# HYPERTENSION NEWS July 2025

Blood pressure and cardiovascular prevention **Exploring measurement, screening practices,** cardiovascular risk, and prognosis

#### IN THIS ISSUE:

WHO report on research priorities for hypertension care

Cardiovascular damage in hypertensive women throughout life

Inflammation and hypertension

The skin and blood pressure control

Hypertension prevention in young people

World Hypertension Day and May Measurement Month



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# INTRODUCTION FROM THE PRESIDENT

## **GEORGE STERGIOU**

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Dear ISH members and friends,

With many of us finding our minds drifting to summer holiday plans rather than work, I am delighted to present a new issue of ISH Hypertension News.

This issue brings together another rich set of interesting contributions coming from around the globe. We include an executive summary of an important report by the World Health **Organization** presenting 10 priority research topics for improving hypertension care. The World Health Organization is currently preparing its 2025 Global Hypertension Report, which is expected to present feasible and scalable solutions for improving hypertension control in a relatively short time, based on recent successful projects.

We also have a summary of the recently published **Hypertension Canada** guidelines. The Canadian guidelines have always been very attractive to me, as they have a unique approach and style, and Canada has historically been among the world leaders in hypertension care. This time they used the **HEARTS** framework developed by the World Health Organization and presented 9 evidence-based and pragmatic recommendations for improving hypertension diagnosis and management. It would be interesting to see how these recommendations compare with the 2025 AHA/ACC Guidelines for hypertension which are expected to be published in a few weeks.

Read about an impressive campaign in Croatia, which effectively reduced salt consumption at

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a national level, and a successful hypertension camp in **Thailand**. We also highlight a report of recent data on the contribution of hypertension to cardiovascular risk, and the central role that blood pressure plays in shaping cardiovascular health and longevity worldwide. And I believe you will be interested to read our articles on prevention in young people, on organ damage in women, and on the links of hypertension with obesity,

Blood pressure measurement is always a hot topic in the ISH Hypertension News, and here we include articles on a home blood pressure score for stratifying patients' risk, on unattended automated office blood pressure measurement, on supine hypertension, and on the impact of **noise** on screening blood pressure measurement. We also feature interesting explanatory research articles, on the role of the **skin** in hypertension, the concept of salt sensitivity, and on inflammation in hypertension.

Last, we are glad to present an article on the ISH Capacity Building Network, and initiatives from several partners around the world for World Hypertension Day, the May Measurement Month global campaign, and Salt Awareness Week

I am grateful to our ISH members and friends who contributed to this edition and invite you all to propose new articles for our next issue.

I hope you will find this issue interesting and informative.

Enjoy reading!









# **NEW PAPERS**

# The special role of arterial hypertension as a cardiovascular risk factor

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For many years, we have been treating patients in primary prevention as well as patients with established cardiovascular disease in the cardiology outpatient clinic at the University Heart and Vascular Center Hamburg, Germany. Every day, we speak about prevention and strive to convey the special importance of known risk factors and the need to optimize them. Their significance has long been clear to all of us.

The recently published studies by the Global Cardiovascular Risk Consortium - one on the effect of classical risk factors on cardiovascular disease and all-cause mortality (Magnussen et al., 2023), and another on the impact of their absence or modification on individual lifespan (Magnussen et al., 2025) - provide a robust evidence base to support our daily clinical practice.

The Global Cardiovascular Risk Consortium dataset currently compiles individual-level data from 133 cohort studies conducted across 39 countries and 6 continents, encompassing over 2 million participants. This constitutes one of the most comprehensive efforts to date in evaluating the impact of risk factors on cardiovascular disease development and life expectancy on a global scale.

Cardiovascular diseases account for approximately one-third of all deaths worldwide. The most well-established risk factors include arterial hypertension, diabetes mellitus, smoking, elevated non-HDL cholesterol, and unhealthy body weight (body-mass index <20 or ≥25 kg/m²). As these risk factors are potentially modifiable, gaining a deeper understanding of their influence on disease incidence and mortality is crucial for guiding effective global prevention strategies.

The first study from the Consortium (Magnussen et al., 2023), which analyzed data from 1.5 million participants, assessed the impact of the five classical risk factors on global cardiovascular disease incidence and mortality. Population attributable fractions (PAFs) were calculated to estimate the proportion of disease theoretically preventable through elimination of a risk factor. The study found that over a 10-year period, more than half of new cardiovascular disease cases - 57% in women and 53% in men - could be prevented by control of the five risk factors. Among them, high blood pressure had the greatest impact, with a PAF of nearly 30%.

In a recently published follow-up study (Magnussen et al., 2025), the Consortium demonstrated that 50-year-olds with normal blood pressure and cholesterol levels, a healthy body weight, who do not smoke and do not have diabetes remain free of cardiovascular disease significantly longer and also have greater overall life expectancy. Among middle-aged individuals, women without any of the five risk factors experienced a delay of 13.3 years and men 10.6 years in the onset of cardiovascular disease compared to their counterparts with all five risk factors. Furthermore, women without risk factors lived 14.5 years longer, and men 11.8 years longer, than individuals of the same age with all five risk factors.

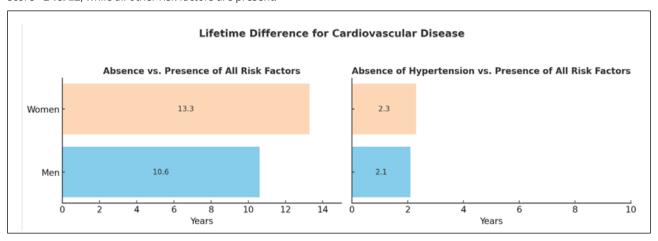
Of course, by age 50, most of our patients already present with one or more risk factors. However, this should not discourage them - or us as physicians. Even in midlife, reducing risk factors can lead to substantial health benefits. For example, controlling high blood pressure between the ages of 55 and 60 results in the







Figure: Lifetime difference (in years) for women and men for cardiovascular disease. The left panel shows the additional life expectancy associated with the absence of the five classical risk factors compared to their presence. The right panel shows the additional life expectancy associated with the absence of arterial hypertension using a dichotomized regional standard deviation score <2 vs. ≥2, while all other risk factors are present.



highest additional life-years free of cardiovascular disease: an additional 2.4 years for women and 1.2 years for men.

The Global Cardiovascular Risk Consortium applied a systolic blood pressure target of below 130 mmHg, a threshold deemed clinically relevant according to international guidelines (McEvoy et al. 2024, Whelton et al. 2018). The findings were clear: the higher the baseline risk factor level, the greater the potential gain in life expectancy from its reduction. Even in midlife, lowering blood pressure can result in a meaningful extension of lifespan. Elevated blood pressure is therefore the most important modifiable risk factor for gaining additional healthy years of life free from cardiovascular disease, and it is also one of the most critical determinants of overall life expectancy.

For patients without a diagnosis of hypertension but with elevated blood pressure values above 130/80 mmHg and an increased cardiovascular risk profile, we recommend initiating lifestyle modifications. These include regular physical activity (at least 150 minutes per week), achieving and maintaining a stable and healthy BMI between 20 and 25 kg/m<sup>2</sup>, adopting a balanced diet - such as the Mediterranean diet - reducing alcohol consumption, and quitting smoking.

Only a portion of our patients are able to successfully implement these lifestyle recommendations. In some cases, it can be challenging to make the decision to initiate antihypertensive therapy after three months of lifestyle changes without meaningful improvement in blood pressure.

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However, the data outlined above provide a strong scientific foundation for these decisions and support more effective communication with patients about the potential long-term benefits.

The five classical risk factors account for more than half of all cardiovascular disease cases. At the same time, their absence at age 50 is associated with over a decade of additional life. Even when a risk factor is present in midlife, modifying it can still result in meaningful gains in life expectancy. These findings highlight the global importance of both preventing and treating cardiovascular risk factors - especially arterial hypertension.

With this knowledge, we will continue conversations about cardiovascular prevention and modifiable risk factors with renewed motivation, confident that the recommended interventions can truly improve both the cardiovascular health and longevity of our patients.

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# **NEW PAPERS**

# Cardiovascular prognosis prediction by a novel home blood pressure stability score: The J-HOP Study

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#### Introduction

Hypertension is one of the most common chronic conditions globally and plays a central role in the development of major cardiovascular diseases (CVD), including stroke, myocardial infarction, heart failure, and renal dysfunction. Traditionally, diagnosis and treatment evaluations were based primarily on office blood pressure (BP) measurements. However, in the digital age, the importance of home BP monitoring (HBPM) is being increasingly emphasized.

HBPM reflects BP fluctuations in daily life settings, making it excellent for detecting white coat and masked hypertension. Measuring BP over several days allows for assessment of variability and longterm trends, improving risk prediction accuracy.1 One key advantage of HBPM is the ability to collect a large number of readings, enhancing the accuracy of averages and increasing sensitivity to variability and outliers. Prior evidence shows that BP variability, both in the office and via ambulatory BP monitoring (ABPM), independently predicts cardiovascular risk.2,3

Given this context, new predictive indicators and treatment targets based on HBPM have recently been developed.<sup>4-7</sup> This article outlines a novel approach to cardiovascular risk prediction incorporating home BP variability, with a focus on the "Home BP Stability Score (HBPS Score)," developed from the nationwide Japanese cohort study J-HOP (Japan Morning Surge-Home Blood Pressure).7

## Composition and Evaluation of the HBPS Score

The HBPS Score is a composite metric combining quantitative (mean) and qualitative (variability) aspects of HBPM. It includes the mean systolic BP (MEave) and three BP variability indicators: Average Real Variability (ARV), Peak SBP (average of the three highest SBP readings), and Time in Therapeutic Range (TTR).

The score ranges from 0 to 10. Higher scores indicate more stable and optimally controlled BP, defined as the "stabilized home BP control status" (Figure 1A, 1B). Those in the optimal score range (9-10 points) had a cardiovascular event incidence of 6.4% per 1,000 person-years (Figure 1C).7

MEave is the average of systolic BP readings taken three times each morning and evening over 14 days. It serves as the fundamental indicator of baseline BP load. A value below 125 mmHg was considered optimal, while values ≥160 mmHg were classified as high risk, consistent with the Japanese Society of Hypertension's home BP target (SBP <125 mmHg) (Figure 2A). Only 26.7% achieved the 125 mmHg target, but those who did showed significantly better long-term outcomes.8

## **Three BP Variability Indicators Used in HBPS**

1. Average Real Variability (ARV) ARV captures day-to-day BP fluctuations by averaging the absolute differences in SBP between consecutive days (Figure 1A). Compared to traditional standard deviation (SD), ARV better reflects real-world fluctuations due to lifestyle stress or irregularities. An ARV ≥8.5 mmHg significantly











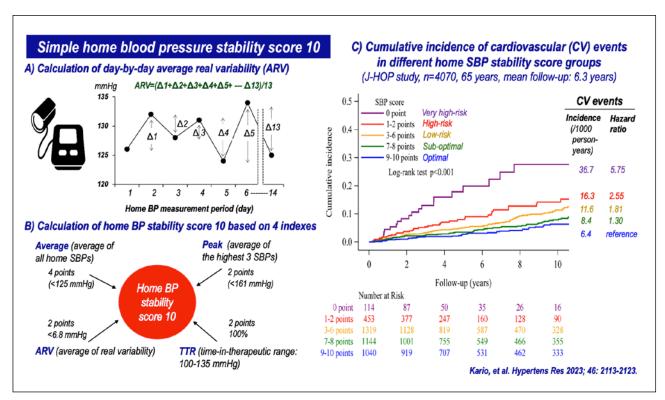


Figure 1. Simple home blood pressure stability score 10

increased event risk (Figure 2B) and has been shown to correspond to an aging-related risk equivalent to 15 years.9

- 2. Peak SBP This is the average of the top three SBP values during the measurement period and visualizes extreme momentary BP spikes not reflected in the average (Figure 2C). It is useful for assessing the risk of acute events such as stroke or heart failure. A threshold ≥173 mmHg was associated with a clear increase in risk, consistent with previous findings<sup>5</sup> and defined as the top quintile.
- 3. Time in Therapeutic Range (TTR) TTR indicates the proportion of time SBP remains within the therapeutic range (100-135 mmHg), reflecting how consistently BP is controlled (Figure 2D). A TTR <15% was associated with a 1.75-fold increase in cardiovascular risk. This threshold has been validated in prior studies.6

## **Predictive Ability of the HBPS Score** for Cardiovascular Outcomes

In the J-HOP study, 4,070 outpatients with hypertension (mean age 64.9 years) recorded 14 days of home BP data for HBPS score calculation. Over a mean follow-up period of 6.3 years, 260 cardiovascular events occurred (stroke, heart failure, coronary artery disease, aortic dissection).

Event rates were significantly lower in higher HBPS score groups. Compared to the most stable group (score 9-10), the most unstable group (score 0) had approximately a fourfold increased risk (adjusted hazard ratio: 3.97, 95% CI: 2.22-7.09, p<0.001) (**Figure 1C**). These associations remained robust after adjusting for age, sex, BMI, diabetes, dyslipidemia, smoking history, and antihypertensive medication use.

## **Clinical Significance and Potential Applications**

The HBPS Score enables risk stratification based solely on home BP, without relying on officebased measurements or expensive diagnostic equipment. It holds particular utility for elderly or immobile patients and in telemedicine. Each component of the score reflects distinct pathophysiological mechanisms: ARV (lifestyle instability), peak SBP (acute stress response), and TTR (long-term BP control). Together, they form a comprehensive risk profile.







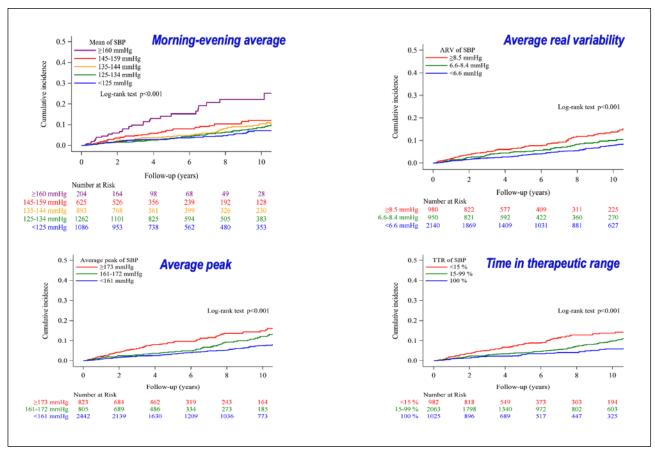


Figure 2. Cumulative incidence of total cardiovascular events by home systolic blood pressure index

Importantly, the HBPS Score supports a paradigm shift from a treatment strategy based only on average BP to one that also values stability and variability. This aligns with personalized and preventive medicine principles.

#### **Limitations and Future Directions**

Several limitations should be noted. First, the 14-day monitoring period may not reflect seasonal or long-term treatment effects. Second, nocturnal BP data were not included. Third, the cohort was limited to high-risk Japanese patients, limiting generalizability to other populations.

Future directions include integrating nighttime and 24-hour BP monitoring, extending measurement duration, and enabling real-time evaluations through digital devices and apps. 10 Incorporating artificial intelligence for prediction enhancement and applying these scores in treatment algorithms are also promising avenues.

#### Conclusion

In clinical practice, using validated BP monitors<sup>11</sup> and applying HBPM-based risk indicators like HBPS can guide optimized, personalized hypertension management. Accelerating research in digital hypertension and integrating multi-dimensional, real-time data could help establish personalized anticipation medicine strategies.<sup>12</sup>

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# **NEW PAPERS**

# AOBP misses the mark in blood pressure diagnosis

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Hypertension is the single most common and modifiable risk factor for cardiovascular disease and mortality<sup>1</sup> and is present in about 1 in 4 Canadian adults. Canada has gained a reputation for being among the world's leading nations in hypertension control rates.2 However, the recent years have seen a decline in hypertension awareness, treatment, and control rates, particularly among women.3 Needless to say, proper measurement is the first step towards optimal blood pressure (BP) control. Automated oscillometric blood pressure measurement (AOBP) is quite common in Canada. BPTru, the pioneering form of AOBP, was originally designed in Canada, and use of AOBP is quite common in family practices nationally. Research has demonstrated that the actual type or brand of AOBP, or the presence or absence of a healthcare worker during the measurement, also does not matter much for BP numbers.4 AOBP however, despite attenuating, does not completely eliminate the problem of white coat effect or white coat hypertension. Our group and others also have reported a higher proportion of masked effect and masked hypertension when using AOBP (as compared to a casual BP measurement) in the past. 5 AOBP also does not provide assessment of variability, or nocturnal dipping and circadian rhythms, which requires 24-hour ambulatory BP monitoring (ABPM). Despite knowing these advantages of ABPM, ABPM remains quite underused in Canada with a mere 14% of family physicians reported using it. The under-utilization of this resource may stem from lack of access (only 5 of 15 jurisdictions in Canada cover ABPM)6 as well as a paucity of existing real-world data on the impact of low ABPM use on hypertension diagnoses.





In this recently published study, we include 964 adult patients who underwent same-day AOBP and ABPM at the Ottawa Hospital Hypertension Clinic, over 4 years (2019-23). Our goal was to determine the proportion of hypertension misclassification and abnormal nocturnal BP patterns detected via ABPM in this real-world setting. Overall, hypertension status of approximately half of all patients were misclassified based on same-day AOBP relative to ABPM. 49% of patients who were normotensive on ABPM had office readings of >140/90 and met criteria for white coat hypertension or white coat effect. 54% of patients with uncontrolled hypertension on ABPM had same day office readings <140/90 and met criteria for masked hypertension or masked uncontrolled hypertension. 36% of patients had non dipping pattern of nocturnal blood pressure and 7% had reverse dipping pattern, both aspects that cannot be identified with an AOBP. These findings should come as no surprise to the readers, but reflect the sober reality, that even at a tertiary care referral clinic, not doing an ABPM would misdiagnose and mistreat roughly half the patients. The underuse of ABPM leads to a lack of recognition of these abnormal hypertension phenotypes, and also under-recognition of non-dipping patterns (roughly a third in this study) and consequent underdiagnosis of the underlying causes.

There were several limitations of the study given that this was a single centre study, with the cohort comprised of patients referred to the hypertension clinic introducing selection bias - these were patients with hypertension uncontrolled in the primary care practices. Additionally, being a crosssectional study, longitudinal outcomes in this











cohort could not be captured. But these data are quite consistent with prevalence data from other geographic locations around the world. Indeed, the main reason ABPM turn out to be cost-effective (and even cost-saving) in many analyses are from the large proportion of white coat hypertensive individuals who no longer need additional treatment and physician visits.7-9 Similarly, for patients with masked effect, especially in setting of uncontrolled BP, epidemiological data suggests adverse cardiovascular outcomes while we await the results of an ongoing trial.<sup>10</sup>

In summary, the results of our study do underscore what we know already about the merits of performing ABPM, but we hope this spurs improved accessibility to ABPM. In Canada we do need a better reimbursement in jurisdictions which do not provide coverage, but this study clearly demonstrates that 1 in 2 patients being seen at a tertiary care referral clinic may be inadequately diagnosed and treated without an ABPM.

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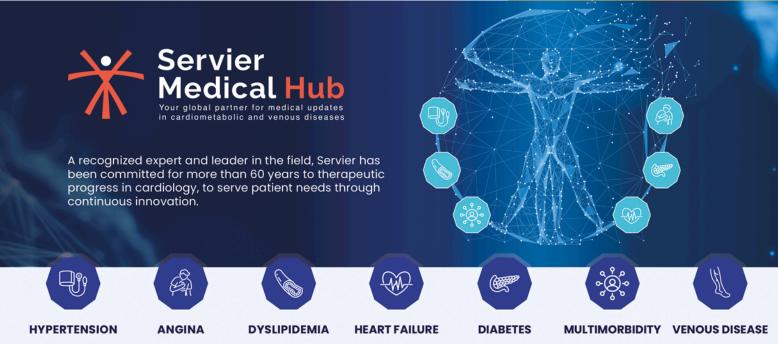












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# **NEW PAPERS**

# Supine hypertension: An overlooked marker of cardiovascular risk?

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When we think about blood pressure (BP) in a clinical setting, we almost always mean the seated measurement. It is the standard approach in clinic offices, hospitals, and even home monitors. However, our recently published analysis from the Atherosclerosis Risk in Communities (ARIC) database has shown that we are missing a critical piece of the puzzle: supine blood pressure.

Our study looked at over 11,000 middle-aged adults from the ARIC cohort and followed them for nearly three decades.1 We wanted to find out whether having high blood pressure while lying down something many patients do most of the night – is linked to cardiovascular disease, independent of seated BP or hypertension treatment.

## **Supine Hypertension Is Common but Often Missed**

At baseline, 37% of participants had supine hypertension, defined as systolic BP≥130 or diastolic BP≥80 mmHg. Notably, 16% of those with normal seated BP still had elevated supine readings. In patients already on antihypertensive medications, more than half had supine hypertension. This means that a significant portion of our patients - especially those we think are wellcontrolled - may have unrecognized hypertension when lying down.1

In current practice, supine blood pressure is something that is only checked when there are concerns of orthostatic changes or syncope.2 Our study makes a compelling case that we may need to revisit that practice, particularly for patients with borderline or unexplained cardiovascular disease (CVD) risk.

## **Supine BP Strongly Predicts Cardiovascular Disease**

The big question is whether this matters for outcomes. We found that it does substantially. After adjusting for traditional risk factors, supine hypertension was independently associated with:

- 60% higher risk of coronary heart disease
- 83% higher risk of heart failure
- 86% higher risk of stroke
- More than double the risk of fatal coronary heart disease
- 43% higher risk of all-cause mortality

Even after accounting for seated BP and whether patients were on antihypertensive medications, the associations remained strong. Supine BP was not just a proxy for poorly controlled seated BP, it was its own, independent predictor of bad outcomes. Supine hypertension alone conferred a higher risk of CVD events than seated hypertension alone. People with high supine BP, but normal seated BP, still had significantly elevated risk for coronary heart disease, stroke, heart failure, fatal coronary heart disease, and death from any cause. In contrast, elevated seated BP alone was associated only with fatal coronary heart disease and all-cause mortality.











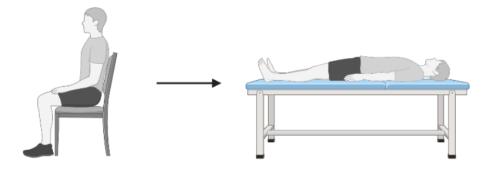
# "Supinatic" Hypertension

(new high blood pressure after lying flat)

Normal Blood Pressure

High Blood Pressure

Acknowledgement: Illustrations from Biorender



## Potential mechanisms:

- (1) Redistribution of fluid volume
- (2) Obesity-related vascular resistance
- (3) Autonomic dysfunction
- (4) Urination urgency from excess kidney filtration
- (5) More accurate/precise blood pressure measurement
- (6) Correlation with seated hypertension

#### Observed risks:

- Cardiovascular disease: coronary heart disease, heart failure, stroke
- (2) Hypotensive-events: falls, syncope
- (3) All-cause mortality

#### What Might Be the Driver?

There are a few possible reasons supine BP could be such a powerful predictor (Figure). First, supine measurement may be more reflective of a person's "true" resting BP. When seated, there is a chance we are underestimating the load the cardiovascular system experiences during sleep or inactivity. Second, supine hypertension could reflect underlying autonomic dysfunction, endothelial issues, or altered fluid distribution, all of which are tied to cardiovascular pathology.3 We know that when people lie down, especially for long periods like during sleep, fluid shifts centrally.4 In individuals with impaired vascular regulation, this may push BP beyond healthy levels. Finally,

it is difficult to ignore the potential overlap with nocturnal hypertension, which is already known to predict cardiovascular risk. 5 Supine BP may act as a proxy in the absence of overnight ambulatory monitoring.

# Clinical Takeaways: Should We **Be Measuring Supine BP?**

Our study raised a provocative concept: supine BP may be a valuable addition to our risk assessment toolkit, especially in patients with normal or borderline seated BP, resistant hypertension, unexplained end-organ damage, elevated nighttime BP (if measured), known autonomic dysfunction or suspected dysautonomia.









For now, it may be useful to measure supine BP selectively in patients where we might be concerned about their overall cardiovascular risk. It may also help explain why some patients still experience cardiovascular events despite having "controlled" BP during routine visits.

**Final Takeaways** 

Our study had limitations. For one, we did not have nighttime BP readings, so we cannot state for certain if supine BP correlates perfectly with what happens while someone is sleeping. In addition, measuring supine BP in the clinic is not standardized. In ARIC, participants rested supine for 20 minutes before BP readings – longer than most of us can do in practice. Still, even a few minutes of rest followed by supine measurement might offer useful insight in clinical practice. This procedure may also be replicated at home. We would like to see future research test shorter rest periods or at-home supine BP monitoring.

In summary, supine hypertension especially is important for patients whose cardiovascular risk appears out of proportion to their seated BP. Whether it is due to underlying autonomic

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dysfunction, vascular stiffness, or mechanisms we have not fully elucidated, supine BP appears to be a powerful risk signal. Until ambulatory monitoring becomes more widespread, conducting supine BP measurement might uncover a hidden risk we have been overlooking.

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# **NEW PAPERS**

# Quiet isn't always required: Rethinking blood pressure screening environments

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Hypertension is a leading cause of cardiovascular disease and mortality worldwide. Controlling blood pressure (BP) is a fundamental strategy to reduce this risk. Accurate BP assessment requires proper measurement techniques, as outlined in clinical guidelines.<sup>1,2</sup> However, these protocols can be challenging to implement, due to lack of space, time, and staffing. Deviations from protocol can result in erroneous BP readings,3 which may have clinical consequences.

Mass screening in public spaces, as is done during May Measurement Month, is an effective and efficient strategy to identify patients with hypertension. By reaching individuals who might not otherwise visit a doctor's office, more at risk individuals are identified, allowing for earlier treatment and prevention of CVD.4 However, if BP readings obtained in such environments are inaccurate, the effectiveness of these efforts may be undermined. Current guidelines recommend measuring BP in quiet, private settings - but creating such environments is often difficult and incompatible with large scale screening efforts.

Surprisingly, limited data exist on the impact of noise and environment on BP readings. Some studies have shown differences in BP measurements depending on timing and location, but few have rigorously separated the effects of noise and setting.5,6 To address this gap, we conducted a randomized cross-over clinical trial to quantify the impact of noise and environment on BP readings.7

We investigated whether BP measurements in a public food market (noisy environment) differed from those in a quiet, private research office at Johns Hopkins University. We enrolled 108 community-dwelling adults, recruited through screening campaigns, mailings to prior participants, and referrals from hypertension clinics. Participants were randomly assigned to the order in which they underwent triplicate BP measurements in three settings: 1) private quiet office (reference), 2) noisy public space (public loud), and 3) noisy public space with earplugs (public quiet). We compared mean BP readings in public loud and public quiet settings to the private quiet reference.

Among the 108 participants, the mean age was 56 years (SD, 17); 84% self-identified as Black, and 41% were female. The mean noise level was 74 dB in the public loud setting and 37 dB in the private quiet setting. Mean systolic BPs (SBPs) were similar in each of the environments: 129 mm Hg (private quiet; reference), 128 mm Hg (public loud), and 129 mm Hg (public quiet). When we determined the average difference in SBP compared to the private quiet setting, these small, non-clinically meaningful differences were even more clear: mean SBP in the public loud environment was 0.66 mm Hg lower than in the private quiet setting (95% CI, -2.25 to 0.93) and mean SBP in the public quiet environment was 0.09 mm Hg higher than in the private quiet setting (95% CI, -1.53 to 1.72) (Table 1). Diastolic BP (DBP) differences were slightly larger but still modest: mean DBP was 1.65 mm Hg higher (95% CI, 0.77 to 2.54) in the public loud environment and 1.45 mm Hg higher (95% CI, 0.64 to 2.27) in the public quiet environment when compared to the private quiet office environment. Results were consistent









Table 1: Mean differences in BP readings obtained in a public loud and a public quiet setting compared to a private quiet setting.

Analytic approach	Public loud - Private quiet	Public quiet - Private quiet
Paired t-tests (for the Primary analysis)		
ΔSBP (95% CI) in mm Hg	-0.66 (-2.25, 0.93)	0.09 (-1.53, 1.72)
ΔDBP (95% CI) in mm Hg	1.65 (0.77, 2.54)	1.45 (0.64, 2.27)
Multivariable mixed effects models* (for the Sensitivity Analysis)		
ΔSBP (95% CI) in mm Hg	-0.79 (-2.35, 0.76)	-0.01 (-1.56, 1.54)
ΔDBP (95% CI) in mm Hg	1.59 (0.78, 2.39)	1.40 (0.60, 2.21)

<sup>\*</sup> Adjusting for age, body mass index, use of antihypertensive medication, upper arm length, arm circumference, and the order of BP measurement sets. In this multivariable linear mixed effects model analysis, the outcome was defined as the average SBP/DBP of triplicate BP measurements, and the treatment effect was modeled as a dummy variable with the following values: 2 for subjects in the public loud group, 1 for those in the public quiet group, and 0 for those in the quiet group (reference). Abbreviations: BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.

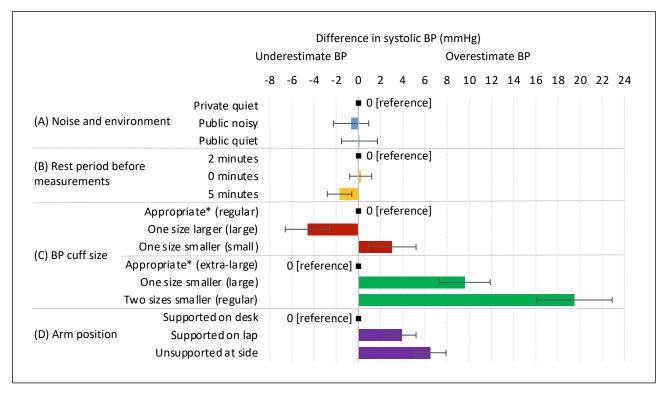


Figure 1: Varying impacts of BP measurement procedures on systolic BP. (A) noise and environment, (B) rest period before measurement, (C) BP cuff size, and (D) arm position. Mean differences in systolic BP are shown relative to guidelinerecommended procedures. Negative values indicate underestimation, while positive values indicate overestimation of BP. Bars represent point estimates; capped gray lines denote 95% confidence intervals. \*Impact of over- and under-cuffing when the regular adult cuff or the extra-large cuff is the appropriate cuff size for the participant.







in multivariable mixed-effects models adjusting for the order of measurements and other factors (Table 1).

Our findings suggest that BP readings in noisy public settings do not differ in clinically meaningful ways from those measured in quiet, private environments. This has important implications for mass screening programs and clinics with limited space and staffing, where creating an ideal measurement environment may not be feasible.

While this study may simplify screening efforts by allowing for greater flexibility, it is important to note that deviating from other standard BP measurement protocols may have greater clinical impact and thus may not be appropriate. Figure 1 summarizes the results from our series of clinical trials that tested the effects of deviations from other recommended measurement steps. 7-10 While shorter rest time before measurement had a similar minimal impact on accuracy as measuring BP in a noisy, public space, malpositioning of the arm during measurement and use of a too-large or too-small cuff during measurement resulted in significant - and in some cases substantial - BP measurement error. Our research underscores the importance of adhering to these two measurement steps during hypertension screening.

Although our study used a rigorous randomized crossover design, several limitations should be acknowledged. It was conducted in the U.S. with a predominantly Black population, and all BP measurements were performed by trained research staff - conditions that may not reflect real-world or resource-limited settings. The noise level in our public environment was 74 dB; the effect of more extreme noise levels (e.g., city traffic >89-90 dB) remains uncertain. Future studies should replicate these findings in broader clinical and community contexts, using pragmatic BP measurement approaches.

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#### **Conclusion:**

In this randomized study, noise and environmental factors had minimal and clinically insignificant effects on BP readings. These findings support the feasibility of conducting hypertension screening in public spaces.

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# PERSPECTIVES IN **HYPERTENSION**

# A life course and health promotion approach to hypertension prevention in young people

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Recently, although the prevalence of hypertension among young people has remained stable or even declined in some high-income countries, it is generally considered to be increasing.<sup>1,2</sup> A metaanalysis of 34 studies from 21 countries, including data from a total of 476,975 individuals aged ≤19 years, reported that the pooled prevalence of hypertension – defined as systolic and/or diastolic blood pressure at or above the age-, sex-, and heightspecific 95th percentile based on at least three measurements - was 4.00% (95% CI, 3.29%-4.78%)1. Moreover, the study showed that hypertension prevalence among children and adolescents increased approximately 4.8-fold from the 1990s to the early 2010s: 1.26% (95% CI, 0.79%-1.84%) in the 1990s, 3.30% (95% CI, 2.69%-3.97%) in the 2000s, and 6.02% (95% CI, 4.38%-7.91%) between 2010 and 2014.1 Although direct comparisons are limited by differences in diagnostic criteria, studies conducted between 2019 and 2024 in various regions of Asia reported hypertension prevalence rates among adolescents aged 10-19 years, ranging from 12.37% to 14.25%, with an increase from 15.0% in 2019 to 22.9% in 2024.2 When hypertension is defined as a systolic blood pressure ≥140 mmHg, a diastolic blood pressure ≥90 mmHg, or current use of antihypertensive medication, the prevalence among U.S. adults aged 18-39 years remained relatively stable, ranging from 7.0% in 1999 to 7.3% in 2014.3 Rapid urbanization has been accompanied

by physical inactivity, increased consumption of high-calorie, high-salt, and high-fat foods, rising rates of obesity, irregular lifestyles, heightened stress

levels, and widespread smoking. These behavioral changes have become urgent public health concerns in low- and middle-income countries. Although public health policies have successfully curbed the increasing number of hypertension cases in some settings, this issue remains far from resolved, even in high-income countries.

Hypertension is majorly associated with social determinants of health and health disparities, including racial and migration-related factors, access to and quality of medical care and education, social and community connectedness, and environmental conditions.4 The rates of awareness, treatment, and control of hypertension are lower in young adults (aged 18-39 years) than in those aged ≥40 years. The lack of regular access to healthcare accounts for 7-16% of this disparity.5

Furthermore, growing evidence has shown that both birth outcomes and fetal origin can affect future health risks. Hypertensive disorders of pregnancy (HDP) are considered high-risk conditions for both mothers and infants and remain a common pregnancy complication with serious health consequences.<sup>6</sup> Globally, 5–10% of pregnancies are affected by HDP, with HDP













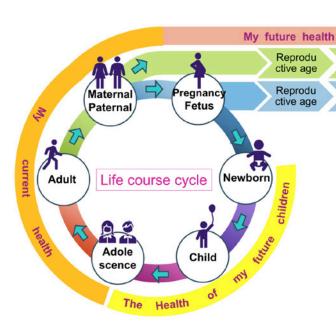


Figure 1: Life course cycle

prevalence increasing due to rising rates of obesity and advanced maternal age.6 Moreover, HDP may result from low birth weight and fetal growth restriction.<sup>6</sup> The frequency of small-forgestational-age infants is higher in the HDP group than in the non-HDP group (7.2% vs. 3.5%).7

Children born to mothers with HDP, including chronic hypertension, who are exposed to elevated blood pressure in utero, are at an increased risk of developing hypertension during youth.<sup>7</sup> Furthermore, fetal growth restriction due to maternal undernutrition and low birth weight is associated with future obesity and the development of hypertension.8

Given these findings, a life course approach that considers the preconception period, pregnancy, and intrauterine environment as starting points is gaining attention as a key perspective for the prevention and early intervention of hypertension in young people.

#### The Importance of a Life Course Approach

An individual's health and risk of disease are shaped by the accumulation and interaction of biological, social, psychological, and behavioral factors at multiple stages across the lifespan, including the prenatal period.9 The World Health Organization promotes a life course approach to health, emphasizing the identification of risk chains and the possibility of disrupting them through timely interventions.9

From this perspective, people need to understand how their current health can influence their future health as well as the health of their children and future generations (Fig. 1). Importantly, we must disseminate the message that appropriate actions can break these chains of risk and lead to better outcomes.

Midlife

transition

Midlife

Older

age

Older

Improving health literacy among individuals and organizations is vital. This includes health education for young people by healthcare professionals, preconception care, interconception care between pregnancies, and educational initiatives, not only in clinical settings but also in schools, workplaces, and local governments.

Education, health, and poverty are interlinked closely. Improved education contributes to better health, 10 and ultimately has the potential to enhance the health and strength of the entire nation.

## Addressing the Challenges in Young Populations

Among young people, hypertension is often underdiagnosed and undertreated owing to its asymptomatic nature and low-risk awareness. Consequently, awareness and treatment rates are lower than those in older age groups, which contribute to poorer cardiovascular outcomes.<sup>3,5</sup> In addition, low participation in routine health checkups and limited access to healthcare services remain major challenges.<sup>3,5</sup>

Considering these issues, we propose an action plan (Fig. 2) as a health-promotion approach tailored to young people's lifestyles, including multifaceted strategies involving diet, physical activity, and connection to medical care.

Youth health lays the foundation for future biopsycho-social well-being. Developing healthy behaviors and habits during this life stage not only reduces future health risks but also contributes to improved educational outcomes.<sup>11</sup> We hope this Action Plan will be applied across various sectors and settings.



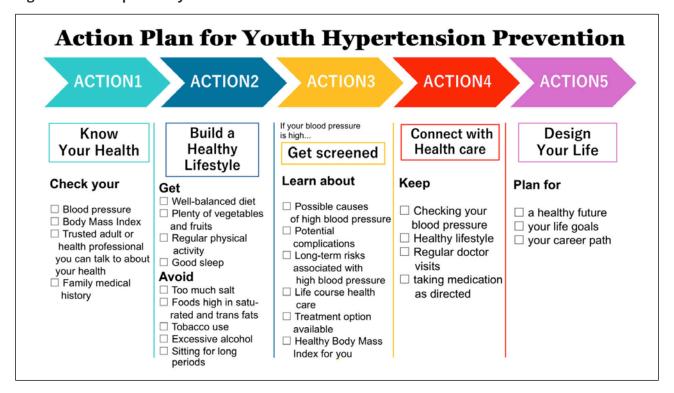








Figure 2: Action plan for youth



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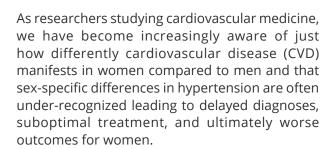


# PERSPECTIVES IN **HYPERTENSION**

# Cardiovascular organ damage in hypertensive women throughout life

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Hypertension is a major risk factor for cardiovascular organ damage. What is interesting is that even though current medical guidelines recommend uniform blood pressure (BP) targets regardless of sex, BP increases differently according to age and sex.1 It is fascinating how woman's cardiovascular risk evolves, beginning even before birth and extending through every stage of life. For women, there are so many hormonal, genetic, and metabolic factors that influence BP from menarche, through pregnancy, and eventually to menopause.<sup>2,3</sup> Understanding these changes is critical to manage cardiovascular organ damage in hypertensive women.

In adolescence, girls typically have lower BP than boys, 1 mainly due to the protective effects of estrogen. Estrogen positively influences endothelial function, lipid metabolism, and vascular responsiveness, providing an early cardiovascular advantage.4 However, this advantage is blunted when concomitant conditions occur, like polycystic ovary syndrome (PCOS) or menstrual irregularities, as the risk for developing hypertension increased.3 Similarly, obesity or insulin resistance, as well as oral estrogen contraceptives, can predispose





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young women to accelerated BP elevation and early onset of hypertension-mediated organ damage (HMOD), including increased left ventricular mass index and arterial stiffening (Table 1).5

Pregnancy is another critical phase and it is often the first major stress test of a woman's cardiovascular system. Hypertensive disorders of pregnancy - gestational hypertension, preeclampsia, and eclampsia – affect up to 15% of pregnancies and significantly increase maternal or child morbidity and mortality and woman's lifetime cardiovascular risk.3,6 Research has shown that women with a history of preeclampsia have a higher prevalence of left ventricular hypertrophy (LVH) and vascular stiffness, even years after delivery. In a notable recent study by Hauge and colleagues,7 women aged 40 to 55 with prior preeclampsia, underwent a cardiac computed tomography, demonstrated double the prevalence of LVH compared to controls. Interestingly, earlyonset preeclampsia conferred a greater risk than late-onset forms (Figure 1), suggesting the need for early and constant cardiovascular assessment after pregnancy complications. In the same study, pre-eclampsia was linked to LVH independently of other CV risk factors, with chronic hypertension explaining only 22% of this







Table 1

LIFE STAGE	CONTRIBUTING FACTORS	SUBCLINICAL DAMAGE	CLINICAL DAMAGE
Adolescence	Obesity, early (<12) or late (>17) menarche, hormonal imbalance, menstrual disorders, polycystic ovary syndrome, altered lipid profile	Endothelial dysfunction, arterial stiffness	Early-onset hypertension, increased lifetime CVD risk
Pregnancy	Preeclampsia, preterm delivery, gestational hypertension, gestational diabetes	Left ventricular hypertrophy, increased arterial stiffness	Chronic hypertension, heart failure with preserved ejection fraction
Menopause	Estrogen level reduction, metabolic syndrome, early menopause, weight gain (central adiposity), uncontrolled hypertension, sodium sensitivity, vascular inflammation, increased RAAS and SNS activity. Late menopause (protective)	Atherosclerosis, diastolic dysfunction, retinal arteriole changes, carotid intima-media thickening, Increased cf-PWV	Coronary artery disease, stroke, heart failure

**Table 1.** Contributing factors, subclinical and clinical damage in women related to sex specific condition over the life course.

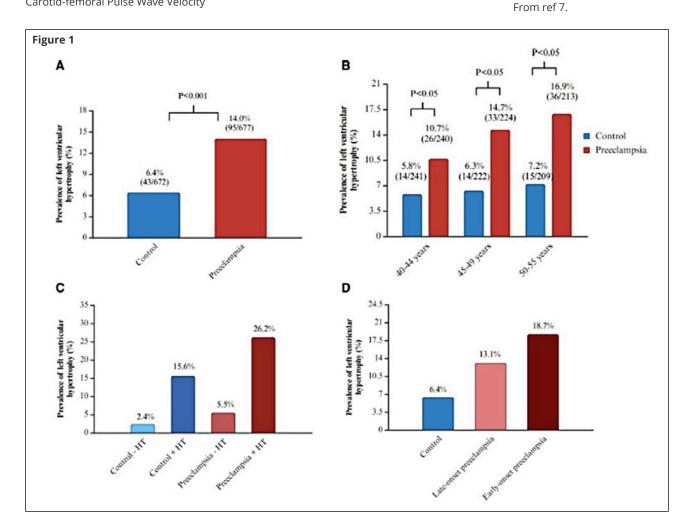
RAAS: renin-angiotensin-aldosteron system, SNS: sympathetic nervous system, cf-PWV: Carotid-femoral Pulse Wave Velocity

ventricular hypertrophy in women with and without a history of preeclampsia. Figure A: Prevalence of left ventricular hypertrophy in women with and without a history of preeclampsia. Figure B: Prevalence of left ventricular hypertrophy % (n) in the preeclampsia group and in the control groups and according to age groups. Figure C: Prevalence of left ventricular hypertrophy in the preeclampsia group and in the control group stratified

according to the presence of

chronic hypertension (HT).

Figure 1. Prevalence of left









association, indicating that other factors such as endothelial dysfunction, systemic inflammation, oxidative stress, and metabolic disturbances, likely contribute to persistent organ damage in these women- even when blood pressure is later wellcontrolled (Table 1).

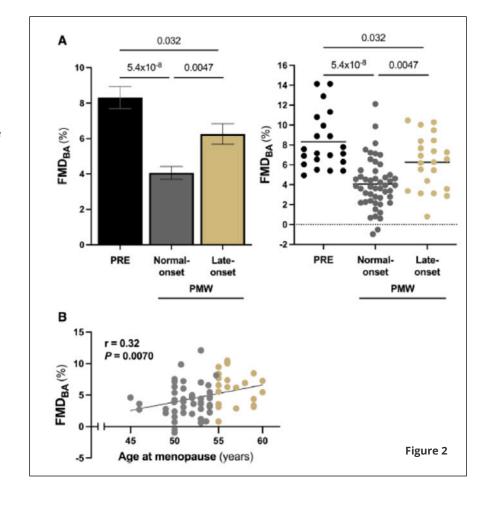
One of the more fascinating aspects of cardiovascular disease in women is how heart diseases affect women differently. Differently to men, women often present microvascular dysfunction without a significant obstructive coronary artery disease (MINOCA) and adverse remodeling leading to heart failure with preserved ejection fraction (HFpEF) partially explained systemic inflammation, oxidative stress and changes of the myocardial extracellular matrix.8

As women transition into midlife, estrogen deficiency disrupts cardiovascular homeostasis once more. Blood pressure rises more steeply, accompanied by increased structural cardiac changes and arterial stiffening (Table 1), with higher risk for CV events like heart failure- even when BP values are only modestly elevated.<sup>6,9</sup> It is

also a time when many women are also dealing with weight gain, reduced physical activity, and changes in cholesterol and insulin sensitivity with adverse consequences. Unfortunately, hormone replacement therapy has not turned out to be the benefit we once hoped it would be.<sup>2,3</sup> While it can help with hot flashes, it does not seem to reduce cardiovascular risk - and may even increase it in some women.<sup>2,3</sup>

Something we found really interesting is that going through menopause later in life might actually be protective against vascular aging and CVD meaning that timing can make a difference. Darvish S, et al<sup>10</sup> demonstrate for the first time that women who experienced menopause at age 55 or later exhibited a better endothelial function compared to normal-onset postmenopausal women with 54% higher brachial artery flowmediated dilation (FMDBA) whereas they show only 24% lower FMDBA than premenopausal women (Figure 3). Additionally, late-onset menopause was associated with and a more favourable lipid metabolite profile and a healthier mitochondrial function, indicating a lower oxidative stress.<sup>10</sup>

Figure 2. Endothelial function in premenopausal women (PRE) and normal- and late-onset postmenopausal women (PMW). Panel A: Endothelial function, assessed by brachial artery flowmediated dilation (FMDBA;%change in diameter), in PRE (black) and normal- (gray) and late-onset PMW (gold). Values are presented as mean±SEM (left) and as individual responses (right). Panel B: Relation between FMDBA and age at menopause. From ref.10.









This attractive finding, though not definitive, may influence how we think about CV risk stratification, highlighting that the timing of menopause has both positive and negative implications. In this context, relatively young women (18-59 years old) with pregnancy-induced hypertensive disorders and early menopause showed increased carotidfemoral pulse wave velocity compared to controls and a higher prevalence of arterial stiffness, independently of blood pressure elevation.11 Similarly, changes in microcirculation (i.e retinal arteriole) may also be found in postmeopausal women which have prognostic impact.<sup>12</sup>

#### **Conclusions: What Should We Do?**

First, we need to start looking at hypertension in women as a continuum that begins early and evolves over time and forsaking the concept that CV risk only becomes "real" after menopause. Second, we have to pay attention to femalespecific risk factors - pregnancy complications, early menopause, PCOS, and more, which are warning signs rather than isolated problems. And finally, we possibly should think differently about prevention assuming that one size does not fits all and that women may need lower BP thresholds for treatment because their risk starts increasing at a lower level.

In conclusion, CV organ damage in hypertensive women is not just a later-life but a lifelong concern. If we can shift our focus earlier, be more sensitive to sex-specific signs, and adopt a more tailored approach, we could possibly change the trajectory for hypertensive women.

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# PERSPECTIVES IN **HYPERTENSION**

# The link between obesity and hypertension: epidemiology, pathophysiology, and interplay

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Obesity and hypertension are closely linked conditions that pose a significant threat to global health. According to the World Health Organisation (WHO), obesity is a major risk factor for developing hypertension, which in turn increases the risk of cardiovascular disease, stroke, and kidney disease. This article reviews the epidemiology of obesity and hypertension, explores the pathophysiological mechanisms underlying the development of hypertension in obesity, and examines the interplay between these conditions.

# **Epidemiology of Obesity**

Obesity is a global epidemic, affecting 1 in 8 people (1). WHO defines obesity as abnormal or excessive fat accumulation that poses a health concern and uses a BMI of 30kg/m<sup>2</sup> or greater to screen for obesity in adults.1 Since 1990, the global prevalence of adult and adolescent obesity has more than doubled and quadrupled, respectively. WHO statistics on overweight and obesity increased from 39% and 13% of adults aged 18 and over, respectively, to 43% and 16% between 2016 and 2022.1

## **Epidemiology of Hypertension**

Hypertension is a major public health concern, affecting over 1.28 billion people, and is the leading cause of death and disability worldwide.2

#### **Abbreviations**

Acronym	Full form
WHO	World Health Organisation
BMI	Body Mass Index
SNS	Sympathetic Nervous System
NHE-3	Sodium-Hydrogen Exchanger 3
RAAS	Renin Angiotensin Aldosterone System
ACE	Angiotensin Converting Enzyme
BP	Blood Pressure

Age-related increases in the prevalence of hypertension make it a significant risk factor for renal disease, stroke, and cardiovascular disease. Additionally, the prevalence of hypertension rises with increasing BMI.3

## **Pathophysiology**

Complex, multifaceted pathophysiological processes contribute to the development of hypertension in obese people including:

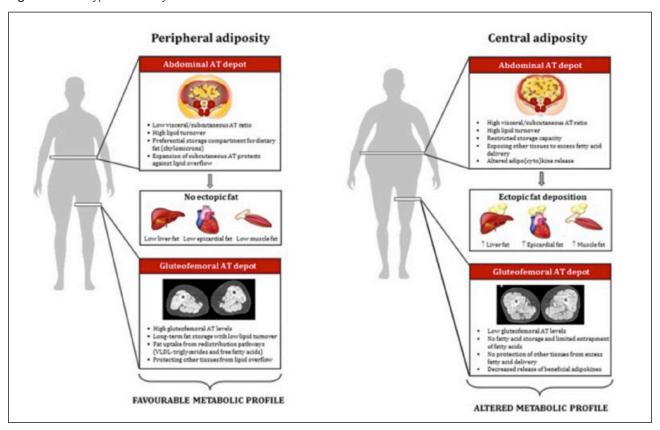
1. Insulin Resistance and Hyperinsulinemia: Obesity causes a state of insulin resistance with hyperinsulinemia, which contributes to hypertension through a variety of mechanisms. Firstly, insulin has sympatho-excitatory effects, as seen by increased muscle SNS activity after insulin







Figure 1: Phenotypes of obesity.10



infusion.4 Secondly, insulin directly promotes renal sodium retention in the proximal convoluted tubule via the sodium-hydrogen exchanger 3 (NHE3), and this is demonstrated in individuals with metabolic syndrome having a higher fractional sodium resorption than those without.<sup>5</sup> Additionally, with insulin resistance and hyperinsulinemia in obesity, vasodilatory effects of insulin are blunted, further enhancing vasoconstrictor tone.

- 2. Increased activity of the sympathetic nervous system: this plays an important role in the development of obesity-related hypertension. Obesity is associated with increased SNS activity, as alluded to above, which contributes to the development of hypertension via elevation in heart rate, cardiac output, and renal tubular sodium reabsorption; occurring as a direct result of  $\alpha$ -adrenergic and  $\beta$ -adrenergic receptor stimulation and indirectly through activation of other systems, such as the RAAS.6
- 3. Renin-Angiotensin-Aldosterone System (RAAS) Activation: Several studies show that obese people have higher levels of plasma renin activity, angiotensinogen, angiotensin-converting enzyme (ACE), and aldosterone, despite the state of volume expansion and sodium retention.7 A number of

pathways may trigger RAAS activation in obese individuals. Firstly, a bidirectional interaction exists between the SNS and the RAAS such that the RAAS increases sympathetic tone and, reciprocally, the SNS activates the RAAS, and secondly, intrinsic RAAS in adipocytes, which appear to produce angiotensinogen and angiotensin II.

4. Kidney Damage and Sodium Retention: Obesityrelated kidney damage and sodium retention also contribute to the development of hypertension. Visceral and retroperitoneal adiposity causes mechanical compression of the kidneys, and in addition, accumulation of perirenal fat may induce inflammation and expansion of renal medullary extracellular matrix, which leads to compression of the renal medulla.8 These mechanisms diminish renal blood flow and decrease sodium delivery distally to the macula densa, stimulating a feedback-mediated reduction in renal arteriolar resistance, increasing renal blood flow, and stimulating renin secretion from the juxtaglomerular cells.8 Ultimately this becomes a maladaptive vicious cycle resulting in nephron injury, glomerular sclerosis, impaired renal function, sodium retention, and elevated arterial pressures.







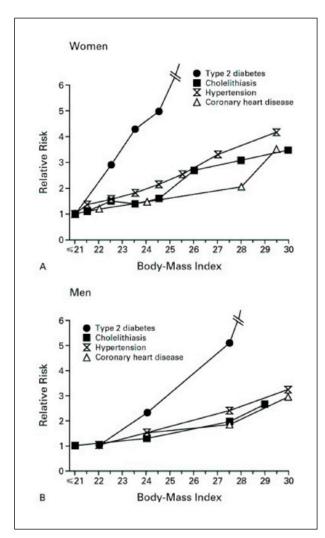


Figure 2: Relation between Body-Mass Index up to 30 and the Relative Risk of Type 2 Diabetes, Hypertension, Coronary Heart Disease, and Cholelithiasis; A- Women, B- Men (3).

5. Sleep Apnoea Syndrome: established cause of hypertension through neurohormonal dysregulation, endothelial dysfunction, inflammation, and increased levels of endothelin. Sleep apnoea syndrome is strongly associated with essential hypertension and has an increased risk of resistant hypertension.9 Also, obesity frequently coexists with obstructive sleep apnea (OSA), with the chronic intermittent hypoxia leading to activation of carotid body chemoreceptors that reflexively upregulate SNS activity, which acts similarly as discussed above to worsen blood pressure control.

6. Leptin-Melanocortin Pathway: Besides its effects on food intake and body weight regulation, it plays a role in regulating SNS activity and blood pressure (BP). Activation of specific melanocortin receptors

leads to sodium retention, circulatory expansion, and elevated BP6 with similar mechanisms to those elucidated above.

#### Interplay

Obesity and hypertension interact dynamically. Uncontrolled hypertension can lead to insulin resistance, hyperinsulinemia, dyslipidaemia, and ultimately obesity through intricate neurohormonal and pro-inflammatory processes. Similarly, obesity can cause or exacerbate hypertension through some of the intricate processes mentioned above.

Obesity has a heterogeneous phenotype, in that individuals with a similar BMI may have distinct metabolic and CV risk profiles, 10 hence the concepts of healthy and unhealthy obesity (Figure 1).10

Nonetheless, modest increases in weight or BMI have been associated with poorer cardiovascular outcomes (Figure 2).3 Thus, BMI is still very useful in identifying individuals at risk.

Conversely, reductions of even 5 to 10% can substantially improve blood pressure, serum lipid levels, and glucose profile and reduce the incidence or improve control of diabetes and hypertension (3). Indeed, this should be the target of therapy in most cases of these 2 diseases of public health concern.

#### **Conclusion and Recommendations**

The link between obesity and hypertension is well-established, with a complex interplay of pathophysiological mechanisms underlying the development of hypertension in obesity. Understanding the epidemiology and pathophysiology of these conditions is crucial for developing effective prevention and treatment strategies.

Maintaining a healthy weight or reducing weight through self- and policy-driven lifestyle modifications will go a long way to reduce the risk of hypertension, T2D, CAD, etc. By addressing obesity and hypertension through lifestyle modifications and evidence-based treatments, we can reduce the burden of cardiovascular disease.











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# PERSPECTIVES IN **HYPERTENSION**

# Salt sensitivity: The hidden factor in hypertension management

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As scientists who study high blood pressure (BP), we often get asked why two people can eat the same salty diet, yet one develops hypertension while the other's BP stays normal. The answer lies in a mysterious trait called salt sensitivity of BP (SSBP) that means that an individual's BP changes in parallel with their salt intake.1 About 50% of people with hypertension and 25% of those with normal BP are salt-sensitive, and this trait comes with higher risks of heart and kidney problems independent of BP levels.2 Yet, it remains underrecognized in routine care and there's currently no quick clinical test for salt sensitivity, making it a "stealth" contributor to cardiovascular risk.3

How, then, do we bring this hidden factor into the spotlight? Let's walk through three intriguing insights from our research journey: (1) the influence of sex on salt sensitivity, (2) an unexpected sodium-sensing role for the lining of red blood cells, and (3) a quick oral salt test that reveals BP's instant reaction to salt. Each of these stories highlights how SSBP can differ from person to person and why recognizing those differences matters for managing hypertension.

# 1. Sex-Specific Differences in Salt Sensitivity

Is salt sensitivity the same for everyone? Not at all – sex matters. It's well documented that before

menopause women have lower hypertension rates than men, yet paradoxically women of all ages tend to be more salt-sensitive than men.<sup>2</sup> We wanted to dig deeper into this sex difference. Would men and women respond differently if we gave them a standardized salt challenge? To find out, we conducted a study with over a hundred young adults (equal numbers of males and females) where we fed them a fixed dose of salt and closely tracked their BP.

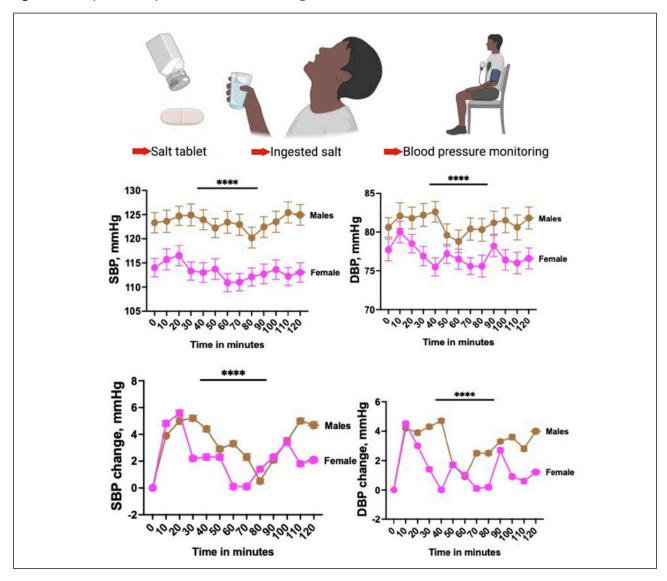
The results (Figure 1) showed that both men and women showed a clear BP rise after the salty drink, but the patterns diverged. Women's BP tended to spike and then settle back to baseline, whereas in men, BP remained elevated for a longer duration.4 In fact, over the two-hour monitoring period, the men's systolic pressures never fully returned to the starting point, unlike in women.<sup>4</sup> This suggests that males experienced a more sustained pressor effect from that single salt load. At first glance, one might think this means men are "more" saltsensitive. However, the story isn't so simple as we'll see next, women demonstrated their own form of salt sensitivity on a cellular level. What our findings did confirm is that men and women manifest salt sensitivity in distinct ways, possibly due to hormonal or physiological differences. Appreciating these nuances is important; for







Figure 1: Blood pressure responses to an oral salt challenge in men versus women.



example, dietary salt recommendations or hypertension treatment might need to be tailored with sex in mind. A one-size-fits-all approach to salt may miss such critical differences.

## 2. Erythrocyte Glycocalyx Sensitivity to Sodium

Our next discovery takes us to red blood cells (RBCs) and their surprising role in salt sensitivity. RBCs have a fuzzy coating of sugars and proteins called the glycocalyx, a negatively charged "sponge" that binds sodium, preventing it from flooding tissues.5 Excessive salt intake, however, can erode this glycocalyx, stripping away its protective barrier and allowing sodium into vessel walls, potentially causing inflammation and arterial stiffness.

To measure glycocalyx vulnerability, we use a test called erythrocyte glycocalyx sensitivity to sodium (eGCSS). High eGCSS indicates greater damage from

salt exposure. Salt-sensitive individuals (based on BP responses) had higher eGCSS values. Interestingly, women showed a stronger correlation between high eGCSS and salt-sensitive BP compared to men.4 Women's glycocalyx appeared more easily damaged by sodium, even though men's immediate BP rise was higher. This suggests women's protection from hypertension pre-menopause may involve short-term compensations, despite greater cellular sensitivity to salt.4 Thus, eGCSS could be a promising biomarker to identify individuals vulnerable to saltinduced cardiovascular risk before BP increases, something we are actively exploring.

## 3. Immediate Pressor Response to Oral Salt

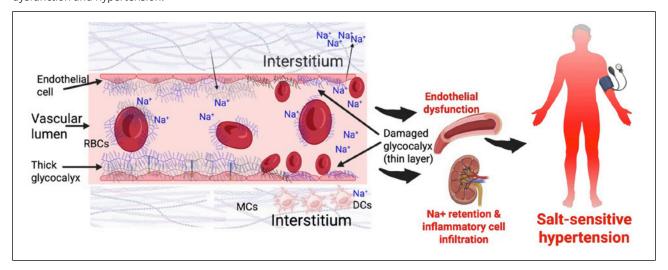
We've all heard that too much salt raises BP chronically. But we wondered: can a single salty meal instantly spike BP? For salt-sensitive individuals, the answer is yes. What we call the







Figure 2: Schematic of the red blood cell glycocalyx as a sodium buffer. This illustration depicts a red blood cell in the bloodstream, coated with a negatively charged glycocalyx (blue brush-like layer). In a normal state (left side), moderate sodium (Na+) intake is buffered as Na+ ions attach harmlessly to the glycocalyx, and the endothelial lining remains protected. In a high-salt state (right side), excess Na+ overwhelms the glycocalyx, and Na+ penetrates to the vessel wall leading to endothelial dysfunction and hypertension.5



Immediate Pressor Response to Oral Salt (IPROS). In our study, two grams of salt raised mean arterial pressure significantly (by ≥10 mmHg) in about 62% of normotensive young adults within 30 minutes, often remaining elevated for two hours. 6 Repeated daily spikes from salty meals could cumulatively damage blood vessels, increasing the risk of heart and kidney problems.6 Practically, IPROS testing, a simple salt challenge, could quickly identify saltsensitive individuals without lengthy dietary tests. Even measuring BP just 30 minutes post-ingestion reliably identifies salt responders, making IPROS testing feasible in clinical settings, enabling tailored guidance or therapies.

## **Embracing Salt Sensitivity** in Hypertension Care

Our exploration of salt sensitivity has convinced us that this hidden factor deserves more attention in hypertension care. While general advice to reduce salt intake is beneficial for everyone, it's critical for salt-sensitive individuals, where salt strongly drives BP spikes and cardiovascular harm. Identifying these individuals through quick tests like IPROS or eGCSS blood biomarkers could soon become routine. With this knowledge, clinicians can provide tailored advice, emphasizing targeted salt reduction, selecting antihypertensive medications designed to counteract salt effects, and closely monitoring salt-sensitive patients. As researchers passionate about this area, we're optimistic:

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increased awareness of salt sensitivity will enhance hypertension prevention and treatment, one salty (or perhaps salt-free!) bite at a time.

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# PERSPECTIVES IN **HYPERTENSION**

# The skin's impact on blood pressure control and hypertension

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Skin is our largest organ. It constitutes the surface of our body and the boundary to the outer environment. We can feel and see it every day, and we all have our associations with skin such as perception of tenderness or pain, scars or crinkles, protection from cold, heat, UV light or from fluid

It is much less known that skin is an endocrine organ which is able to synthesise and release a multitude of hormones and mediators, many of which are involved in the regulation of blood pressure.1 Among those cutaneous, vasoactive hormones are catecholamines, angiotensin II, aldosterone, substance P and bradykinin. For all these molecules, there is evidence that they can be synthesised locally by cutaneous cells and residing immune cells suggesting that their tissue concentration does not depend on supply from the circulation but can be regulated locally. Cutaneous cells such as keratinocytes or dermal fibroblasts express receptors for these vasoactive hormones which again points to local effects.

This article will discuss four mechanisms by which the skin and cutaneous hormonal systems potentially impact blood pressure regulation: a) Regulation of the diameter of cutaneous resistance vessels, b) Activation of cutaneous water conservation mechanisms, c) Regulation of sodium storage in skin, and c) Regulation of sodium excretion by sweat.

## a) Regulation of the diameter of cutaneous resistance vessels

Subcutaneous tissue harbours a dense network of resistance arteries. Generally, an increase in the diameter of cutaneous resistance arteries within a large area of skin triggers the lowering of systemic blood pressure. This has been shown for cutaneous vasodilation induced by irradiation of half of the body surface with UV-A light.3 However, until very recently, it was not known whether local, cutaneous hormones can have an impact on systemic blood pressure by changes to the diameter of cutaneous resistance arteries, although experiments in isolated cutaneous vessels had proven responsiveness of these arteries to vasoactive hormones such as angiotensin II.4 A study published in May 2025 in Nature Communications has now provided evidence using genetically altered mice that angiotensin II locally synthesised in skin increases systemic blood pressure through constriction of cutaneous resistance arteries.5

# b) Activation of cutaneous water conservation mechanisms

Based on preclinical data, the group of Akira Nishiyama recently developed a novel concept suggesting that in case of renal water loss because of tubular damage and renal dysfunction, compensatory water conservation mechanisms in the skin are triggered such as vasoconstriction leading to reduced skin blood flow and less











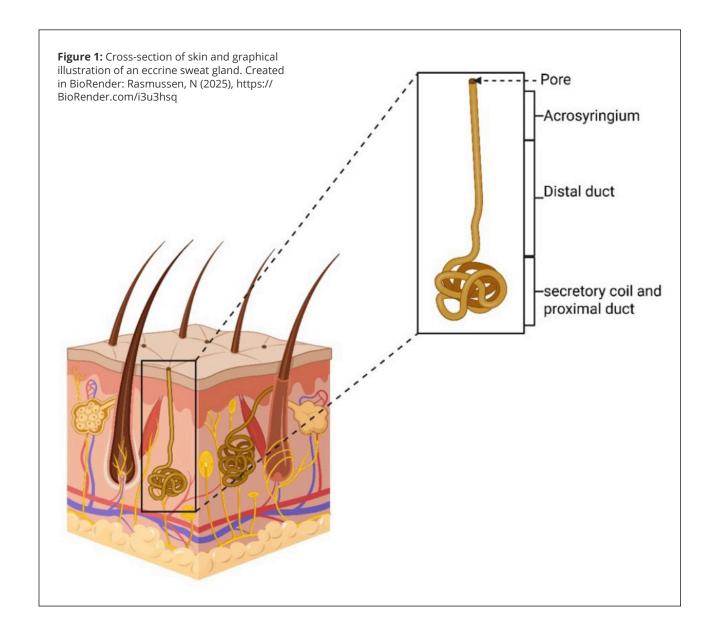
trans-epidermal water loss. These compensatory mechanisms can "outperform" the original renal fluid loss thus leading to an increase in body fluid volume and subsequently hypertension.6

#### c) Regulation of sodium storage in skin

It is now well established that skin has the capacity to store significant amounts of sodium.<sup>2</sup> This suggests an impact of cutaneous salt on fluid homeostasis and systemic blood pressure - an association that is indeed supported by some studies, but there is also controversy.7 Moreover, the mechanisms by which cutaneous, accumulated sodium may influence blood pressure are poorly understood.

## d) Regulation of sodium excretion by sweat

Human skin harbours so-called eccrine sweat glands in high density. Sweat glands consist of the secretory coil in which sweat is produced and of the (proximal and distal) sweat gland duct, which connects the secretory coil to the pore on the skin surface (Fig. 1). Interestingly, cells lining the distal eccrine sweat gland duct have striking similarity with cells of the collecting duct of the nephron. They possess the sodium channels and transporters ENaC and Na+/K+-ATPase and are capable of reabsorbing Na+ and water from the lumen of the duct.8 Moreover, these cells express mineralocorticoid and probably also angiotensin receptors which indicates that Na+/









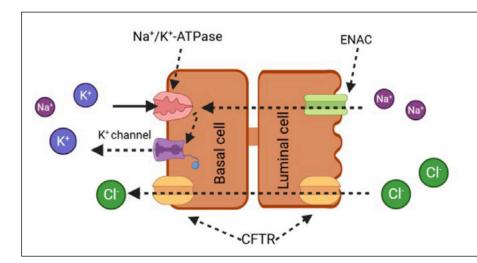


Figure 2: Schematic illustration of an eccrine sweat gland duct cell showing its similarity with cells of the renal tubular system. ENaC: Epithelial sodium channel. Created in BioRender: Rasmussen, N (2025), https:// BioRender.com/yig6vis

water reabsorption by these cells is controlled in a similar way as Na+/water reabsorption in the kidneys. There is actually evidence from two clinical studies that these "cutaneous mini-kidneys" (which are small but abundant in very high number) may have a role in blood pressure control by their impact on Na+/water reabsorption and, thereby, on extracellular volume. This is indicated by the fact that both studies found a negative correlation between Na+ concentration in sweat and blood pressure levels in subjects with hypertension.<sup>9,10</sup> Or in other words: a lower Na+ content in the sweat of hypertensive patients indicates a higher rate of Na+ (and water) reabsorption thus leading to an increased extracellular volume, which may contribute to the higher blood pressure levels.

Collectively, recent accumulating evidence suggests that the skin has been underestimated as endocrine organ and in view of a potential role in the control of sodium and fluid homeostasis and consequently blood pressure. Our comprehension of the role of skin for blood pressure control is still in its "childhood days" and many more studies are needed to understand the net contribution of the skin to the control of systemic blood pressure, the local, cutaneous blood pressure-relevant control mechanisms including local hormonal systems and the impact of the effect of antihypertensive drugs on cutaneous systems for their therapeutic effect.

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# PERSPECTIVES IN **HYPERTENSION**

## Inflammation in hypertension: from mechanisms to therapeutic perspectives

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Hypertension remains a leading global health concern, affecting over a billion individuals worldwide. As clinicians, we typically manage hypertension by targeting conventional mechanisms- fluid overload, renin-angiotensin system activation, or sympathetic overactivity. However, an expanding body of evidence now positions chronic inflammation as a critical contributor to the pathogenesis and progression of hypertension. Understanding the inflammatory underpinnings of hypertension may offer innovative therapeutic pathways beyond standard blood pressure management.

#### **Clinical Evidence Linking Inflammation and Hypertension**

Inflammation's role in hypertension is clearly demonstrated through clinical observations. Patients with inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, and periodontitis have significantly higher risks of developing hypertension. Epidemiological studies have shown that individuals suffering from psoriatic arthritis, rheumatoid arthritis, or chronic periodontitis are substantially more likely to develop hypertension, with reported increases in prevalence approaching 90%, 50%, and over 20% respectively when compared to individuals without these conditions. 1-3 Furthermore, elevated levels of inflammatory biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNFα), or IL-1β have been associated with higher systolic and diastolic blood pressure values highlighting a link between systemic inflammation and elevated blood pressure.4 Evidence from large cohort studies such as NHANES and the UK Biobank has shown that individuals with higher levels of circulating proinflammatory immune cells - including monocytes, neutrophils, and activated lymphocytes- tend to exhibit increased systolic and diastolic blood pressure. 5 These observational findings are bolstered by Mendelian randomization analyses (a method that uses genetic variants as instrumental variables to infer causality in observational data, helping to strengthen causal inference) leveraging genome-wide association study (GWAS) data, which indicate that elevated lymphocyte counts may play a causal role in blood pressure elevation.6

#### **Mechanistic Insights: How Does Inflammation Drive Hypertension?**

Inflammation promotes hypertension through interconnected immune mechanisms involving immune cell activation, cytokine release, and neuroimmune interactions. Activated immune cells-including TH17 lymphocytes, cytotoxic CD8+ T cells, macrophages, and dendritic cells- migrate from secondary lymphoid organs, notably the spleen, to target tissues such as kidneys, vascular walls (particularly perivascular fat and adventitia), the heart, and the brain. Within these tissues, they secrete cytokines (IL-17, IFNy, TNFα, IL-6, and IL-1β), promoting local inflammation. For example, IL-17 and IFNy directly induce endothelial dysfunction through oxidative stress, whereas IL-1β – activated







via the NLRP3 inflammasome- enhances renal inflammation and sodium reabsorption.7-9 (Table 1)

Recent evidence also highlights other key inflammatory players contributing to hypertension. Activation of the complement system- particularly its alternative pathwaygenerates pro-inflammatory mediators that exacerbate renal inflammation, endothelial injury, and vascular remodelling. Additionally, neutrophils have emerged as critical contributors, promoting vascular damage through the formation of neutrophil extracellular traps (NETosis), further intensifying endothelial dysfunction and inflammation.9

These inflammatory processes collectively amplify systemic inflammation and sympathetic nerve activity, ultimately driving sustained blood pressure elevation. Conversely, regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs) act as protective counter-regulators by limiting inflammatory responses 9 . Tregs suppress inflammation by secreting anti-inflammatory cytokines such as IL-10, while MDSCs help mitigate blood pressure elevation and vascular inflammation, highlighting their potential therapeutic relevance.

Chronic activation of the sympathetic nervous system further reinforces inflammation by stimulating spleen-mediated immune responses, perpetuating hypertensive disease.

#### **Targeting Inflammation: Emerging Therapeutic Strategies**

Given inflammation's role in hypertension, therapeutic strategies targeting inflammatory pathways offer promising new approaches.

In preclinical animal models (e.g., mouse and rat studies), monoclonal antibodies targeting pro-inflammatory cytokines, such as IL-17 and IL-6, have demonstrated the potential to reduce

**Table 1**: Key Inflammatory Actors in Hypertension

Cells	Description	
TH17 lymphocytes	CD4+ T cells producing IL-17, promoting inflammation	
Cytotoxic CD8+ T cells	Eliminate infected or damaged cells, release pro-inflammatory cytokines	
Macrophages	Innate immune cells involved in inflammation, tissue remodelling	
Dendritic cells	Antigen-presenting cells, activate T cells	
Regulatory T cells (Tregs)	Suppress immune response, produce anti-inflammatory IL-10	
Myeloid-derived suppressor cells (MDSCs)	Counter-regulatory myeloid cells, limit inflammation and vascular damage	
Neutrophils (via NETosis)	Promote endothelial dysfunction through formation of neutrophil extracellular traps (NETs)	
Cytokine		
IL-17	Enhances local inflammation and tissue injury	
IFNy	Promotes vascular inflammation and immune activation	
TNFα	Triggers systemic inflammation, endothelial dysfunction	
IL-6	Systemic inflammatory mediator, increases vascular stiffness	
IL-1β	Activated by NLRP3 inflammasome, drives renal inflammation and sodium retention	
Complement (C3, C5)	Generates pro-inflammatory mediators exacerbating endothelial injury and vascular remodeling	







blood pressure and attenuate hypertensive organ damage. Similarly, inhibition of the NLRP3 inflammasome, a multi-protein complex of the innate immune system responsible for detecting cellular stress signals and activating pro-inflammatory cytokines like IL-1β, has shown promising effects in reducing hypertension and associated organ injury in these animal models. In humans, indirect approaches aiming to reduce systemic inflammation, such as the treatment of periodontitis and other inflammatory comorbidities, have yielded significant cardiovascular benefits. Indeed, evidence from clinical trials and observational studies highlights that even low-grade chronic inflammation in hypertensive or high-risk cardiovascular patients should be actively addressed. Particular attention should be given to oral health in humans, as periodontitis represents a modifiable inflammatory trigger with demonstrated clinical relevance in hypertension management. Future therapeutic strategies for humans might also include innovative bioelectronic approaches aimed at modulating inflammatory pathways through nerve stimulation, and the use of nanoparticle-mediated targeted delivery of immunosuppressants directly to inflamed tissues. Such strategies, although still under investigation, hold promise for more precise and effective inflammation control in hypertension.<sup>10</sup>

Despite these promising approaches, rigorous clinical studies are essential before widespread implementation of inflammation-targeted therapies can be recommended in routine clinical practice.

#### **Conclusions and Clinical Perspectives**

The link between inflammation and hypertension provides clinicians with novel insights and potentially transformative therapeutic targets. Future management of hypertension may increasingly include therapies aimed at reducing systemic inflammation, potentially improving outcomes beyond simple blood pressure control. Biomarkers of inflammation could become critical tools for patient stratification and risk prediction.

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# ISH CAPACITY **BUILDING NETWORK**

# Forming new collaborations: perspectives of an early-mid career researcher

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I want to share my personal experience of forming collaborations. I presented a short talk about this topic at the ISH Capacity Building Network symposium in Cartagena in September 2024. At the meeting ISH generously supported two Collaboration and Exchange grants. These grants were designed for early career researchers who met new, more senior colleagues at ISH2024 and identified an opportunity to collaborate. This short article will discuss my experiences in forming new collaborations on the back of conversations at scientific meetings and some tips on ways to start, build and maintain these collaborations.

#### **Networking takes many forms**

I have been extremely fortunate to attend several ISH meetings and congresses of other organisations as a junior researcher, PhD student and early postdoc. As an introverted person, I struggle to talk to people until I really get to know them. Being an introvert makes formal networking events feel awkward, and this was especially so early in my career when I didn't know many people. I found introducing myself to new people daunting (still do!), especially at these events when everyone always seems to be deep in conversations. But, over time, I've learned the importance of making the most of conferences. Having everyone in the same place, at the same time offers a rich opportunity to explore conversations about important topics, throw ideas around and importantly get to know one another.

For me, my collaboration with Dr Rémi Goupil that started on the back of a scientific meeting didn't involve any of the above, but instead, came

#### Ingredients for successful collaborations

### Building

- Opportunity to work together or visit
- Develop a research question or project idea
- Regularly communicate to build rapport and trust
- Time and capacity

### Maintaining

- Open and honest communication
- Accountability
- Developing track record of work together
- Seek funding where needed
- · Time and capacity

### Starting

- Mutual interest
- Get along well
- Complementary skills/ ideas/ expertise/ perspectives
- Time and capacity













about through viewing a poster, and contacting the presenter directly. I just couldn't find Rémi at the conference despite looking everywhere. I have found that if you reach out to people and are genuinely interested in their work, they are very open and willing to meet and discuss with you and from there opportunities to collaborate can start to emerge. It probably goes without saying but not every conversation is going to lead to a longer-term collaboration – that is unrealistic.

#### Key ingredients for starting, building and maintaining collaborations.

Starting collaborations. Having a mutual interest is critical, being open, that you like each other as people and can see potential for a synergistic, symbiotic collaboration! Having complementary skills and bringing different perspectives to research questions probably also helps. As a nonclinician, new collaborations that I have formed have invariably been with clinician-researchers.

Building collaborations: This can only occur by creating an opportunity to work together on a project or do a collaborative exchange. Although I had never met Rémi, in person, over time we started working on more projects and I was fortunate to receive a collaboration grant to visit Rémi's team, which gave us the opportunity to build a stronger connection. In other words, you just get to know each other. This helps build trust and through discussions, new interesting opportunities to work together hopefully emerge.

If you don't have your own data available, think creatively about open access data sources that might be able to answer a question or systematic reviews that would be useful contributions to the field. Again, here, we had systematic review questions to work on together.

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Maintaining collaborations: Although my career is relatively short so far and these collaborations are still fairly new, I think having open, honest communication is important. Being accountable to each other and when you don't hold up your end of the bargain, accepting responsibility for that. The more you work together, the stronger your collaborative track record becomes, which can give you a better chance in research funding applications.

In my career to date, I have been lucky to have different opportunities to explore and foster international research collaborations. I have found that pursuing collaborative projects has enriched my research knowledge by opening my mind to different perspectives, expertise, points of view and lived experience of others from different regions of the world. Rémi and I hope that sharing this story and some practical tips may help others explore these opportunities.

#### **Acknowledgements:**

Thank you to Dr. Rémi Goupil for his feedback on this article.



From left to right: Remi Goupil, Prof. Mohsen Agharazii & Dean Picone.

The ISH Capacity Building Network offers career development and networking opportunities for early and mid-career researchers and those from under-represented backgrounds. Launched in 2023, it is co-led by Chair of the ISH New Investigator Committee Dean Picone; Chair of the ISH Women in Hypertension Research Committee Yan Li and Chair of the ISH Mentorship and Training Committee, Lebo Gafane-Matemane.











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# ISH AFFILIATED SOCIETY REPORTS

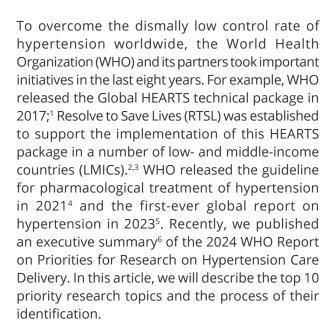
## Executive summary of the WHO report on priorities for research on hypertension care delivery

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Several members, including the two of us, from WHO, Johns Hopkins University, and Resolve to Save Lives first identified a leadership team of ~15 experts with representation of geographic areas and relevant expertise. Then, the leadership team decided on the scope and objective of this project. Our objective was to identify priority research topics that immediately and directly are related to the delivery of hypertension care. We then identified five themes: (1) Healthcare workforce; (2) Service delivery system; (3) Patient retention/ adherence; (4) Financing care delivery system; and (5) Research gaps acknowledged in the WHO 2021 hypertension treatment guideline.4

We hosted a webinar for each theme from March through September 2022. Before

each webinar, we sent "prewebinar survey" to webinar invitees (experts in the relevant fields in addition to the leadership team members), asking them to propose up to five priority research questions and five articles relevant to the webinar theme (e.g., Healthcare workforce). According to the feedback from the pre-webinar survey, the leadership team made a "post-webinar survey" with several questions to curtail potential priority research topics. We administered the post-webinar survey at the end of each webinar. Based on the response to the post-webinar survey, the leadership team constructed several priority research topics for each theme as well as their relevant study designs (e.g., qualitative studies, implementation studies, and randomized controlled trials). Lastly, the leadership team determined the top 10 priorities across the five themes by voting.

Our top 10 priority research topics are wellbalanced across the five themes (Table 1). Tasksharing was a cross-cutting theme and was relevant to four of the 10 priorities (priorities #3, 4, 8, and 10). Task-sharing would be pertinent to priority #2 as well, which evaluates a new system allowing hypertension care closer to home. There were three priority topics related to medications under different themes: priority #1, cost-effectiveness of











**Table 1**. Top 10 priority research topics for improving hypertension care

Ranking	Theme	Research Priority	Examples of study designs
1	Gap in the WHO 2021 Guideline	Cost-effectiveness of combination therapy in LMICs, especially single-pill combinations, relative to monotherapy	RCT, simulation/modeling study
2	Patient retention and medication adherence	Evaluation of a system allowing hypertension care closer to home (e.g., community clinics or even in the patient's own home)	Quasi-experimental Studies, cluster RCT, implementation research,
3	Healthcare workforce	Effectiveness and safety of health system reform allowing trained community health workers (CHWs) to refill or even initiate/titrate antihypertensive medications under the supervision of appropriate professionals (e.g., physicians and/or nurses)	Quasi-experimental Studies, cluster RCT
4	Healthcare workforce	Effectiveness and safety of health system reform allowing nurses to diagnose and treat hypertension	Quasi-experimental Studies, cluster RCT, implementation research
5	Financing of healthcare	Exploration of gaps in the medication supply	Root cause analysis
6	Service delivery system	Efficacy/effectiveness of a new approach integrating the management of hypertension and other chronic diseases	Quasi-experimental Studies, cluster RCT
7	Patient retention and medication adherence	Effectiveness of a digital approach for improving medication adherence and patient retention	Quality improvement project, RCT
8	Healthcare workforce	Identification of optimal approaches to training healthcare workers to support task-sharing	Cluster RCT, qualitative research, implementation research, quality improvement project
9	Financing of healthcare	Cost-effectiveness or cost analysis of different approaches to financing hypertension care in a specific region/country	Cluster RCT, simulation/ modeling study
10	Service delivery system	Implementation research on an approach to task-sharing that addresses barriers in relevant settings	Implementation research, qualitative study

LMICs=low- and middle-income countries; RCT=randomized controlled trial







single-pill combination therapy in LMICs; priority #5, exploration of medication supply gaps; and priority #7, effectiveness of digital approaches for improving medication adherence. The other two topics were integration of care for hypertension and other clinical conditions (priority #6) and costeffectiveness of different approaches to financing hypertension care (priority #9).

Usually, investigators come up with their research topics according to gaps in the literature, their perspectives (e.g., clinical observation), and public needs. In that context, this project was unique for us by hosting five webinars with over 200 invited experts from Africa, the Americas, Asia, Europe, and Oceania to identify top priority research topics for improving hypertension management on a global scale.

We anticipate that these research priorities will guide individual researchers. In this regard, it was nice to see a recent simulation study addressing our priority #1 topic about the cost-effectiveness of single-pill combination.7 Furthermore, these

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priorities should call on governments, funding agencies, and expert organizations to consider supporting these critical research areas.

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# ISH AFFILIATED SOCIETY REPORTS

### Canadian hypertension guidelines taking on a new look

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#### A New Guideline Approach

Canada boasts a rich tradition in hypertension, being among the world's leading nations in terms of hypertension treatment and control rates.1 However, recent years have witnessed somewhat of a setback with a gradual decline in hypertension treatment and control rates across the country.<sup>2,3</sup> While the reasons behind this decline are likely multi-factorial and incompletely understood, some theories have included overly complex guideline recommendations, confusion surrounding optimal blood pressure targets, underdeveloped implementation strategies, and inadequate engagement with primary care.4 Further compounding these challenges, there has been a time gap in national recommendations due to leadership changes and the COVID-19 pandemic such that the most recent set of Hypertension Canada guidelines were published in 2020.5

We viewed this time lapse as a unique opportunity to re-imagine the structure the guidelines should take to better serve the Canadian population by addressing these known challenges. The new guideline approach is a two phase process. 6 The first phase involved producing a primary care-specific set of guidelines. As primary care is where the vast majority of hypertension care takes place, we felt that that targeting this audience would be paramount to combat the current worrisome trends in hypertension that we are experiencing in Canada. The goal was to work alongside primary care providers to develop pragmatic recommendations and algorithms for efficient implementation into everyday clinical practice. The second phase will be a more traditional comprehensive hypertension guideline. However, rather than updating all topics simultaneously, we will be making updates on a rolling topic-by-topic basis such that there will be a "living" guideline which is constantly being updated. We believe this approach will enhance the efficiency and quality of our guidelines.

#### **Primary Care Guidelines**

Our primary care guidelines were designed to serve as a framework for managing the majority of cases of hypertension in primary care. The committee developing these guidelines consisted primarily of primary care providers (family medicine physicians, pharmacists, and nursing) along with hypertension specialists and a GRADE methodologist. We also









worked alongside a group of patient-partners with lived experience with hypertension which provided feedback throughout the guideline development process and led the creation of a patient support tool which was released concurrently with the guidelines. In essence, this patient support tool provides a public-/patient-facing dissemination of our guideline recommendations. Our committee placed a priority on limiting the number of recommendations to those most relevant to hypertension management in primary care to keep the guidelines streamlined and pragmatic.

We developed a total of nine recommendations under the topics of hypertension diagnosis and hypertension treatment. We rated the strength of recommendation and certainty of evidence by applying the GRADE framework.8 Diagnostic recommendations included a standardized approach to measuring blood pressure and confirming hypertension as well as providing a uniform definition for hypertension. Treatment recommendations included setting blood pressure targets, promoting healthy lifestyle changes, and providing stepwise guidance on optimal drug choices for patients requiring pharmacotherapy. Notable changes within these guidelines relative to prior Hypertension Canada guidelines include the promotion of initial low dose combination therapy for patients requiring pharmacotherapy, the adoption of ≥130/80 mmHg as the threshold to define hypertension, and setting a systolic blood pressure treatment target of <130 mmHg. We acknowledge that these recommendations do not apply to all clinical scenarios; rather, they provide a simple pragmatic approach to hypertension management that can be applied to the majority of hypertension cases encountered in the primary care setting.

Additionally, we used HEARTS to develop suggested algorithms for both the diagnosis and treatment of hypertension in primary care. HEARTS is a framework developed by the World Health Organization which outlines principles regarding optimal diagnostic approaches and simplified directive algorithms to improve hypertension control at the population level.9 HEARTS has a strong track record of success, having been utilized successfully in a number of countries to improve hypertension care. 10 In our primary care guidelines, we adapted HEARTS to the Canadian context to develop standardized protocols that we believe will help to improve population-wide blood pressure control. These include providing specific medication recommendations based on factors such as drug efficacy and tolerability, cost, coverage, availability, and protection from future drug shortages. We also will utilize HEARTS wellestablished implementation policies to engage primary care providers in an effort to optimize the uptake of our guideline recommendations.

#### **Comprehensive Guidelines**

With our primary care guidelines now publicaly available, we are now turning our attention to updating our comprehensive guidelines. These guidelines will be designed to serve as a resource for more specialized and nuanced aspects of hypertension care. As opposed to a traditional all-encompassing set of guidelines, we will be developing a "living" set of comprehensive guidelines within which topics are continually being updated on a rolling basis. For this endeavour, we will be partnering with Hypertension Australia to share the costs of evidence synthesis and harmonize our guidelines. This new approach was chosen to optimize efficiency and allow us to focus on specific priority topics within hypertension for which new and practice-changing evidence emerges. We are currently in the process of conducting a priority setting exercise among our Hypertension Canada members and other key stakeholders to determine which initial topics to update first. We aim to release the first set of these priority topic-specific guidelines toward the end of this year or early next year. Going forward, each year we will plan to update multiple topics. Thus, our comprehensive guideline will be continuously evolving in parallel with the latest available literature.

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# ISH AFFILIATED SOCIETY REPORTS

## Croatian Action on Salt and Health (CRASH) less salt, more health

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In 2006, the main aim of the CRASH was to decrease salt intake in Croatia by 16%. We have organized educational activities to increase awareness on salt harmfulness, define food categories of prime interest, collaborate with industry and determine salt intake (24 h urine sodium excretion). This is a brief report of the Croatian successstory, which is based on our enthusiasm, dedication, determination and persistence (Figure 1). Our motto is Failure in not an option.















#### First Period (2005-2014)

Initial Steps of the Croatian Society of **Hypertension and Croatian Food Agency** 

One year after the announcement of the World Action on Salt and Health program, a Declaration on the importance of starting a national campaign to reduce salt intake in Croatia was accepted at the Congress of the Croatian Society for Hypertension in 2006, and in 2007 the Croatian initiative (Croatian Action on Salt and Health—CRASH) and the national program were presented with the motto Less salt, more health (Figure 1).









These first actions have already led to initial results. Public awareness of the harmful effects of excessive salt intake and the importance of reducing it increased, and parts of the industry have started to reduce voluntarily the NaCl content in their products.

#### Table 1. Actions and achievements in the first period

- (1) The average intake of salt was determined (11.3 grams per day)\*
- (2) The relationship between the amount of consumed salt and BP values was established \*
- (3) An insufficient awareness of the general population about the harmfulness of high intake of salt was determined\*
- (4) The proportion of salt in bakery products has been determined (ranging from 1.56% to 2.0%)\*
- (5) The proportion of daily salt intake from bread and bakery was determined (2.46 g per day)\*
- (6) Education was organized for health workers, as well as public health actions (Figure 2).
- (7) Negotiations with the food industry, restaurants and catering facilities have begun.
- (8) A position paper on the harmfulness of excessive intake of salt was launched.
- \*24-hour urine sample, national, representative random sample of adult population in Croatia

#### Second Period (2014-2019)

#### **Action Plan for Salt Reduction in** Croatia, Ministry of Health

These initial steps were the basis for the action plan for salt reduction in Croatia which was prepared according to the WHO recommendations for reducing the intake of salt in the population: (1) To decrease salt intake by 16% over 4 years (4% per year in period of 2014-2019). (2) To increase awareness on salt harmfulness. (3) To define food categories of prime interest. (4) To determine salt intake by measuring 24-hour urine sodium excretion. (5) To develop new recipes in collaboration with the food industry. (6) To monitor salt intake, in collaboration with the food industry and analyse trends in awareness.

#### Table 2. Actions and achievements in the second period

- (1) The Ministry of Agriculture, Forestry and Fishery adopted the Ordinance on Cereals and Cereal Products, and determined that the proportion of salt in ready-to-eat baked bread should not exceed 1.4%
- (2) The largest meat industry in Croatia, PIK Vrbovec, made a reformulation of meat products and reduced the proportion of salt in all its products by an average of 25%.
- (3) We have continued with educative public health actions that increased awareness about salt (Figures 2 and 3)
- (4) The control of the implementation was performed by analysing the share of salt in bakery products (the amount of salt was reduced to 1.21 - 1.34%) (Figure 3).
- (5) The bakery industry was found to be compliant: 72% and 66% of breads and bakery products had a salt content <1.4%, respectively.
- (6) Unfortunately, the data showed that the intake of salt had not decreased. However, salt intake was estimated using spot morning urine samples, which is not reliable.











#### Third Period (2020-2025)

#### Continuation of activities under leadership of the Croatian Hypertension League

Although officially the Action Plan of the Ministry of Health surprisingly and unexplainably has not been continued the Croatian Hypertension League and partners have proceeded with all previously planned activities.

#### Table 3. Actions and achievements in the third period

- (1). The Ministry of Agriculture, Forestry and Fishery adopted the second Ordinance on Cereals and Cereal Products determining that the proportion of the salt in ready-to eat baked bread and bakery products should not exceed 1.3%.
- (2) Two position papers were launched: on salt in bread and bakery products, and on salt in meat products
- (3) We have continued with numerous educational activities for the general population further expanding them by launching the digital educational platform Hunting for the Silent Killer. https://tihiubojica.hr/
- (4) Awareness of the harmful effects of high salt intake increased (Figure 3).
- (5) The average salt intake was determined (8.6 g/day) (Figure 4).
- (6) The intake of salt was reduced by an average of 15.9% (22.8% and 11.7% for men and women, respectively) (Figure 5)\*.
- (7) Decrease of salt intake was associated with decrease of BP at the population level, and with decrease of stroke mortality (Figure 5).
- (8) Predictors of high salt intake were determined, and regional differences were observed.
- (9) Proportion of subjects who ingested less than of 5 grams of salt per day increased, but still a high proportion of population is ingesting high and very high amount of salt per day (Figure 4).
- (10) The iodine intake was assessed, and the largest number of the adult population (71.7%) had iodine intake above recommended 100 µg/l\*.
- \*24-hour urine sample; national, representative random sample of adult population in Croatia

#### Future Plans — to decrease salt and increase potassium intake

In addition to reducing the high intake of salt in the next phase of the CRASH we added importance of an increase in potassium intake which is too low in our population. We will continue our negotiations with food industry, restaurants and catering services and we will work even harder on education. The educational program of the Croatian Hypertension League for increasing health literacy will be additionally targeted to subsets of the population determined to ingest higher amounts of salt. It will have two arms—one organized by using classic public health methods, and the other using digital technology. The success of the programme will be measured using the same methodology.

#### Conclusion

The CRASH has been very successful: salt consumption was substantially reduced, and awareness about the harmful effects of high salt consumption significantly increased. A very good collaboration with the food industry has been established. Our nice story might be a good lesson to other countries showing that improvements can be made even without the official support, endorsement and the help of politicians. However, undoubtedly, these results would be even better with long-term multisectoral collaboration, and it is our hope that this will be achieved in the near future. If not, we will continue anyhow.











Figure 1. Croatian Action on Salt and Health – flow-chart of long-lasting activities

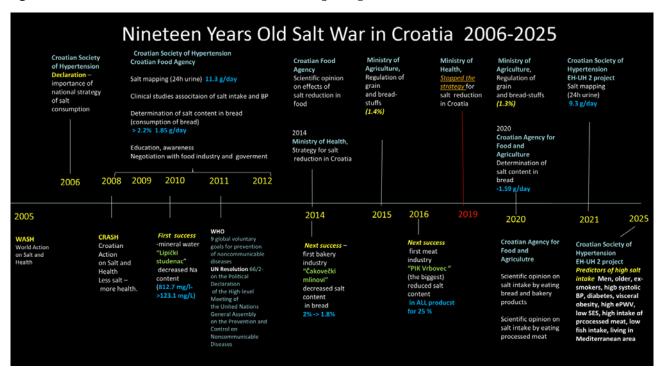
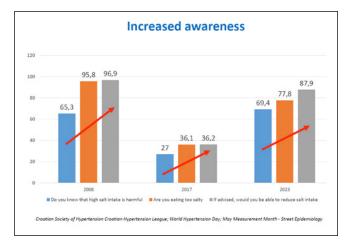


Figure 2. Educational materials - increasing health literacy through various channels



Figure 3. First achievements – increased awareness and decreased salt content in bread



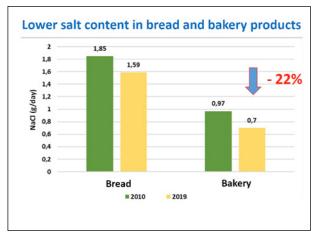


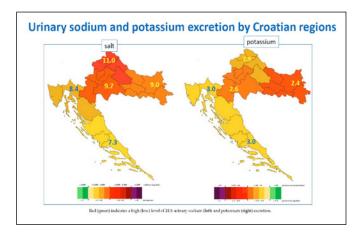








Figure 4. Salt and potassium intake in Croatian adult population - on the road to success



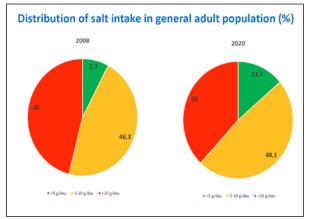
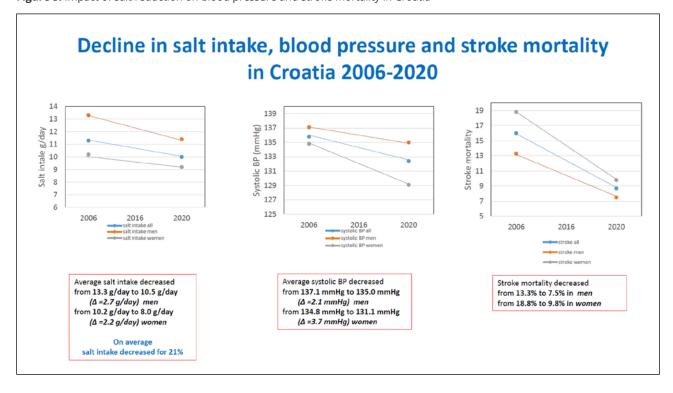


Figure 5. Impact of salt reduction on blood pressure and stroke mortality in Croatia



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# ISH AFFILIATED SOCIETY REPORTS

### The story of Hypertension Camp in Thailand

APICHARD SUKONTHASARN

President of the Thai Society of Hypertension



Thailand is facing a significant risk of increasing cardiovascular disease especially in stroke in the very near future. Data from the Thai Ministry of Health revealed that mortality from stroke in Thailand was the highest ever in the year 2023, with a total of 350,934 cases (961 cases per day) and 47,275 deaths (130 deaths per day). Rates of both coronary artery disease and stroke are still increasing. The way to best control this dreadful threat is to have better blood pressure control.

In Thailand we have increasing prevalence of high blood pressure due to several risk factors such as increasing obesity, urbanization, socioeconomic stress, alcohol abuse, and poor salt intake control. Most of all, we have a very significant threat from ambient air pollution which occurs every year from March to June. Many cities in Thailand had the level of PM2.5 about 5 to 10 times higher than WHO's recommended threshold during the dry season. Addressing the underlying risk factors for high blood pressure will be a long-term challenge.



Unfortunately, awareness of high blood pressure in Thai people is still low, and the result of the latest National Health Survey indicates that this awareness is even lower than in the past decade. In 2024, the Thai Hypertension Society announced new Thai hypertension guidelines. Notably, blood pressure readings of 130-139/80-89 mmHg are now defined as "BP at risk" instead of "high-normal" and the recommendation for diagnosis is simpler and faster, with just one outpatient visit with careful standard blood pressure measurement. The Thai ministry of health has tried to encourage health centers all over the country to adopt earlier hypertension diagnosis with just one or two outpatient visits, but progress has been slow and diagnostic inertia persists across most health centers.

In 2019, the Thai Hypertension Society, the International Society of Hypertension (ISH), together with the Asia Pacific Society of Hypertension, arranged a successful one-week Summer School in Ayutthaya Province, Thailand. This impactful event inspired numerous scholars from several countries in the region including Vietnam, South Korea and Japan. Inspired themselves, participating Thai faculty and scholars strongly encouraged the Thai Hypertension Society to host more meetings in Thailand, designed in the same manner, to educate, inspire and train the next generation of Thai physicians and address this critical national health issue.

Following discussions with Abbott Thailand and with support from the ISH, the first hypertension camp, a full-day training event, was successfully launched on 14 March 2024, with a second held on













15 August of the same year. The third camp proved even more successful than the previous two, attracting a larger number of physicians and other health care personnel team from hospitals from all regions of Thailand. Participating physicians primarily included general practitioners, internists, and family physicians from secondary and tertiary care hospitals. Invited scholars and their teams delivered presentations on self-selected hypertension topics, followed by faculty feedback and suggestions focusing on scientific content, presentation quality and time management. Nurses and pharmacists from each participating hospital were also invited to attend as part of their team. Feedback from all attendees indicated that these meetings were both fun and very useful for their clinical practice.

The Thai hypertension camp aims to address the critical challenges in the country's major health issues, identify common pitfall in clinical practice, and facilitate opinion sharing to determine optimal solutions for individual hospitals. Participant feedback and engagement exceeded expectations, and faculty members also learned a lot from the presenting scholars. All feedback received was used to improve the content and processes of future camps.

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Building upon the success of the previous three hypertension camps, the Thai Hypertension Society has established a valuable network that facilitates the collection of crucial patient data for the May Measurement Month project, established and supported by ISH. This network also supports data gathering for several prospective clinical and observational epidemiological research studies.

The fourth hypertension camp is already scheduled for 23rd of August this year, with a focus on enhanced practical application and greater utility for practitioners and health care professionals. The Thai Hypertension Society intends to continue this hypertension camp project for the foreseeable future with the support of the ISH, contingent on funding and the continued high prevalences of hypertension in Thailand.









# WORLD HYPERTENSION DAY

World Hypertension Day, May Measurement Month and Salt Awareness Week all happened in May. Here we report on some of the activities which took place around the world, shared with us by our members and partners.

### Malaysia

A community event organised by a clinic in Cheras, Kuala Lumpur in Malaysia, linked to World Hypertension Day and Salt Awareness Week, aimed to:

- raise awareness about hypertension
- educate the public on the harmful effects of excessive salt intake
- and promote health interventions for disease prevention and management.

The event, organised by Klinik Kesihatan Cheras Baru, in collaboration with the Cheras District Health Office, featured interactive talks and educational booths offering hands-on learning experiences.

ISH member Siti Zulaikha Shazali, Family physician in Malaysia, was part of activities.





Over 60 participants from the local community were enthusiastic in their participation.





In conjunction with May Measurement Month 2025, the Malaysian Society of Hypertension and the Malaysian Society for World Action on Salt, Sugar and Health (My-WASSH) organized multiple awareness initiatives across Malaysia. Key activities included free public blood pressure screenings at shopping malls, the annual MSH Hypertension Conference, and participation in a diabetes awareness run. Additionally, as educational webinar emphasised the health benefits of

reducing dietary salt intake. Yook Chin Chia, member the ISH Asia Pacific Regional Advisory Group, was part of these activities.













Pakistan Hypertension League, in collaboration with the Pakistan Cardiac Society, the Pakistan Society of Internal Medicine, and Go Red for Women Pakistan, arranged a symposium at Nishtar Medical University, Multan, Pakistan, on World Hypertension Day.

Session topics included the prevalence of hypertension and cardiovascular risk factors.

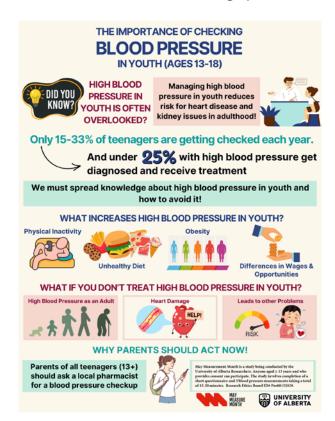




Pakistan Hypertension League, together with Pakistan Cardiac Society, held a health awareness walk and a yoga session to spread the message of a healthy lifestyle.

### Canada

Hypertension Canada and a research team at McMaster University in Canada launched blood pressure screening for teenagers (13-18 years old) during May Measurement Month at local pharmacies. The team created a video and infographic.











### China

The Chinese Hypertension League (CHL) launched a nationwide campaign for World Hypertension Day 2025, promoting early detection and effective management of hypertension.

The campaign activities included:

- Free health screenings and public education, with hospitals and community centres across China offering free blood pressure checks and interactive sessions to empower citizens with actionable health knowledge
- A global webinar with speakers including World Hypertension League President Gianfranco Parati and CHL President Jiguang Wang
- Digital outreach, including short videos, infographics and live Q&A sessions which reached millions online
- The promotion of Stride BP online training, designed to standardise blood pressure measurement techniques worldwide.

Activities by the CHL this year attracted over tens of thousands of people, including both elderly hypertensive patients and health-conscious younger individuals, demonstrating broad population coverage.

Medical professionals delivered in-depth knowledge on hypertension prevention, treatment, and daily management.





Additionally, more than thousands of copies of educational materials were distributed, significantly enhancing public awareness and understanding of hypertension.











### Japan

An event made possible through the support of the Japanese Society of Hypertension and the Japanese Association of Hypertension was held in Hiroshima City on 16 May.

The event featured community blood pressure screening and a series of lectures on public health, offering a chance for citizens to better understand the importance of blood pressure control and take steps towards healthier lifestyles.

A total of 218 citizens participated in the blood pressure screening. Many took the opportunity to ask attending physicians detailed questions about their blood pressure readings. All participants received a record of their blood pressure values along with a handout entitled, '10 Tips for Managing Your Blood Pressure,' which offered practical lifestyle guidance. Some participants with



elevated readings expressed their intention to visit a nearby clinic, signalling a positive step toward follow-up care.

The public lectures drew a crowd of 154 people, far exceeding the initial capacity. The talks proved popular with attendees.

Local businesses and medical institutions were part of the event, which organisers believe made a significant contribution to raising awareness about hypertension and promoting preventive healthy behaviours.









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