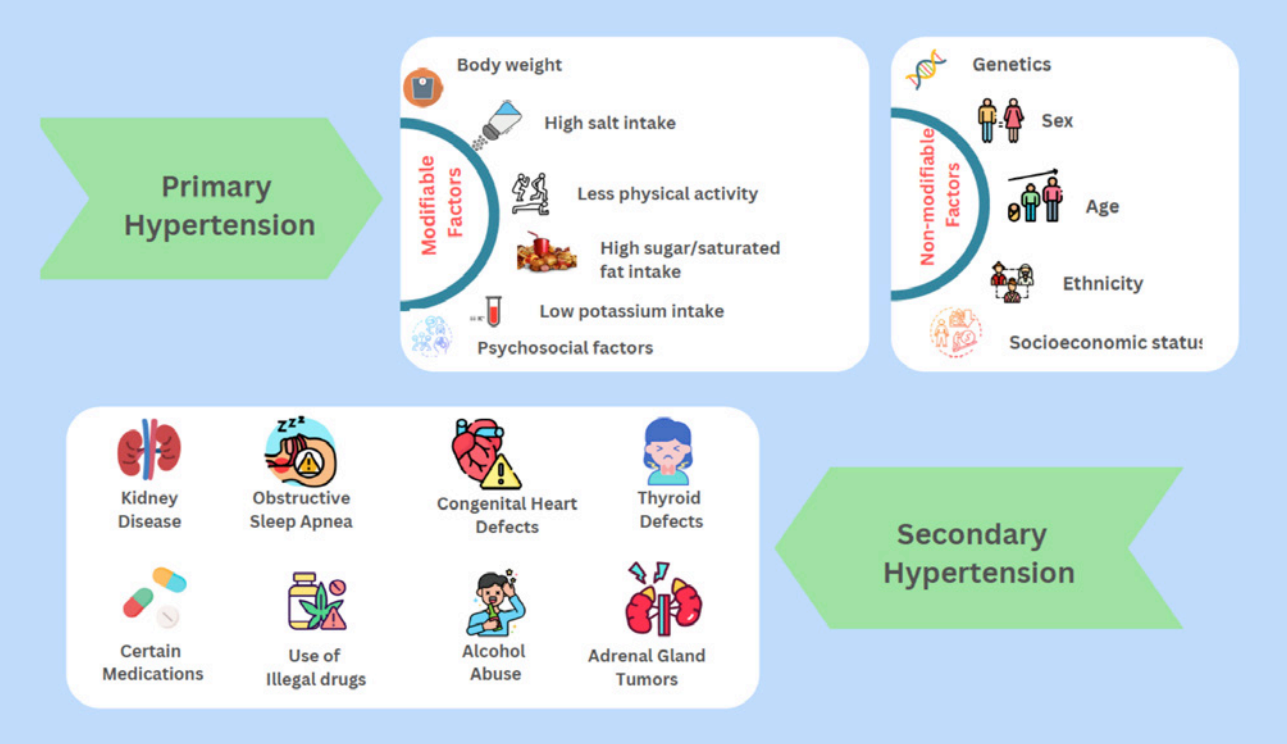
How common is primary hypertension in youth?

The prevalence of primary pediatric hypertension has risen markedly in recent years, primarily due to increasing rates of childhood obesity, excessive salt intake, low physical activity, and a growing intake of processed foods. Studies suggest that 5–8% of children and adolescents have hypertension, and an additional 10–14% have elevated BP, often referred to as prehypertension.[2] A meta-analysis revealed that the prevalence of hypertension in children increased from just over 1% in the 1990s to 7% between 2010 and 2014.[3] While this alarming trend highlights the need for heightened awareness and targeted interventions to address the growing burden of pediatric hypertension, it is noteworthy to add that these global prevalence rates are highly underrepresented of LMICs.

Current challenges in pediatric hypertension care

Despite the rising prevalence, pediatric hypertension care remains inadequate. Many healthcare providers remain unfamiliar with the complex hypertension diagnostic criteria, which rely on age, sex, and height percentiles rather than fixed thresholds. In addition, conflicting guidelines contribute to underdiagnosis, with organizations such as the American Academy of Pediatrics and Hypertension Canada advocating for annual BP screening starting at age 3, while others, including the U.S. Preventive Services Task Force, do not recommend routine screening.[4] In practice, screening and follow-up care are insufficient. Studies from the USA reveal that only 15–33% of children undergo annual BP measurements, and fewer receive appropriate follow-up for elevated readings.[5] Fewer than 25% of children with hypertension are accurately diagnosed, less than half receive lifestyle counseling, and only 6% are

Figure 1: Risk Factors of Pediatric Hypertension



prescribed antihypertensive medications when indicated.[6] Families, too, often underestimate the significance of hypertension in children, perceiving hypertension as a condition that primarily affects adults, which highlights the need to upscale health education even at household level.

What increases the risk of primary hypertension in youth?

Pediatric hypertension is multifactorial, with both genetic and environmental factors playing significant roles.[7] Currently, primary hypertension is the main driver in context of increasing rates of obesity due to unhealthy dietary intake, high salt and low potassium intake and sedentary lifestyle among children (**Figure 1**).

Consequences of untreated hypertension in youth

Progression or tracking to Adult Hypertension

Children with hypertension are at significant risk of persistent hypertension in adulthood.[8]

Cardiovascular outcomes

Hypertension can cause structural and functional changes in the heart and blood vessels, including left ventricular hypertrophy (LVH) and arterial stiffness.[9,10] These are precursors to severe cardiovascular diseases and events in later life.

Increased Risk of Long-Term Complications

Studies link childhood hypertension with a higher likelihood of early cardiovascular and kidney events.[11] Jacobs et al. (2022) showed that childhood combined-risk z score were strongly associated with cardiovascular events in midlife, and especially higher relative risk for fatal and non-fatal cardiovascular events in adults younger than 47 years.[10]

Strategies to optimize pediatric BP screening and hypertension care

To optimize pediatric blood pressure (BP) screening and hypertension care worldwide, a comprehensive, multi-faceted approach is essential (**Figure 2**). This includes implementing standardized screening protocols across healthcare settings, developing unified international guidelines in collaboration with organizations like ISH, and integrating BP measurement into routine care such as annual well-child visits and school health checkups. Using validated BP devices designed for children can improve accuracy and reduce variability in measurements.

Enhancing provider education and training through continuous medical education (CME), distributing resources like reference guides and management algorithms, and focusing on educating providers

in rural and underserved areas can significantly improve care. Leveraging health information technology, such as incorporating alerts within electronic medical records (EMRs) to remind providers to check BP and using data analytics for targeted interventions, is also crucial. Expanding telehealth services for follow-up consultations and BP monitoring can particularly benefit families in remote areas.

Promoting family and community awareness through education campaigns, school-based or pharmacy-based programs, and community outreach can help educate parents and caregivers about the importance of regular BP checks and healthy lifestyle choices. Improving access to care and resources by establishing multidisciplinary hypertension clinics, ensuring affordable home BP monitors, and advocating for policies that reduce barriers to care is vital.

Fostering research and surveillance by creating centralized registries to track pediatric hypertension cases, supporting implementation studies, and prioritizing research on underrepresented populations can address health inequities. Finally, incentivizing quality care by developing performance metrics to assess BP screening rates and management outcomes in pediatric care settings can drive improvements in care and outcomes.

Why we need to act now?

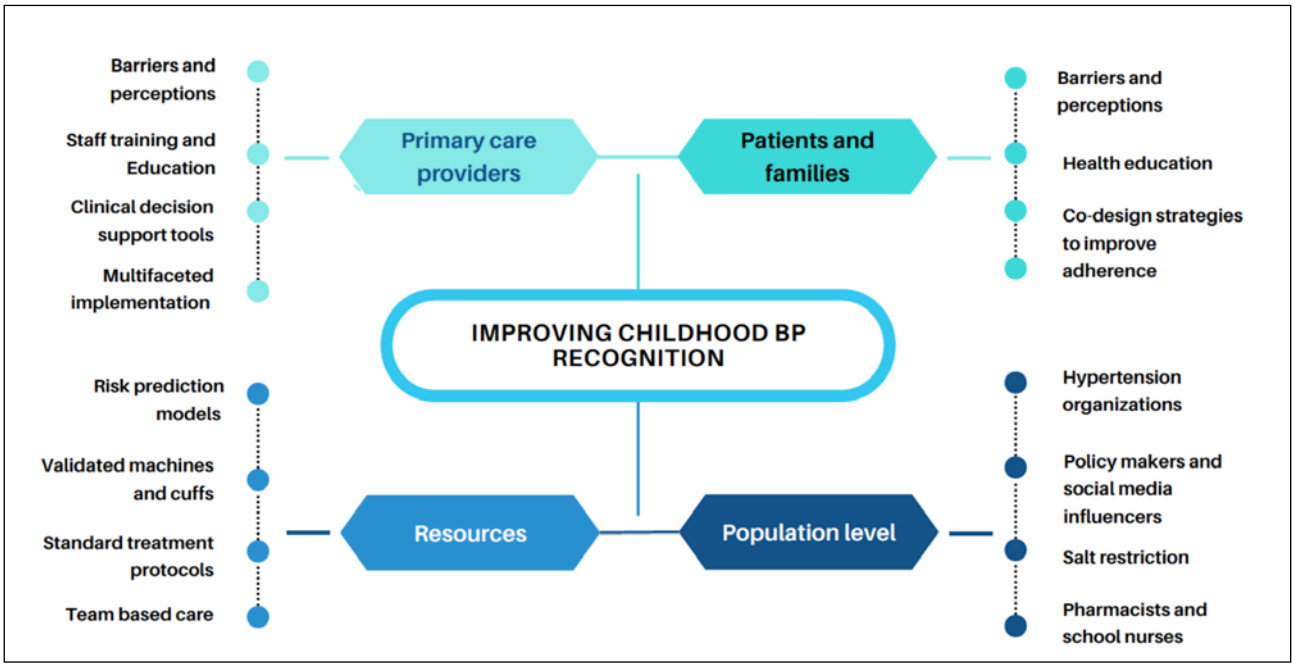
Hypertension in children is not just a future health concern; it is a public health issue today. Screening blood pressure can identify those at risk, particularly children with obesity, a family history of hypertension, or other risk factors. Early interventions – including dietary changes, increased physical activity, and medical management when necessary – can effectively lower BP and prevent complications.

Unfortunately, most children with high BP remain undiagnosed and untreated due to systemic gaps in care. Addressing these issues requires:

- Improved awareness among healthcare providers and caregivers
- Proper recordkeeping of blood pressure vitals in pediatric patient files
- Clearer, evidence-based guidelines for screening and management
- Enhanced access to diagnostic and therapeutic resources

By prioritizing pediatric hypertension as a public health concern, we can significantly reduce the risk of serious illnesses in adulthood.[12] This enhanced focus on pediatric hypertension can serve as a cornerstone for healthier communities, underscoring the importance of preventive care in transforming health outcomes globally.

Figure 2: Strategies to improve pediatric hypertension recognition and management



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Development of a patient educational package for BP management

Patient education is key to effective blood pressure (BP) management

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Patient education is the delivery of information to support individuals to engage in behaviours and decision-making to manage their health.[1] Previous research has shown that patient education improves BP control[2] and engagement with self-management activities including lifestyle changes and medication adherence.[3,4,5]

Delivery of education often fails to appropriately meet patient needs.

In the clinical setting, healthcare professionals experience barriers to implementing strategies to adapt education delivery to meet the diverse needs of patients due to low awareness, lack of training and limited resourcing.[6,7] Meanwhile, online patient education resources deliver information that does not align to guidelines and does not meet patient learning needs.[8,9]

To be appropriate for use, patient education materials should provide evidence-based information via diverse communication methods (i.e. written text, graphics, video) with content in plain language (grade 8 or lower).[10,11] Working in partnership with patients, known as co-design, is also recommended because this approach integrates the experiences and needs of patients in the development of educational materials.[12] The need to improve patient education and increase patient engagement to improve BP management has been emphasized recently by key peak bodies including the American Heart Association, American Medical Association, World Heart Federation and Australian Hypertension Taskforce.[10,13,14]

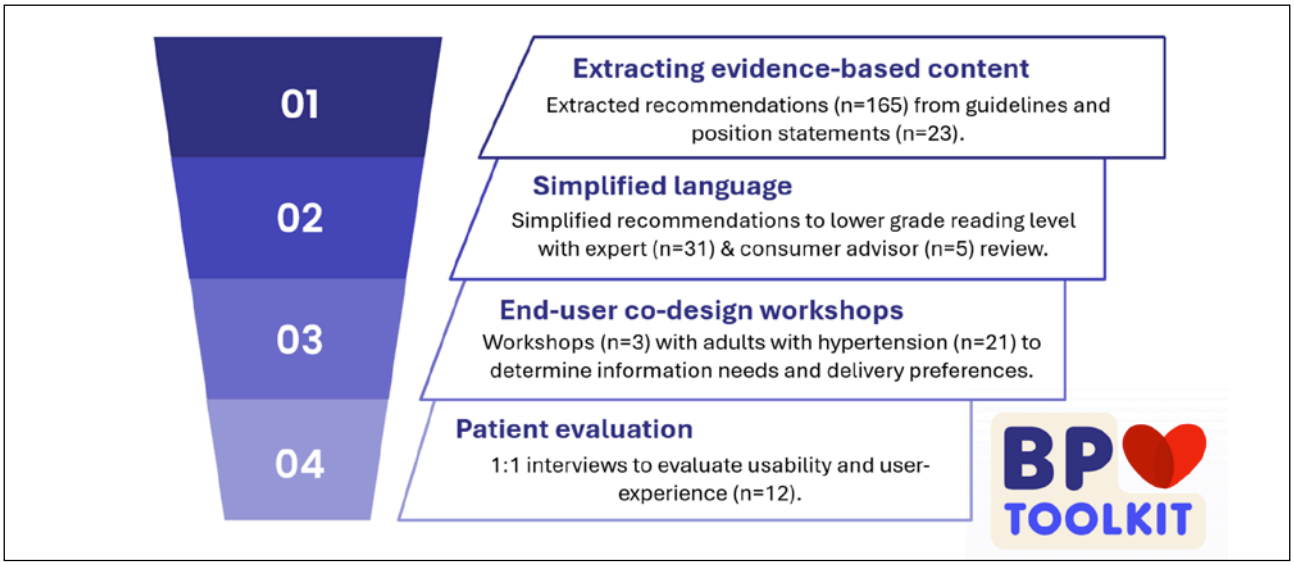
Development of an evidence-based patient education package in partnership with patients.

In 2023 we began development of an educational package for patients to support BP management called the "BP Toolkit" using best-practice co-design methods (**Figure 1**).

Extracting and translating evidence-based content into accessible plain language

Recommendations (n=165) made by guidelines and position statements (n=23) were extracted for inclusion in the BP Toolkit. This evidence-based information covered the following topics: BP thresholds, BP measurement in healthcare settings, BP measurement at home, lifestyle changes and medication usage.

Figure 1. Development of the BP Toolkit.



Each recommendation was simplified to plain language (BP Toolkit content achieves grade 6.4 reading level on average) and reviewed by BP experts and consumer advisors to rank understandability of the statements and agreement in meaning between the plain language statement and the original recommendation using head-to-head comparison.

Workshops to determine how to present BP Toolkit content

Workshops (n=3) were undertaken with patients with hypertension (n=21) according to user-design methodology to determine if the BP Toolkit content addressed patient information needs and to understand how the information should be presented (video, audio, written text, infographics) and delivered (paper-based, website, app).

We found that individual patient information needs were highly varied; depending on specific circumstances, motivation and stage of BP management journey as one's information needs may change over time as patients adapt from initial diagnosis to ongoing management.

Participants had diverse preferences for how the BP Toolkit content should be delivered. Overall, it was important that the BP Toolkit catered for a personalised approach to navigating information and met the unique preferences of patients with different abilities, learning needs and IT skill levels. This included presenting information to support printing at home, complementing content with instructional videos or images, a text-only option to support software aids for people that were hard of hearing, and the ability to move through content at their own pace.

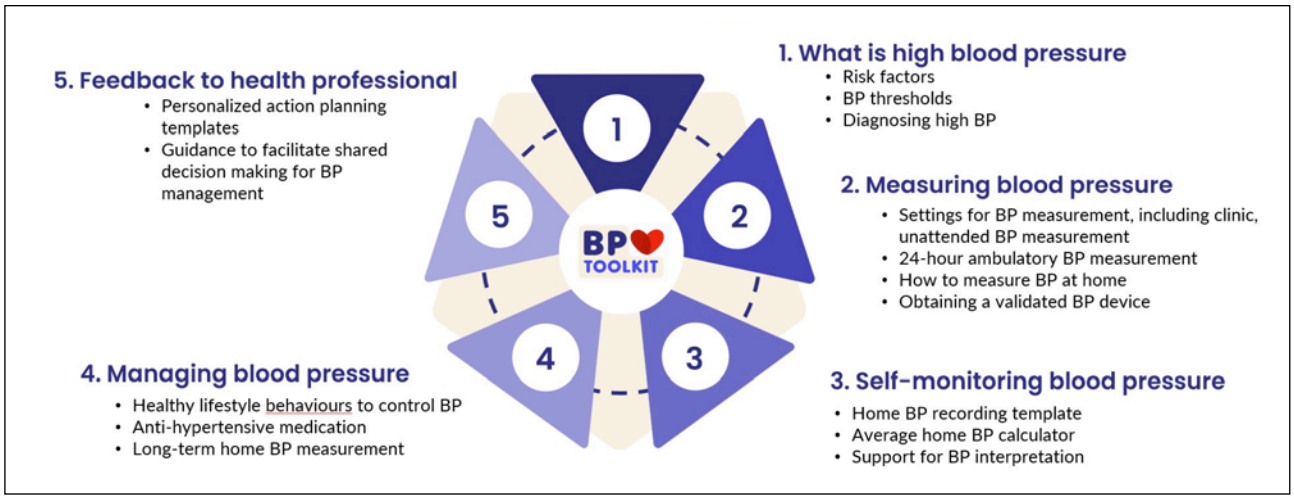


Figure 2. Information for BP management delivered by the BP Toolkit.

Next steps: evaluation, adaptation and implementation

The BP Toolkit will be evaluated through user-testing via 1:1 interviews with patients with hypertension and/or experience of BP management to determine the usability of the website.

Cultural and linguistic adaptation of the BP Toolkit for Chinese-speaking migrant populations in Australia will be undertaken via linguistic translation and workshops to explore if this content meets the cultural and health needs of Chinese migrants.

We plan to explore if the BP Toolkit improves BP control via an individual randomised clinical trial in pharmacy in NSW, Australia. In this trial we will determine if delivery of the BP Toolkit lowers systolic BP among patients taking anti-hypertensive medications with uncontrolled BP.

The BP Toolkit will be regularly updated to incorporate new evidence and recommendations for BP management and address feedback from end-users. Our aim is to achieve widespread dissemination and uptake of the BP Toolkit in healthcare services, community settings and clinical research settings.

Please contact Dr Niamh Chapman (Niamh.chapman@sydney.edu.au) for more information about the BP Toolkit. We would like to thank the University of Sydney, NSW Health and the Foundation for High Blood Pressure Research Australia for providing seed funding to develop to BP Toolkit.

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PERSPECTIVES IN HYPERTENSION

Effectiveness of educational interventions on hypertensive patients' self-management behaviours – findings from an umbrella review

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As a researcher deeply invested in the health and well-being of hypertensive patients, I find it important to evaluate how educational interventions shape self-management behaviours. Hypertension, a global health crisis affecting over 1.28 billion adults, remains one of the primary causes of morbidity and mortality. While pharmacological treatments have advanced, the persistent challenge of uncontrolled hypertension underscores the need for comprehensive management strategies that include educational interventions. My team members and I synthesised and evaluated the effectiveness of educational interventions in enhancing blood pressure control and promoting self-management practices among individuals living with hypertension.

Background and objective

Hypertension management requires an integrative approach where patients actively participate in their care.[1] This includes medication adherence, monitoring blood pressure, maintaining a healthy diet, engaging in physical activity, and avoiding harmful behaviours.[2] However, barriers such as low health literacy, limited support systems, and socioeconomic factors often hinder these efforts. Educational interventions aim to empower patients with knowledge and skills to overcome these barriers and sustain self-care behaviours.[3] In this umbrella review, we synthesised findings from 21 systematic reviews to evaluate the effectiveness of educational interventions on self-management practices and blood pressure control.

Methods

Our study adhered to a rigorous methodology, including a comprehensive search across six databases from their inception to December 2024. We have published the protocol for this review.[4] We included systematic reviews that examined educational interventions targeting adults with hypertension. Interventions included diverse delivery methods such as in-person counselling, group workshops, digital platforms, and community-based programs. Outcomes of interest focused on self-management practices, blood pressure control, and health-related quality of life.

Key findings

From the 21 systematic reviews encompassing over 360,000 participants and 716 primary studies, we observed diverse strategies and outcomes (**Table 1**):

Blood pressure control

Educational interventions showed moderate success in improving blood pressure control. While interventions focused solely on education often lacked clinically significant blood pressure reductions, integrating these with other strategies, such as digital tools or peer support, yielded better outcomes. Salt reduction programs combined with educational efforts showed measurable reductions in systolic and diastolic blood pressure.[5]

Table 1: Key findings from included reviews

First Author/ Publication Year	Key Findings
Gorina et al 2018	Improving chronic disease management in people with long-term conditions has proven to be essential for building coping skills and delaying disease progression.
Kengnea et al 2024	Non-pharmacological interventions utilized in support of medication adherence can be crucial when used alongside pharmacological therapies to treat chronic diseases.
Schroeder et al 2010	The review confirmed that most interventions do not appear to lead to large improvements in adherence and BP reductions.
Guzman-Tordecilla et al 2019	The review provides evidence that there is no single strategy that increases pharmacological adherence. Nevertheless, the review identified that all strategies that improve adherence include 'accompanying processes' on patients to utilize their medicines.
Chen et al 2019	Findings from the review showed that BP levels in older adults with HTN exposed to health education were lower than those in care groups, using systolic and diastolic blood pressures as metrics.
Pasha et al 2021	Several studies were excluded because they did not detail BP before and after the intervention or did not provide information on the number of patients.
Yuan et al 2019	Community pharmacy services have significant positive clinical outcomes, particularly in reducing systolic blood pressure, DBP and HbA1c
Santschi et al 2014	Pharmacist interventions improve BP control in outpatients compared with usual care.
Schroeder et al 2004	The study concludes that the simplification of dosing regimens could be the most promising intervention to improve medication adherence. It also concludes that evidence on the effectiveness of motivational interventions was inconclusive.
Radhakrishnan 2012	The review showed that tailored interventions may not be more effective than standard interventions in improving self-management behaviours in individuals with long-term conditions such as hypertension, asthma and diabetes.
Mills et al 2017	Multilevel, multicomponent strategies followed by patient-level strategies are most effective in BP control among hypertensive patients.
Aliasgharzadeh et al 2022	Results of the meta-analysis suggest that salt substitution and nutrition education are effective strategies for lowering systolic and diastolic blood pressure.
Israfil et al 2022	Results of the study found that health education interventions via mobile devices increase patient knowledge, monitor blood pressure, as well as increase medication adherence and ultimately facilitate BP control.
Fahey et al 2006	This review shows that a rigorous approach in terms of follow-up and treatment with antihypertensive medications could be translated to reductions in cardiovascular mortality. The use of educational interventions alone is unlikely to cause any clinically significant reductions in BP.
Garcıa-Lizana & Sarria-Santamera 2007	The conclusion of this review was that the benefit of controlling chronic diseases with the use of information and communication technology (ICT) is limited.
Jin et al 2020	Salt reduction by salt substitutes had abundant high-quality evidence on the effect of lowering BP among Chinese adults, particularly in patients with hypertension.
Glynn et al 2010	Antihypertensive drug therapy should be implemented by means of a vigorous stepped-care approach when patients do not reach target blood pressure levels. Self-monitoring is a useful adjunct to care while reminder systems and nurse/pharmacist-led care require further evaluation.
Ebrahim & Smith 1998	Non-pharmacological lifestyle interventions are difficult to test in RCTs because the techniques used in drug trials to improve internal validity (i.e. double-blinding, standardization of intervention) are not possible.
Xun et al. 2023	Findings suggest that behavioural change interventions centred on salt reduction can effectively lower salt intake levels and decrease blood pressure levels. However, to enhance effectiveness, behavioural interventions for salt reduction should be combined with other salt-reduction strategies
Krishnamoorthy et al. 2018	To conclude, peer support intervention is effective and causes clinically and statistically significant reduction in HbA1C and SBP levels and helps in achieving better control status among DM and HTN patients.
Tan et al. 2019	Education that was conducted at home showed better medication adherence than education conducted in clinics. Medication adherence was improved after two to three sessions, but no significant differences were found after three sessions.

Medication adherence

One of the critical challenges in hypertension management is medication adherence. Simplifying medication regimens and enhancing patient understanding through education improved adherence rates. Mobile health (mHealth) education further bolstered adherence and facilitated regular blood pressure monitoring.[6]

Lifestyle modifications

Behavioural interventions targeting lifestyle changes, such as dietary adjustments, physical activity, and stress management, were effective. Programs emphasising salt reduction significantly lowered blood pressure levels, particularly when combined with other supportive strategies like peer-led initiatives.[7]

Delivery modes and contextual factors

Delivery methods significantly influenced intervention success. Home-based education yielded better adherence compared to clinic-based programs. Digital platforms and telehealth services emerged as promising tools for scalability and accessibility, especially in resource-constrained settings. Culturally tailored interventions were particularly impactful, aligning content with the values and beliefs of target populations.[8]

Peer and community support

Peer-led interventions demonstrated substantial benefits in fostering behaviour change and achieving clinical outcomes, including BP reduction. Community-based programs emphasised the importance of involving local leaders and culturally relevant materials to enhance engagement.[8]

Challenges and limitations

Despite the promising findings, several challenges persist. Some of the challenges include heterogeneity of interventions such as variability in design, delivery, and evaluation metrics complicating evidence synthesis and comparison. Additionally, only a few studies included long-term follow-up, restricting insights into the sustained impacts of these interventions. Findings from our study showed that certain demographic groups, such as low-income populations and ethnic minorities, were underrepresented, limiting generalisability.

Implications for practice and policy

To maximise impact, educational interventions should be integrated with pharmacological treatments and multilevel strategies targeting individual, community, and systemic factors. Policymakers should prioritise investments in digital health technologies to enhance reach and efficiency. Training programs for healthcare providers can further empower them to deliver effective educational content.

Conclusion

Educational interventions hold transformative potential in addressing hypertension's critical challenges. By enhancing self-management behaviours, improving medication adherence, and fostering sustainable lifestyle changes, these programs empower patients to take control of their health. However, the variability in intervention approaches and the underrepresentation of certain populations call for further research to refine, standardise, and ensure inclusivity. We are optimistic that integrating these insights into practice will drive meaningful improvements in hypertension management.

This article is based on work from the following individuals:

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PERSPECTIVES IN HYPERTENSION

Hypertension prevalence, health policy and guidelines across nine countries in Africa in 2024

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Hypertension is a global burden that increases mortality from cardiovascular and kidney diseases. In 2019, the prevalence of hypertension reached 1.3 billion worldwide.[1] The prevalence of hypertensive heart disease (HHD) has also risen globally and was the main cause of 1.16 million deaths and 21.5 million disability-adjusted life years (DALYs) in 2019.[2] In Africa, the cumulative estimated prevalence of hypertension is 27.0%.[3]

According to the Global Burden of Disease (GBD), the prevalence of CVD and DALYs almost doubled. The number of CVD deaths increased steadily from 12.1 million to 20.5 million from 1990 to 2021.[4] Around two-thirds of cardiovascular deaths occur in low- and middle-income countries where delays in diagnosis and incomplete and interrupted treatment of hypertension can lead to poor health outcomes and premature deaths.[1]

Hypertension management in Africa faces significant challenges, including low awareness, limited access to healthcare, overburdened health systems, workforce shortages, unaffordable medications, and non-adherence to treatment plans.[5]

We searched nine African countries in 2024 to assess the pillars of the hypertension control program and guideline mapping versus the estimated hypertension prevalence. Our main objective was to map the hypertension-related health policies versus hypertension prevalence in Eswatini, Ethiopia, Ghana, Kenya, Malawi, Nigeria, Somalia, South Sudan, and Sudan. Our specific objectives were to map the hypertension control programs within nine African countries, to contrast the findings of the mapped hypertension programs with the estimated hypertension prevalence from the GDB-2019 study, and to compare the findings across the study countries.

We conducted a scoping review and meta-analysis for the nine African countries mentioned above. An expert from each country was enrolled in a panel; a structured tool was used to map the pillars of the hypertension control program versus the estimated hypertension prevalence in the countries from the Global Burden of Disease study. Analysis was done using content analysis, percentages, and Spearman's corrélations.

Our results indicated that hypertension prevalence (both genders) varied from 27% in Ethiopia to 43% in Eswatini. Females had a higher prevalence than males (30% in Ethiopia to 47% in Eswatini) suggesting gender-specific risk factors or disparities in healthcare access/utilization.

Sudan had the second highest prevalence at 44%, following Eswatini. However, Eswatini implemented blood pressure control measures, unlike Sudan. High prevalence was also found in countries with functional policies (Eswatini, Kenya, Nigeria, South Sudan), suggesting the urgent need for improvement in healthcare delivery, policy enforcement, and addressing other risk factors. Ghana and Somalia had lower hypertension prevalence, though fewer policies. Kenya, Nigeria, and Ethiopia leverage trained non-physician community health workers in hypertension management, more than Somalia

and Sudan, thereby improving treatment access and adherence. Negative correlations were found between national responses and hypertension prevalence. The treatment guidelines, based mainly on international guidelines, were moderately negatively correlated with hypertension prevalence.

There needs to be more than the mere presence of guidelines as in Kenya, and Malawi. Kenya did not have a specific blood pressure response, which might suggest the need for more targeted interventions. Salt Intake Surveys also had a negative correlation with hypertension prevalence, highlighting countries like Ethiopia and Nigeria with salt intake surveys and lower prevalence, reinforcing the effectiveness of dietary factors in managing hypertension. These findings highlighted the multifaceted nature of hypertension and the disparities in hypertension control programs in the studied African countries which require a comprehensive approach encompassing considerations of gender, socioeconomic factors, lifestyle, salt reduction, policy implementation, healthcare access, and a unified African hypertension guideline. Favorable outcomes necessitate alignment of all the activities to create a successful program.

Figure 1: Heatmap illustration for both health system pillars and the prevalence of hypertension, the age-standardized prevalence (30-70 years) per 100,000 was transformed into categories; high, moderate, and low and denoted 3,2, and 1 for visualization purposes.

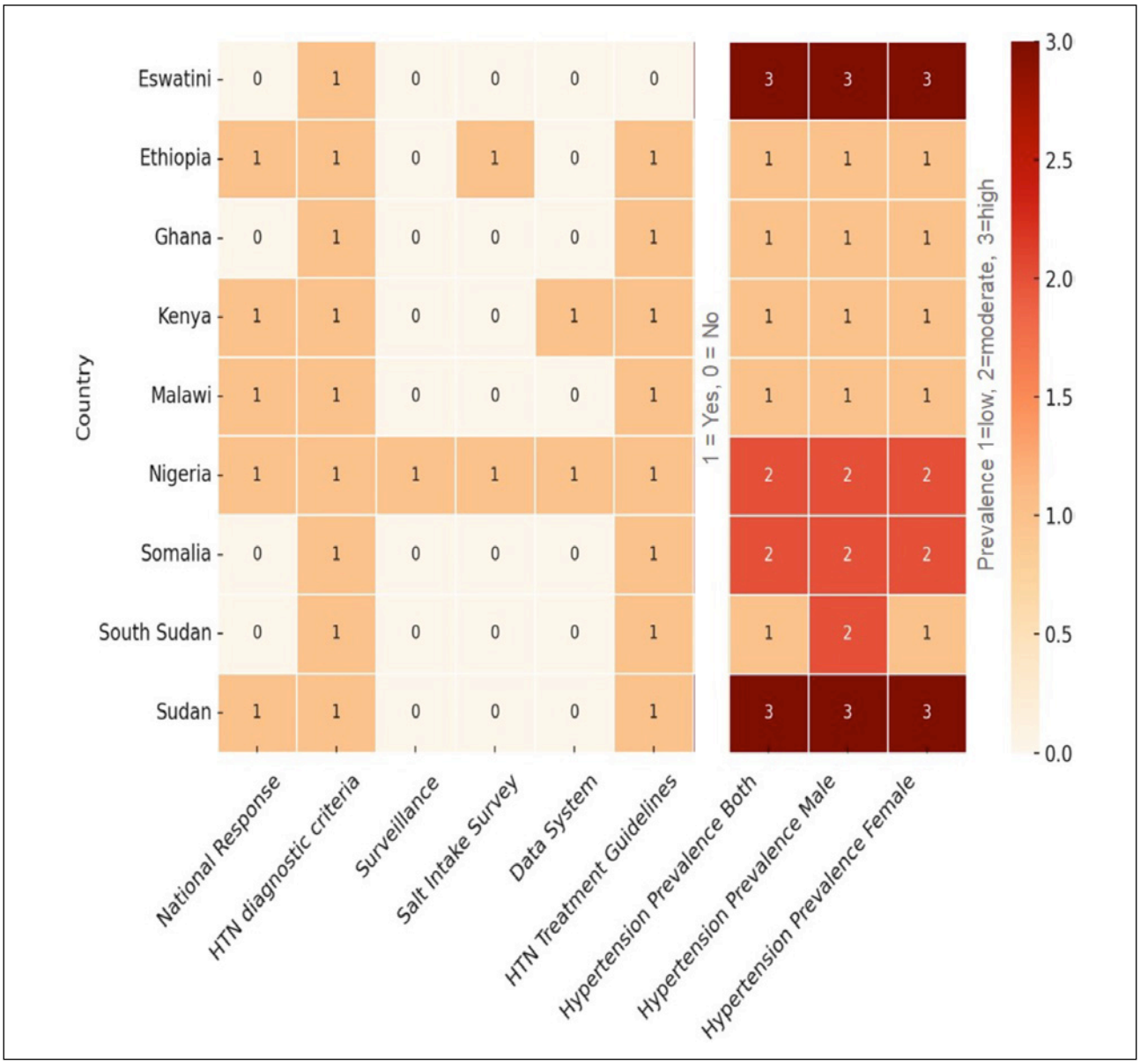
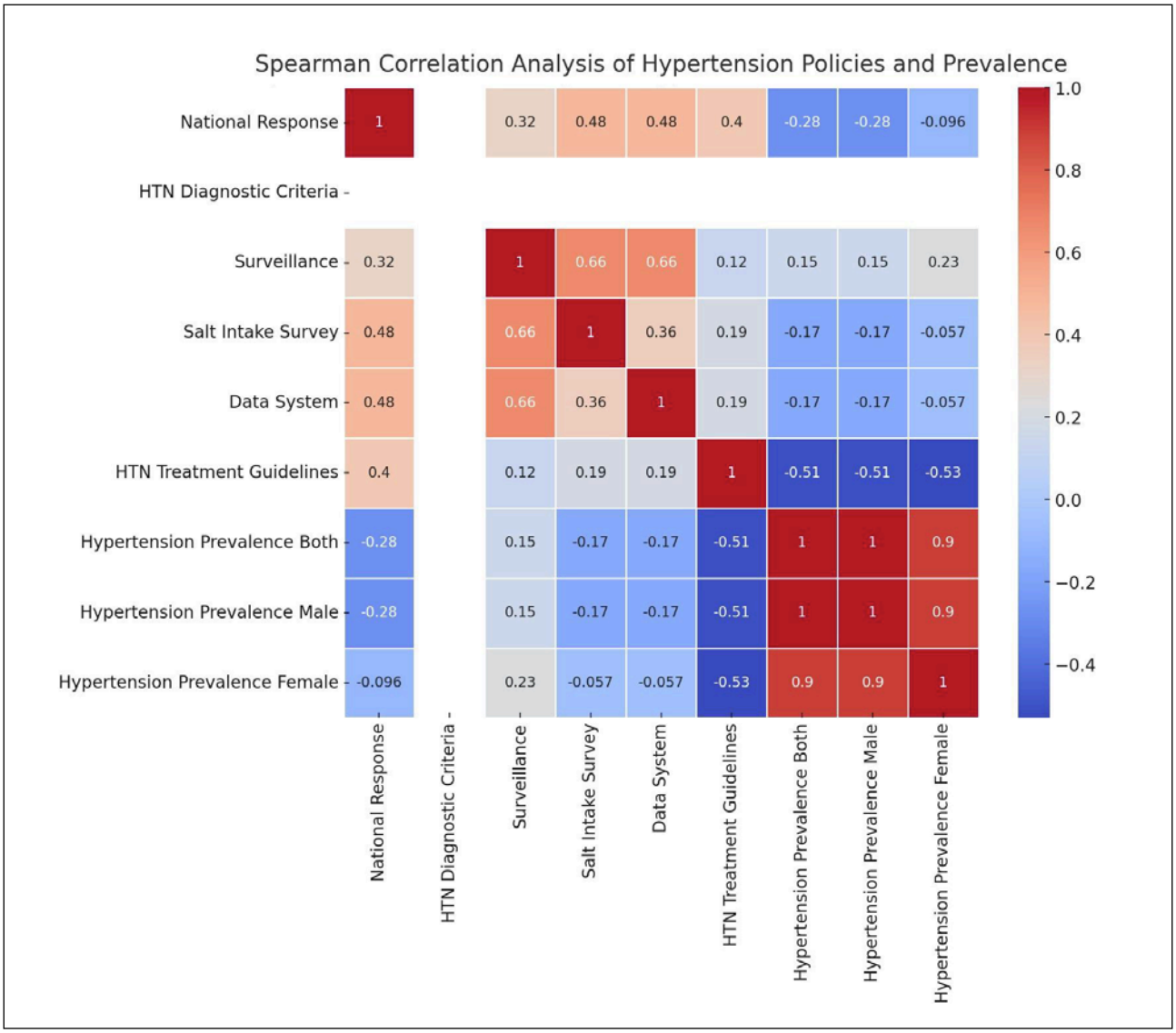


Figure 2: Spearman's correlation matrix



This scoping review provides insight into and compares outcomes of hypertension control strategies and their impact on the prevalence of hypertension in nine African countries.

Our recommendations include:

- System-thinking approach: this should be used in the development of all hypertension control modules and activities.
- Cultural and socio-economic risk factors: special attention must be paid to risk factors such as gender disparities in hypertension in Africa.
- Innovative and collaborative programs: regional, national, and international efforts should be made to improve knowledge and experience sharing and fast-track the implementation of programs such as the WHO HEARTS technical package and the World Hypertension League Call to Action to improve detection, monitoring, and treatment strategies in Africa by 2030.
- Engagement of African communities through health-promoting environments that promote hypertension risk factor control practices such as reduced salt consumption, obesity control, and general lifestyle improvements.
- Training non-physician community health workers: this can improve treatment access and adherence in hypertension management.
- Implementation of the ISH Pan African Hypertension Guideline: – a project currently in development which intends to be a version of the ISH guidelines specifically for Africa.

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PERSPECTIVES IN HYPERTENSION

Harnessing demographic diversity in hypertension research and trials

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Global public health initiatives such as the May Measurement Month campaign and novel out-of-clinic blood pressure (BP)-measuring technologies are becomingly increasingly available enabling earlier detection of high BP. In addition, novel BP-lowering technologies such as Zilbesiran ribonucleic acid interference therapeutic agent and catheter-based renal denervation procedure have emerged as adjunctive treatment options for patients in whom lifestyle modifications and high-intensity antihypertensives medications do not adequately reduce BP. Nevertheless, cardiovascular risk conferred by suboptimal BP management remains high.[1] Concerningly, the extent of BP treatment and control are markedly heterogeneous across sex, age, race/ethnicity, socioeconomic status, or underlying comorbidities even within a narrowly-defined population.[2]

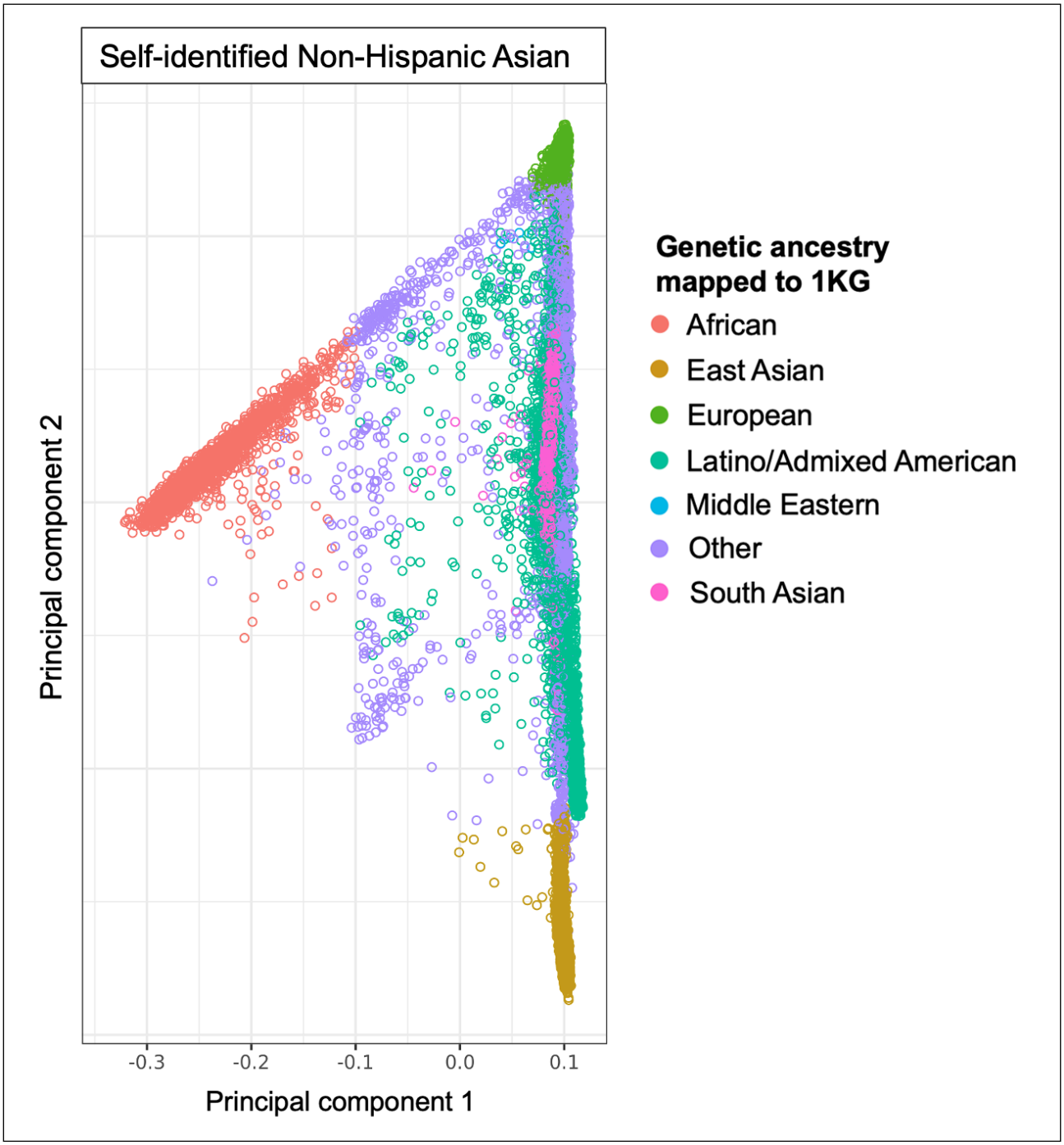
To facilitate timely, sustained, and safe management of high BP, clinical practice guidelines undergo periodic updates based on meta-analysis of novel and accumulated randomized controlled clinical trials and rigorous inspection of observational study findings. However, in some circumstances, the evidence from event-based trials is unavailable for treatment decision-making in certain demographic or clinical populations. Such is the case for populations of heterogeneous demographic background.

Inclusion in biomedical cohort and event-based trials has historically been disproportionate across sociodemographic and clinical characteristics contributing to systemic disparities in evidence-based health care.[3] Consequently, clinical trials and epidemiologic studies often rely on oversampling, model recalibration, or broad generalization and are interpreted within limited context and applicability.[4] However, these are incomplete attempts to capture substantial heterogeneity in treatment effect[5] as well as distributions of multilevel risk factors – ranging from physical and structural environment, healthcare utilization, to lifestyle, and genome-wide variation – that affect BP management.

A notable recent effort to mitigate persistent disparities in hypertension knowledge gaps include delineating the distinct epidemiology and contribution of elevated BP to cardiovascular outcomes across Asian subgroups. The Asian population is generally presumed to be with low cardiovascular risk compared to other racial or ethnic populations. Nonetheless, the frequently used "Asian" category masks a substantial gradient of hypertension prevalence across major subgroups[6], ranging from 34% among Chinese and Korean to 43% among South Asian immigrants residing in the U.S.[7]; even in native populations, 68% of native South Asian adults with either undetected or untreated hypertension compared with 44% of East Asian adults.[2]

The recent work6 on disaggregating East- and South Asian-specific BP trajectory demonstrates an early divergence of BP levels with both self-identified and genetically-inferred South Asian

Figure 1. Heterogeneity of genetic ancestry within a self-identified non-Hispanic Asian category in All of Us

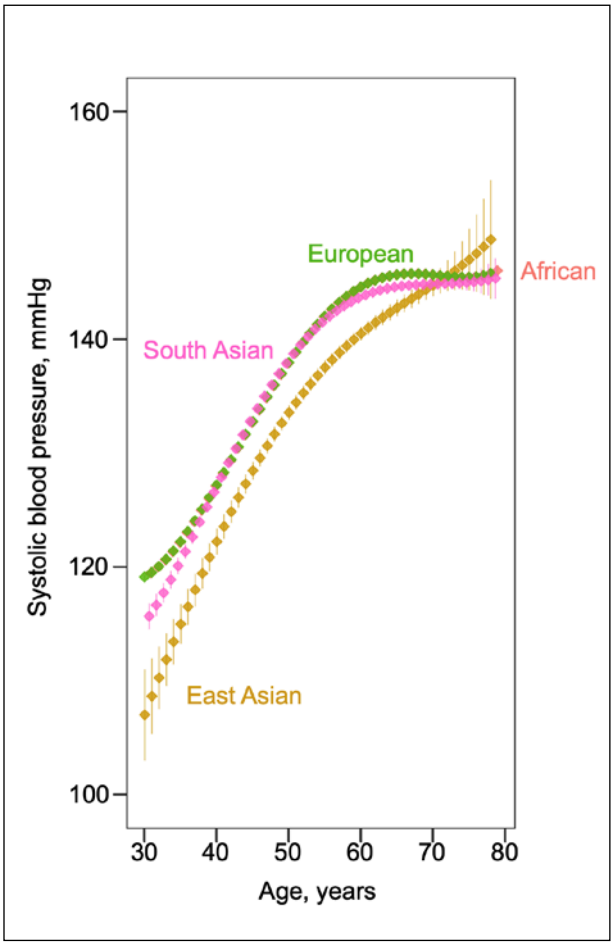


individuals having more premature and rapidly increasing BP compared with the East Asian population. Additionally, the between-group BP differences were most evident during young adulthood in men compared to midlife in women. With South Asian individuals undergoing more premature and accelerated BP elevation, young adulthood BP was significantly associated with lifetime atherosclerotic cardiovascular disease. On the other hand, East Asian individuals exhibited lower and delayed age-associated BP increase with midlife BP strongly predictive of lifetime stroke risk. Given Asian subpopulation-specific BP patterns and their age-differential associations with cardiovascular disease, the study informs opportunities to tailor BP screening and treatment initiation timing across individuals of different self-identified and genetic ancestry.

Dedicated initiatives such as the United States' National Institutes of Health's All of Us Research Program[8] or the Multi-ethnic Observational

Study in American Asian and Pacific Islander Communities (MOSAAIC)[9] are emerging to study longitudinal expression of BP phenotype as well as genomic and contextual BP markers in underrepresented populations. In conjunction, contemporary pharmacogenomics focuses on the identification of potent BP-related variants or candidate genes responsible for inter-individual variability in response to antihypertensives. In the context of precision medicine, such efforts can correct long-standing bias resulting from disproportionate representation, timing of preventive strategies, uncover heterogeneous antihypertensive treatment effects to maximize benefit-to-harm for each unique individual, and equitably prioritize future clinical trial candidates.

Figure 2. Early divergence of lifetime blood pressure trajectory across genetic ancestry groups in UK Biobank



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PERSPECTIVES IN HYPERTENSION

Hydrostatic pressure: another missing link in accurate blood pressure measurement

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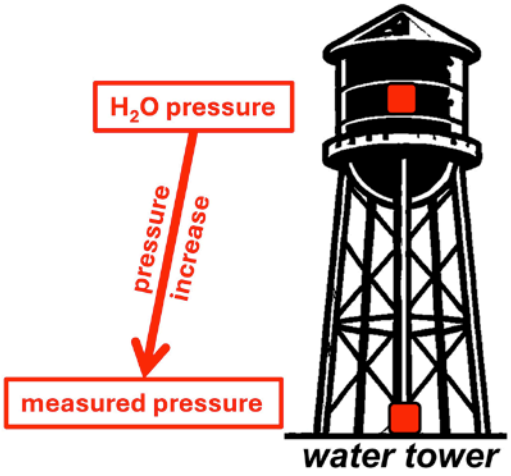
For years, I have been troubled by the limitations of our conventional blood pressure (BP) measurement techniques.[1] Emerging evidence has made it clear that failing to account for hydrostatic pressure differences – changes in pressure caused by the vertical distance between the BP measurement cuff and the heart – can lead to significant misclassification of hypertension and an misinterpretation of cardiovascular risk.[2,3]

In our recent study published in Hypertension Research, my colleagues and I examined how body position affects ambulatory BP (ABPM) measurements. We discovered that when a patient lies on their right side, the BP cuff is frequently positioned above the heart. This creates a negative hydrostatic pressure, averaging nearly –10 mmHg, which causes a notable underestimation of the true BP. When we corrected for this hydrostatic effect, 27.5% of subjects were reclassified regarding nocturnal hypertension, and 37.3% experienced changes in their dipping patterns—affecting almost half of the participants. In short: changes in body position during ABPM lead to substantial changes in diagnostic evaluation.[2]

In parallel, a large-scale prospective study published in JAMA Cardiology provided equally compelling evidence from another angle. This study, involving over 11,000 middle-aged adults, demonstrated that supine office BP measurements (OBPM) are more closely linked to adverse cardiovascular outcomes than seated measurements. Remarkably, even when seated BP was normal, the presence of supine hypertension was associated with increased risks of coronary heart disease, heart failure, stroke, and mortality.[4]

This study challenges the decade-old reliance on seated OBPM as gold-standard for initial BP assessment. Even beyond that, it poses questions on why supine OBPM may (!) be superior to seated OBPM. Potentially, and in my opinion most likely, the effect of eliminating the hydrostatic difference between the heart and the arm is crucial. Whilst measurements are supposed to be conducted in accordance with the best practice guidelines for BP measurement – arm positions are often not ideally standardised.[5,6] This is evermore so true for measurements conducted outside of clinical study settings.

The clinical implications are clear and urgent: There are uncounted patients whose cardiovascular risk profiles do not match their seated blood pressure readings. It is now apparent that failing to account for hydrostatic pressure differences can mask (or induce) underlying hypertension and lead to inappropriate risk stratification. For clinicians, this means rethinking how we measure blood pressure in both the office and ambulatory settings. For clinician researchers, this now creates an impetus to provide more conclusive data. Adjusting for hydrostatic pressure is not an academic nicety – it appears to be a practical necessity that can improve diagnostic accuracy and patient outcomes. In the medium-term, the international societies will have to have the uncomfortable conversation of whether the long-trusted OBPM practice recommendations need to be rethought.



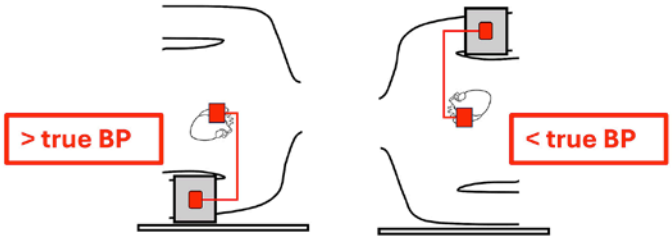


Figure 1 - Hydrostatic Pressure: The left side of the figure shows a water tower, highlighting the difference in hydrostatic pressure between the reservoir and the measurement point at the bottom of the tower. The right side of the figure highlights the same effect between the true BP (at heart level) when the measurement point (cuff, grey) moves above or below the heart level. The picture is partly adapted from.[2]

Technological advances offer a direct solution to this problem. I envision a new generation of blood pressure monitors equipped with posture-detection sensors that automatically adjust readings based on the relative position of the cuff to the heart. This is especially attractive for ABPM (and potentially home BP measurement) settings, where standardisation is impossible.[3] By integrating such corrections, devices could standardize measurements across different settings, ensuring that the values obtained truly reflect arterial pressure rather than artifacts of body position. At the same time, it will allow us researchers to investigate whether and how we need to adjust for this effect. All the while, we need to communicate the importance of hydrostatic pressure to our patients; and our colleagues who treat them.

When putting the insights of all these novel studies together, I feel compelled to at least consider a shift in our paradigm of BP measurement. In an era in which the push for individualised precision medicine is palpable everywhere, our field cannot cling to 20th century measurement beliefs if there is compelling data posing more and more questions. Without ensuring the accuracy of our diagnostic tools, precision medicine is impossible. Embracing technological solutions not only refines our measurements but also guides more effective treatment decisions, ultimately saving lives.[7]

I am committed to making that future a reality – let's make it happen together.

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PERSPECTIVES IN HYPERTENSION

Need to know in hypertension: Exploring the central regulation of hypertension

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Brain pathways controlling arterial pressure are distributed throughout the neuroaxis in topographically selective networks. The medulla oblongata, a key region in arterial pressure regulation, the nucleus tractus solitarius (NTS) is the primary site for integrating cardiorespiratory reflexes. Lesions or disturbances in the NTS can elevate arterial pressure (AP), and recent studies reveal two distinct neuronal subpopulations within the NTS that influence AP in opposite ways. Commissural NTS neurons, located along the midline, may contribute to hypertension maintenance, as small lesions in this area significantly reduce AP. Additionally, two regions of the ventrolateral medulla—the caudal (CVLM) and rostral (RVLM)—play a crucial role in blood pressure regulation. CVLM neurons receive baroreceptor inputs and send inhibitory projections to the RVLM, which helps regulate sympathetic outflow. The absence of this inhibition may contribute to hypertension development. Meanwhile, the RVLM is essential for tonic and reflexive AP regulation. Experimental models of hypertension show that RVLM neurons receive increased excitatory inputs, leading to heightened sympathetic activity—an essential factor in the development and maintenance of hypertension. Essential hypertension affects millions globally, and while the sympathetic nervous system's role in arterial pressure control is clear, its exact contribution to hypertension remains debated. Clinical and experimental evidence suggests increased vascular resistance as a key factor in hypertension, raising the question of whether neural or humoral factors initiate the condition. Recent findings emphasize the importance of neural mechanisms, particularly those in the medulla oblongata, in driving and sustaining hypertension.[1]

Historically, hypertension treatment in the 1930s and 1940s was largely surgical, focusing on interrupting sympathetic pathways through splanchnic nerve interruption or sympathetic chain removal. These procedures led to the development of pharmacological approaches that mimicked surgical sympathectomy, rendering surgery obsolete. However, the idea of sympathetic nervous system involvement in hypertension has persisted, reinforcing the need to further explore central neural mechanisms in blood pressure regulation. Overall, I must highlight the significant role of the medulla oblongata in essential hypertension. By integrating baroreceptor and sympathetic inputs, regions such as the NTS, CVLM, and RVLM are central to arterial pressure control. Emerging evidence supports a renewed focus on the neural contribution to hypertension, emphasizing that increased excitatory drive within brainstem circuits may be a critical factor in its development and persistence.[1]

As a researcher in the field of neurovascular regulation, I have always been fascinated by the complex interplay between central neural circuits and cardiovascular function. One crucial area of interest is the nucleus of the solitary tract (NTS), particularly its commissural subdivision (cNTS), which has emerged as a key player in the central regulation of hypertension. Several works from my laboratory and others have significantly contributed to our understanding of how the cNTS integrates and

processes baroreceptor and chemoreceptor signals, ultimately influencing autonomic outflow and cardiovascular homeostasis. We have demonstrated that the cNTS is not merely a passive relay station but actively participates in modulating sympathetic and parasympathetic activity. This modulation occurs through intricate synaptic connections with the rostral ventrolateral medulla (RVLM), the paraventricular nucleus of the hypothalamus (PVN), and other brain regions implicated in blood pressure regulation. A fundamental aspect of cNTS function is its neurochemical environment. Our and other's studies have shown that glutamatergic and GABAergic neurotransmission within the cNTS critically influences autonomic output. Excitatory glutamatergic signalling enhances baroreflex sensitivity, whereas inhibitory GABAergic input suppresses it, potentially contributing to hypertension in conditions where this balance is disrupted.

One particularly intriguing aspect of my work involves the role of nitric oxide (NO) and angiotensin II (Ang II) within the cNTS. NO is a well-known vasodilator that facilitates baroreflex function, whereas Ang II has sympathoexcitatory effects that may contribute to the pathogenesis of hypertension. Indeed, I suggest that alterations in the NO-Ang II balance within the cNTS could be a key factor in the development and maintenance of high blood pressure. Experimental models of hypertension have provided valuable insights into how cNTS dysfunction contributes to increased sympathetic drive. In hypertensive animals, there is often a reduction in inhibitory neurotransmission and an increase in excitatory input within the cNTS, leading to sustained sympathetic activation and elevated blood pressure. This central dysregulation suggests that targeting cNTS pathways could be a promising therapeutic strategy.[2] Understanding the precise mechanisms by which the cNTS influences neurovascular control has far-reaching implications. Pharmacological interventions aimed at restoring the excitatory-inhibitory balance within this nucleus could offer novel treatment avenues for hypertension.[3,4] Additionally, emerging neuromodulatory approaches, such as optogenetics and deep brain stimulation, hold

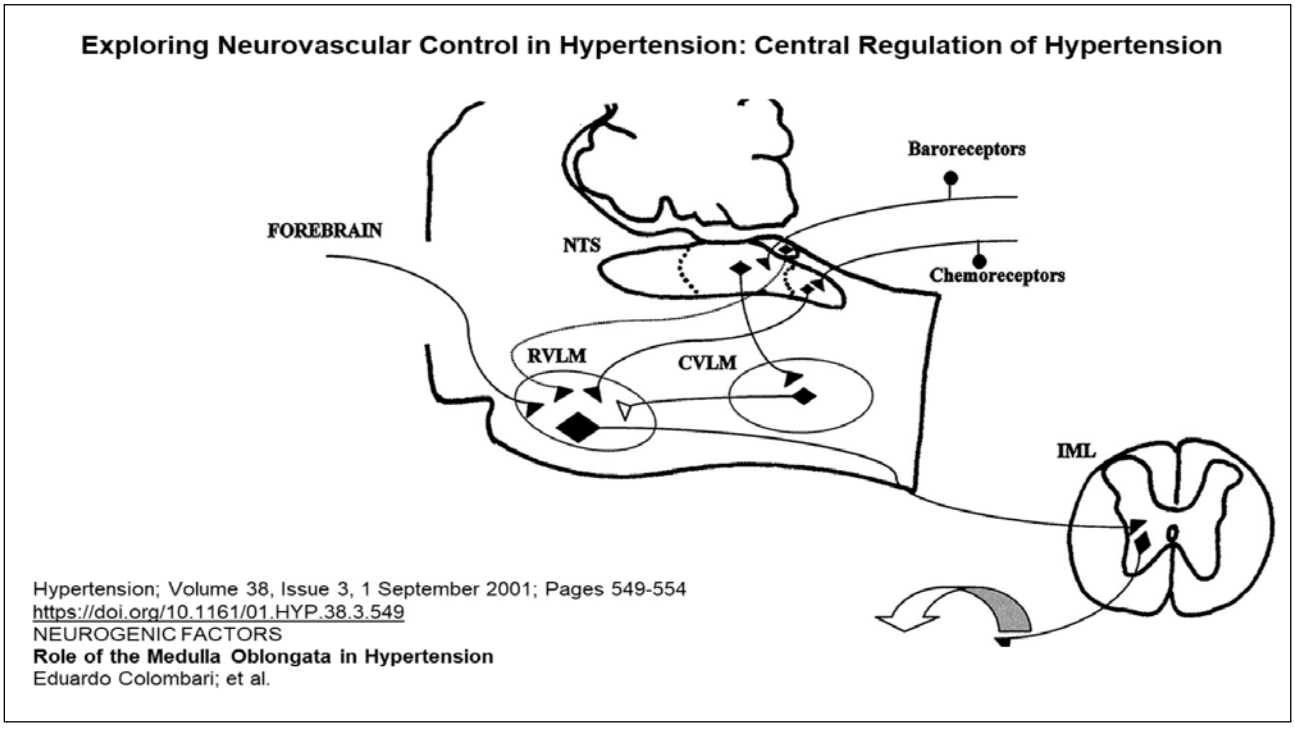

Figure 1: Schematic sagittal view of the medulla oblongata depicting neural pathways involved in neurogenic hypertension. Premotor neurons of the RVLM provide excitatory drive to preganglionic neurons in the intermediolateral cell column (IML), which provide sympathetic output to target organs. RVLM neurons receive excitatory inputs from (1) forebrain structures, (2) commissural NTS, and (3) area postrema, and inhibitory inputs from the CVLM. The intermediate and commissural NTS represent the primary site of projection of afferent fibers arising from baro- and chemoreceptors. Increased excitatory inputs and/or decrease of inhibitory inputs result in enhancement of RVLM activity, thus increasing sympathetic output, a common feature of different forms of hypertension.

potential for selectively modulating cNTS activity to achieve blood pressure regulation. See schematic representation of the medulla oblongata circuit (**Figure 1**).

As a mechanical result of hypertension, the central nervous system inside the cranium is also affected by shear stress increased within cerebral vascular system. In a recent study we could observe the lack of the blood brain barrier at the initial phase of the renovascular hypertension in animal model. Briefly, the mechanisms by which changes in intracranial pressure (ICP) occur during hypertension are unclear. The experimental 2K1C (2-kidney, 1-clip) hypertension is a model characterized by sympathetic and renin-angiotensin system overactivation in which ICP still needs investigation. We analysed ICP alterations during the development of 2K1C hypertension using invasive and non-invasive ICP recording methods. We also tested the importance of AT1R (angiotensin II type 1 receptor) activation for the ICP changes and investigated the integrity of the blood-brain barrier within central cardioregulatory nuclei in 2K1C hypertensive rats. 2K1C hypertension was induced in 6-week-old male rats (150 g). In the fourth week of 2K1C hypertension induction, when mean arterial pressure reached 162±2 mm Hg, ICP significantly increased, ICP pulse waveforms changed, increasing the ratio between the two peaks (P2/P1 ratio) of the ICP waveform. In the third week of 2K1C hypertension induction, blood-brain barrier disruption was detected within the hypothalamic paraventricular nucleus, rostral ventrolateral medulla, and nucleus tractus solitarius. In the sixth week, intravenous losartan (AT1R antagonist) or the vasodilator hydralazine acutely reduced arterial pressure to normotensive levels. Losartan, but not hydralazine, partially reduced the increase of ICP and P2/P1 ratio in hypertensive rats.[5] These results show significant changes in ICP in 2K1C hypertensive rats and suggest that AT1R activation may contribute to elevated ICP during hypertension—an effect possibly intensified by the blood-brain barrier disruption in important central cardioregulatory nuclei in renovascular hypertensive animals (See **Figure 2**[5]).

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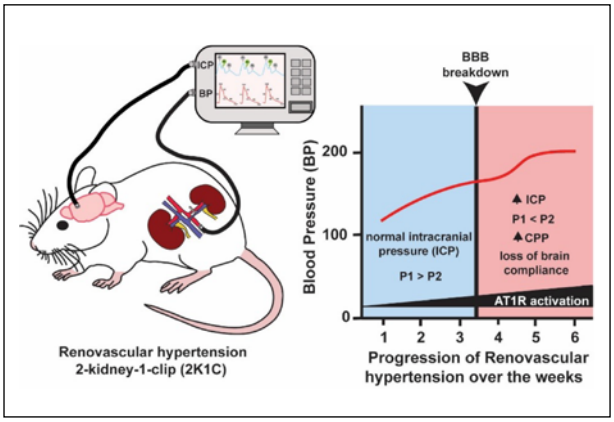

Figure 2: Intracranial Pressure During the Development of Renovascular Hypertension. Fernandes, MV; ... Colombari, E. Hypertension. 2021; 77:1311-1322.

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FROM THE NEWS DESK

ISH/ESH 2028: ISH and ESH to host joint 2028 Scientific Meeting

George Stergiou (ISH President) and Thomas Weber (ESH President) announced in January 2025 that the ISH and ESH will hold a joint Scientific Meeting in 2028 in Europe, in the tradition of several successful joint meetings in the past.

We are now in the process of considering bids to host the meeting. Find out how you can bid. (Deadline: 31 March). Dates and details will be announced in due course.

In the meantime, the next ISH Scientific Meeting will take place in Dubai from 22 to 25 October 2026.

Save the date, and watch this space for more details soon!

Two ISH Collaboration Exchange Scholarships of 5,000 USD awarded to ISH members

Two early career investigators have each been awarded ISH scholarships worth USD 5,000 to develop international collaborations which began at the 2024 ISH Scientific Meeting.

For the **Collaboration Exchange Scholarships** – launched by the ISH Capacity Building Network (CBN) – both awardees will be hosted by more established researchers who will support joint activities in 2025.

The scholarships were launched to give early to mid-career investigators support to continue collaborations initiated at ISH meetings, which they may not otherwise have the resources to pursue.

The ISH awardees

Arinola Akinnibosun

Federation University, Australia

Continued on next page.

Awarded a PhD in 2024 by Federation University, Australia, has conducted work in genomics, with her research including work on telomere therapy for chronic kidney disease.

She will be hosted for four weeks this year by Prof Ruan Kruger at the North-West University, South Africa. Ruan is President of the Childhood Hypertension Consortium of South Africa (CHCSA). Arinola will contribute to the CHCSA's national blood pressure screening project and genomics research of the childhood projects in the Hypertension in Africa Research Team. She will expand collaboration between groups in the study of childhood hypertension and will help to advance genomics initiatives targeting chronic health issues in African communities.

Caroline Cristina Pinto Souza

São Paulo State University, Brazil

Caroline Cristina Pinto Souza has a bachelor's degree in Biomedical Sciences. She is a PhD student in Biotechnology at the Institute of Biosciences of Botucatu, Department of Biophysics and Pharmacology, São Paulo State University, Brazil. Her research focuses on proteomics and the identification of pharmacological therapeutic targets for preeclampsia.

For the Scholarship, Caroline will be hosted for six weeks in 2025 by Dr. Ana Carolina Palei, Associate Professor at the University of Mississippi Medical Center, USA. Dr. Palei has extensive research experience investigating mechanisms and therapeutic targets in preeclampsia, and Caroline will collaborate with her to identify proteins that may serve as biomarkers for diagnosis, treatment, and prevention in preeclampsia using a proteomics approach in selected tissues of a well-established rat model of this hypertensive disorder of pregnancy – the Reduced Uterine Perfusion Pressure.

Launch of the scheme

The scheme was initiated by Niamh Chapman, co-Chair of the CBN. She said: "ISH meetings provide a platform for networking and the start of collaborations, but early to mid-career researchers can find it challenging to continue these activities after meetings are over, due to a lack of resources. We wanted to address this problem, through targeted funding for early to mid-career researchers to work with more senior investigators."

Buna Bhandari and Ching Siew Mooi, members of the ISH Women in Hypertension Research Committee, who also support the CBN, played a key role in administering the scheme.

Vice President of the ISH Hiroshi Itoh was Chair of the review panel for the scholarship, and said: "The competition among applications for these scholarships was exceptionally strong, and the ISH Reviewer Panel faced a challenge in choosing the eventual recipients. The scholarship proposals from the two successful applicants were outstanding, demonstrating excellence across all evaluation criteria. We look forward to seeing the outcomes of both projects."

George Stergiou, President of the ISH, said: "Congratulations to both awardees. An important mission of the ISH is to help foster collaboration between investigators around the world. These projects are excellent examples of the kind of joint working we want to encourage. It is particularly gratifying to be able to support early and mid-career investigators, and I'd like to thank members of the ISH Capacity Building Network for their work in launching this Collaboration Exchange Scholarship.

ISH COMMITTEE AND AFFILIATED SOCIETY REPORTS

The Chinese Hypertension League guidelines 2024

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The title of the guidelines

The title of the Chinese Hypertension League (CHL) guidelines include two medical keywords, "prevention" and "treatment", and did not use the general term of "management".[1,2] The goal is clear. Prevention targets not only the progression from normotension to hypertension, from normal to abnormal structure and function of target organs, and from subclinical or compensated to clinical or decompensated organ damages or complications, but also the occurrence of any diseases behind blood pressure elevation, as either secondary or primary causes of hypertension. Treatment targets blood pressure control with lifestyle modifications, antihypertensive drugs, and device therapy, interventions for various subclinical and clinical complications, and medical, surgical, and device therapies for various secondary and primary causes of hypertension.

Key aspects of the guidelines

A core concept of the CHL hypertension guidelines 2024 is the prevention and treatment of hypertension according to blood pressure classification, disease severity, and the pathogenesis or pathophysiology of hypertension or mechanisms of blood pressure dysregulation or elevation.[3] The diagnostic threshold for the definition of hypertension is still 140/90 mmHg. The reason is simple and clear. Only at this level of blood pressure and above is there evidence on the benefit of antihypertensive drug treatment. There is no evidence, whatsoever, on benefit of treating those with a systolic/diastolic blood pressure in the range of 130-139/80-89 mmHg, although there is indeed epidemiological evidence of increased cardiovascular risk.

The key issue is the lack of evidence on risk reversibility by current antihypertensive drug treatment. Nonetheless, lifestyle modifications are important for those with high-normal blood pressure. In addition, we continue to classify hypertension into stages 1 to 3, because in China there is still a high prevalence of stage 3 hypertension that requires different treatment from stage 1 and stage 2 hypertension. In this new guideline, both office and out-of-office, either ambulatory or home blood pressure monitoring are recommended for the diagnosis and therapeutic monitoring of hypertension.

The CHL hypertension guidelines recommend comprehensive assessment of target organ damage for the classification of disease severity into three phases, i.e., no damage, subclinical or compensated organ damage, and decompensated organ damage or clinical complications. Renal dysfunction should best be detected at the stage of microalbuminuria and early stages of reduced glomerular filtration rate (GFR). The recommended measurements include urine routine test, albumin excretion by either 24-h urine collection or urine albumin-to-creatinine ratio, and serum concentrations of urea, uric acid, creatinine and cysteine.

Blood pressure control should be intensified in the presence of albuminuria and end-stage renal disease (ESRD), with the proper use of renin-angiotensin system inhibitors, especially the recently approved angiotensin-receptor neprilysin

inhibitors (ARNIs) for hypertension.[4] Cardiac structure and function can be evaluated with electrocardiography (ECG) and various imaging modalities, such as echocardiography, magnetic resonance (MR) imaging, etc., for the early detection of left ventricular hypertrophy (LVH), left atrial enlargement, and systolic and diastolic dysfunction. These findings of cardiac abnormalities also help in the choice of antihypertensive therapy, again the use of renin-angiotensin inhibitors. Brain MR imaging and angiography and carotid and vertebral-basilar arterial ultrasound imaging are increasingly available. Early detection of white matter lesions and abnormalities in the cerebral circulation will provide clue for the prevention of ischaemic and haemorrhagic stroke, which is still the main complication of hypertension in the Chinese population. Several measurements of haemodynamics and large and small arterial properties are widely performed in hospitals in China, such as ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV), flow-mediated dilatation (FMD), central haemodynamics, retinography, etc. However, these measurements are not sufficiently used in guiding antihypertensive treatment, to some extent, because of insufficient evidence and lack of guideline recommendations.

The CHL guidelines recommend treatment of hypertension according to the pathogenesis or pathophysiology of hypertension or at least the mechanisms of blood pressure dysregulation. This principle requires systematic screen for prevalent secondary causes of hypertension, especially those severe and curable diseases, such as primary aldosteronism,[5] obstructive sleep apnoea syndrome (OSAS), renal artery stenosis, various renal parenchymal diseases, and drug-, food- and toxin-induced hypertension.

With the increasing use of advanced imaging and biochemical technologies, there seems an increasing detection of several previously-believed rare causes of secondary hypertension, such as clinical and subclinical hypercortisolism, pheochromocytoma/paraganglioma, primary and secondary hyperthyroidism and hypothyroidism, aortic coarctation, etc. There is also increasing evidence to support the description of pathophysiology or mechanisms of blood pressure dysregulation in the so-called primary hypertension. In the young, metabolic disorders are the most often seen factors that may be the mechanisms of blood pressure dysregulation or elevation. The mechanisms often involve endogenous and exogenous hyperinsulinemia, enlarged central-to-peripheral pressure amplification,[7] and reduced arteriolar lumen-to-wall ratio.

There is now treatment or even cure for these disorders, which is glucagon-like peptide-1 (GLP-1) receptor agonist. In middle-aged people, sympathetic overactivation or autonomous nervous dysregulation plays a crucial role in blood pressure elevation and development of hypertension, usually as the consequence of psychological disorders, such as press, anxiety and depression, under the high pressure of work, life and society. There are several classes of antihypertensive drugs that target this system. That is why the CHL guidelines continue to recommend β-blockers as one class of the primary antihypertensive agents,[6] and possible use of renal denervation in selected patients with resistant or difficult to treat hypertension, especially those with the suspicion of sympathetic overactivation. In the elderly, large arterial stiffness might be a driving factor for blood pressure elevation, either because of vascular hypertrophy, fibrosis, or disseminated calcification. Vasoactive drugs should be preferentially used in the treatment of hypertension in these patients with stiffened arteries.

New approaches and technologies

The CHL guidelines emphasize the importance of technological platforms and recommend the construction of infrastructural and technological platforms. The control of hypertension involves the interaction between hypertension specialists in hospitals and primary care physicians and other health professionals from community health centres. An infrastructure including these different parties has been well established in the developed areas of China.[8]

Technological platforms are playing an increasing role in the control of hypertension.[9] This platform includes a web-based and -linked office and out-of-office blood pressure measurement system, integrated imaging, functional and biochemical measurements for the assessment of structure and function of target organs, including the

kidneys, heart, brain, arteries and retina, and big-data and artificial intelligence (AI)-based phenotyping according to causes of hypertension.

Conclusion

We set up a goal of blood pressure control in China by 2030, and started several initiatives to overcome the major barriers of hypertension control, which include low awareness in general and low control rate in treated hypertensive patients.[10] The goal is to treat 70% of patients and to control blood pressure in 70% of treated hypertensive patients, leading to a 50% control rate of hypertension in China by 2030. The goal seems far from reaching, but is in fact feasible with the increasing use of innovative blood pressure measurement [11,12] and antihypertensive treatment[13] and evolving technological platforms.[9] With the implementation of the core concept of prevention and treatment, and establishment of the new platforms, the control of hypertension will ultimately transform from the current "care" to the future "cure", and help prevent most if not all cardiovascular events.

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ISH COMMITTEE AND AFFILIATED SOCIETY REPORTS

Reflections on the mentor/mentee experience

Mentee's perspective

Keneilwe Nkgola Mmopi
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Upon returning to Botswana after completing my PhD in South Africa in 2021, I was faced with a challenge of how to do research in cardiovascular science because I didn't have any local research collaborations or research funds to start me off. In my country cardiovascular science research is a relatively unentered area. I felt stuck and was not sure how to go about advancing my research as well as move forward to the next level of my career. I realised that I needed a mentor to help me navigate that.

I chose Lebo Gafane-Matemane as my ISH mentor because I admired her distinguished career as a cardiovascular researcher. I opted for 18 months as the duration of the mentorship. To start off, I wrote an action plan with timelines for the duration of the programme. I set goals which were quite ambitious because I wanted the mentorship to be worthwhile and beneficial to my aspirations. When I shared my ambitious goals with Lebo she didn't modify or question them, instead she agreed that we should go for it, showing that she believed they were achievable goals. We agreed to meet every 6 weeks online and our first meeting was in April 2024. At the end of each meeting we agreed on action items to report on for the next meeting. This ensured that I actively worked on my goals so as to meet the set timelines.

Some of my goals were to have more opportunities for research, collaborations and secure research grants. Because of the support from my mentor, I also felt inspired to apply for opportunities of service and networking in international cardiovascular science platforms. In this regard, I'm grateful to say that I'm currently serving in the International Society of Hypertension Membership Committee. In 2024 I was selected for the inaugural cohort that was trained in Leadership and Advocacy by the World Heart Federation. I'm happy that I have recently been invited to be part of the Abstract Reviewing Committee of the European Society of Cardiology Congress 2025. What is even more outstanding for me is that by the end of 2024 I had applied for two large international grants as the project lead. Lebo gave me the space to lead the applications while encouraging me all the way. This made me realise that I had the competency to lead a grant application, what I only needed was the confidence. I'm excited that my application

for the research fellowship grant has since been conditionally approved for support. I'm still waiting for the outcome of the other application. I'm grateful that this experience has given me the launching pad that I needed to apply for other grants as the lead investigator.

Almost a year into the mentorship programme, I'm happy to say that I'm well on track towards realising most of my mentorship targets. I would like to thank Lebo Gafane-Matemane and the International Society of Hypertension for this wonderful mentorship opportunity.

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Mentor's perspective

Lebo Gafane-Matemane
Chair ISH Mentorship and Training Committee, and Hypertension in Africa Research Team, North-West University, Potchefstroom, South Africa

Since I joined the ISH Mentorship and Training Committee (MTC) in 2021, I have had the privilege of working on the pairing of early-career researchers with established researchers within ISH. I have been mentored by global leaders in hypertension who had been part of the ISH leadership. It is for this reason that I was not sure if I was ready to be a mentor to an emerging researcher and be able to make a meaningful contribution to an individual's career path. When reflecting on my decision to serve as a mentor for Keneilwe and others, the most important element was that even though I am an early career researcher myself, carrying out the mentorship under the ISH MTC provided some safety net. Resources such as the mentee handbook from the MTC came in handy at the beginning and from there the relationship evolved naturally as opportunities for growth that aligned with Keneilwe's goals arose.

An important lesson for me here was that context is important in mentorship. Even though I was technically Keneilwe's peer, in South Africa I had many opportunities in hypertension research activities, mentorship, and seed funding as well as international exposure through the ISH which in turn propelled my career faster than my peers who are basic scientists. My peers such as Keneilwe were inspired by that and at that point in their careers, the kind of support needed was for someone who could show them how to move from one stage in their early career to another. This is quite important as some individuals experience challenges immediately after the completion of PhD due to the cessation of mentorship. Being

able to relate had a significant bearing on how the mentorship started and facilitated trust and open communication.

This experience has shown me that peer mentoring is as valuable as being mentored by a senior or established researcher, depending on an individual's needs at that particular time. Additional benefits include building solid collaborations with balanced power relations, clear expectations, and more opportunities for networking and growth for both the mentor and mentee. Peer mentoring has the potential to make a remarkable difference in supporting career development, especially in environments where it might be challenging to find a senior researcher with spare time to contribute to mentorship. In addition to the support of the mentee, this mentorship has opened more doors for collaborations between North-West University and the University of Botswana through new connections.

There are not sufficient mentorship opportunities in some regions in the world such as in Africa, especially for upcoming and sometimes mid-career researchers and basic scientists with an interest in hypertension. Given the limited number of senior experts in the field and subsequently limited time to mentor more early career researchers, peer mentorship may be a good option. This will support career growth and foster collaborations to build the next generation of well-supported researchers in hypertension and cardiovascular medicine.

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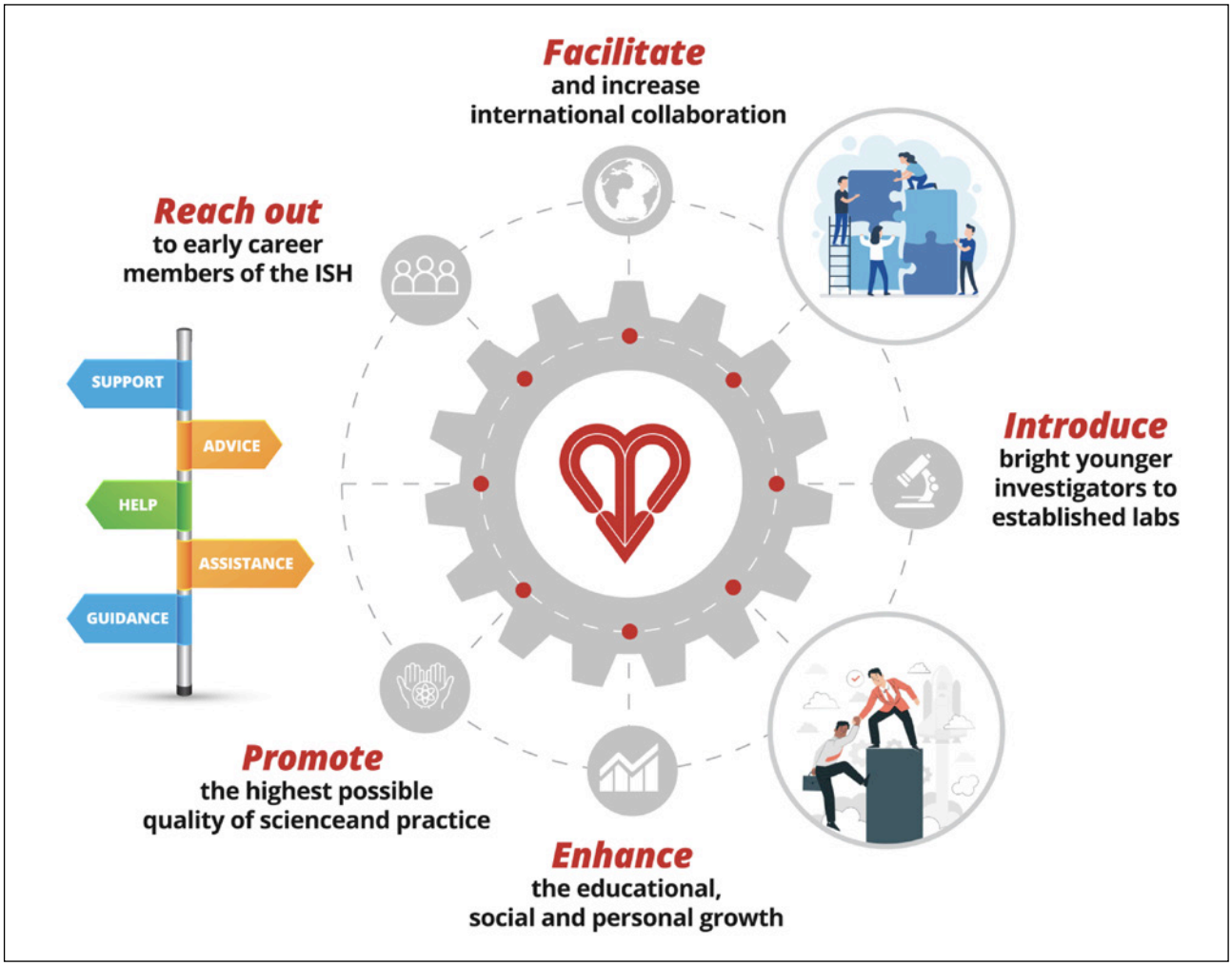

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