NEW DIMENSION SERIES

Sustainable Development Goals (SDGs) for Hypertension Zero in the era of Anthropocene.

CATEGORY A: HYPERTENSION AND LIFE ENVIRONMENT

Hypertension as the life-environment disease

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1. Hypertension as an Environmental Disease

Until now, hypertension and subsequent cardiovascular (CV) events have been considered lifestyle-related diseases, as an individual's living behavior deeply influences their occurrence. However, in recent years, it has become evident that environmental factors such as cold weather and air pollution also have a significant impact on an individual's blood pressure (BP). Furthermore, it has been observed that in the case of environmental disruption due to disasters, hypertension and CV events can be triggered. Therefore, hypertension and CV diseases can be regarded as environmental diseases.[1]

2. Disasters Disrupting the Living Environment and Triggering 'Disaster Hypertension' Leading to a High Incidence of Cardiovascular Diseases

Japan is a country prone to frequent earthquakes. I myself have experienced two of these, the Hanshin-Awaji earthquake and the Great East Japan earthquake, and have been involved in disaster medicine. The stress from disasters and the disruption of the living environment significantly impacts the body's homeostasis, resulting in the onset of CV events.[2-5] One crucial factor contributing to this is the elevation of BP.[2] The hypertension that arises during disasters is known as 'disaster hypertension',[3] and its causes are believed to include increased salt sensitivity due to factors such as sympathetic nervous system overactivity, disruptions in circadian rhythms, and increased salt intake during meals.[3, 4] The increase in CV events stemming from disaster-induced hypertension can be controlled. After a disaster occurs, monitoring BP in shelters and homes allows for the identification of poorly managed disaster hypertension and subsequent therapeutic intervention.[2]

To be prepared for immediate use during disasters, we have developed a disaster cardiovascular prevention (DCAP) risk score based on the extent of damage and medical history, as well as a Prevention Score that assesses lifestyle factors, including salt reduction, and environmental factors like noise, light, and temperature.[2, 3]

3. What Is Thermo-Sensitive Hypertension?

CV events aren't solely caused by abrupt environmental changes like disasters. Routine environmental factors also significantly affect BP, altering the risk of CV diseases. In countries with distinct climate season changes, such as Japan, there is an increased occurrence of CV diseases like stroke, coronary artery diseases, heart failure, and aortic dissection during the winter. BP also exhibits similar seasonal fluctuations, with early morning BP rising more during the winter and an increase in BP variability. Early morning represents the time when BP changes from nighttime to daytime are most pronounced. In patients undergoing antihypertensive therapy, early morning BP

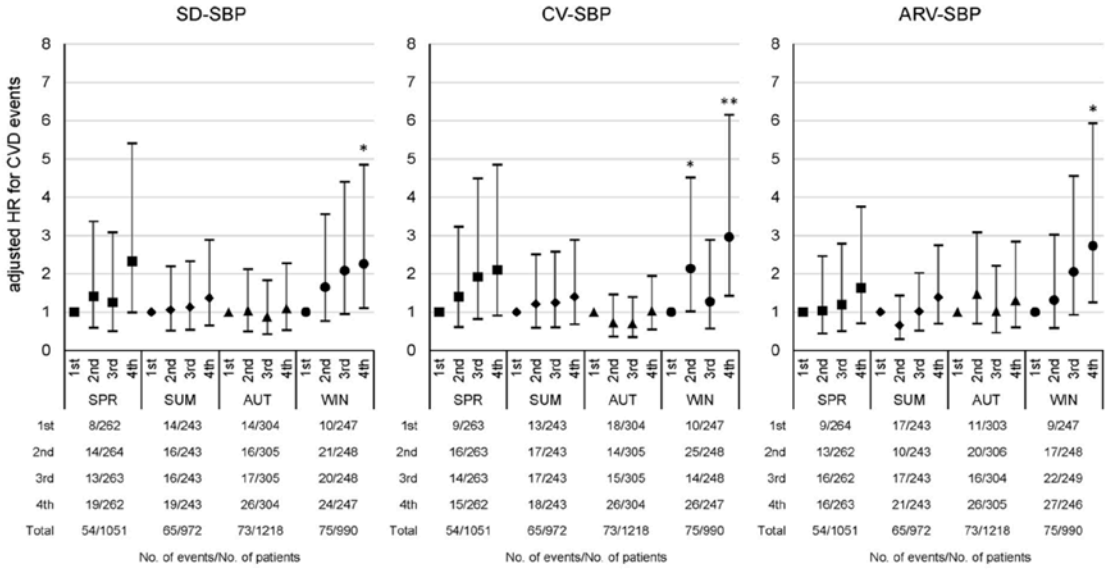
before taking medication is a critical blind spot where the antihypertensive effect is at its lowest.[6]

It's widely known that morning surges in BP and early morning home BP levels are associated with risks like stroke and myocardial infarction.[6, 7]

Moreover, an increase in the variability of home BP and peak values (an average of up to three points within a two-week period) are clear risk factors for onset of stroke.[8] Especially, the increased BP variability during the winter is linked to a higher risk of stroke **(Figure 1)**.

Figure 1. Seasonal variation of impact of BP variability on cardiovascular event risk

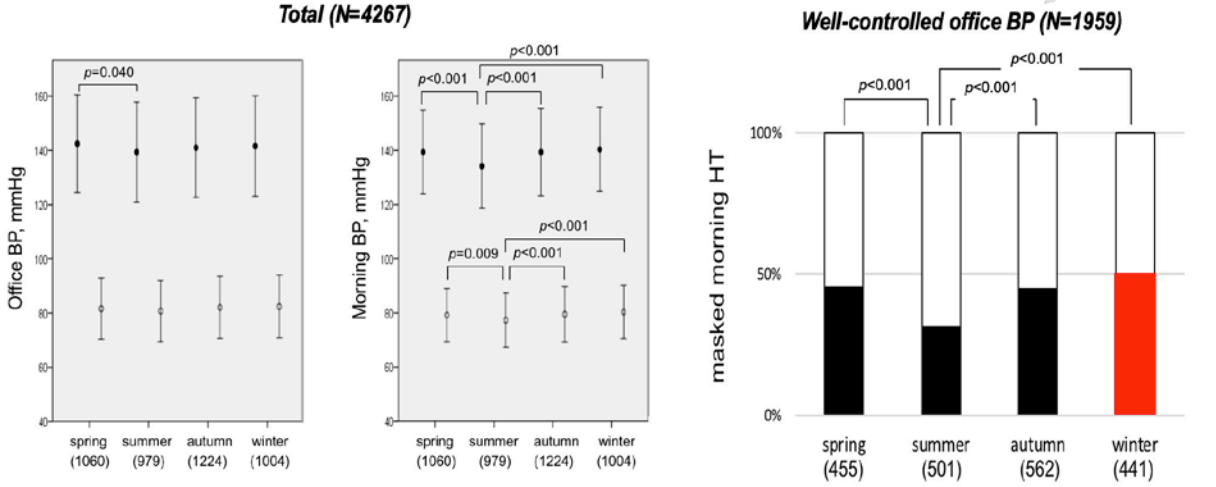
4231 patients of the nation-wide J-HOP study (Japan Morning Surge-Home Blood Pressure)



Narita K, Hoshide S, Kario K. Hypertension; 2022; 79: 2062-2070

Figure 2. Seasonal variation of blood pressure and masked morning hypertension

Data from nation-wide J-HOP study (Japan Morning Surge-Home Blood Pressure)

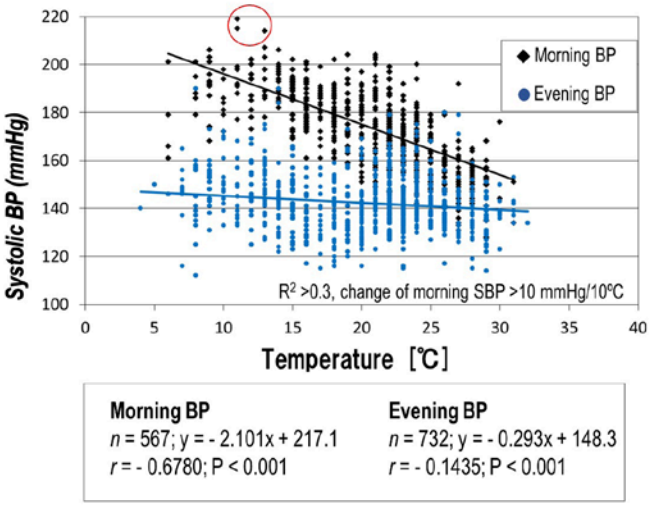


Narita K, Hoshide S, Fujiwara T, Nanegae H, Kario K. Am J Hypertens 2020; 33: 620-628.

Figure 3. Thermosensitivity and seasonal variation of actisensitivity

A. Thermosensitivity (the slope of BP against temperature)

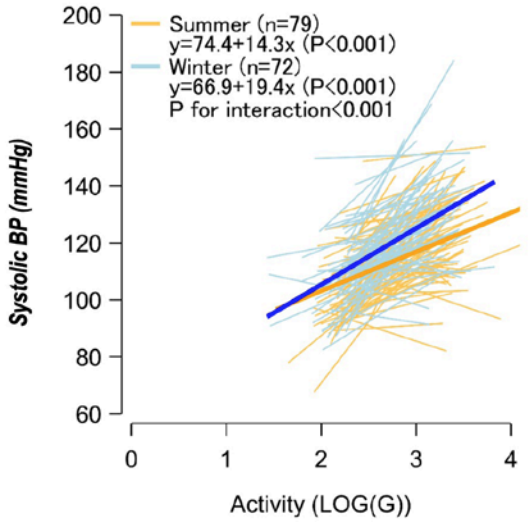
Thermosensitive hypertension *is defined by the* ***thermosensitivity*** *≥10 mmHg-increase in systolic BP/10°C-decrease in temperature*



Morning BP	Evening BP
n = 567; y = - 2.101x + 217.1	*n* = 732; y = - 0.293x + 148.3
r = - 0.6780; P < 0.001	*r* = - 0.1435; P < 0.001

Kario K. Am J Hypertens. 2021; 34: 783-794.

B. Actisensitivity (slope of BP against physical activity)



Kario K, et al. Prog Cardiovasc Dis 2017; 60: 435-449.

Previous studies using Ambulatory Blood Pressure Monitoring (ABPM) have reported that nighttime BP increases during the summer, and early morning BP rises during the winter. The morning BP surge in winter has been identified as a CV risk factor for the elderly. Recent research in home BP measurements has shown that a rise in morning BP (135/85 mmHg or more) during the winter has been observed in approximately half of hypertensive patients whose office BP is controlled below 140/90 mmHg **(Figure 2)**. Furthermore, studies on nighttime home BP monitoring have found that even when morning, evening, and daytime home BPs are controlled to below 135/85 mmHg, masked uncontrolled nighttime hypertension is more frequent during the summer at 45.6% compared to 24.9% during the winter.[9] This may partly be attributed to a higher salt intake against dehydration, a decreased dose of antihypertension drugs, poor sleep quality, etc. during hot summers.[6] It has become evident that 24-hour blood pressure fluctuations are modulated by seasonal changes and temperature.

In particular, the nationwide research study known as 'Smart Wellness Housing Survey' conducted simultaneous measurements of indoor temperature and morning home BP, revealing that morning BP fluctuates under the influence of temperature, notably increasing at lower temperatures. We define the strength of this relationship as 'thermo-sensitivity,' which quantifies the extent of BP change (in mmHg/°C) in response to a 1°C temperature change **(refer to Figure 3A)**.[6] An inclination with a value equal to or greater than 1 is categorized as 'thermo-sensitive hypertension.' Thermo-sensitivity among individuals with an average age of 80 is approximately 1.02, whereas for younger individuals around 30 years of age, it is around 0.38. This thermos-sensitivity is even more pronounced in older, slender individuals. The World Health Organization (WHO) recommends maintaining indoor temperatures at or above 18°C; however, the correlation between indoor temperature and morning BP tends to diminish at around 25°C for elderly men and around 20°C for those in their early thirties.[1] For elderly individuals, it is desirable to maintain indoor temperatures of 22°C or higher even during the winter. Furthermore, this study highlights that the patients residing in non-insulation retrofitting housing are significantly affected by outdoor temperatures, and there is a considerable discrepancy in morning and bedtime home BP, along with substantial daily fluctuations.[1]

Furthermore, physical activity leads to an increase in BP, but during the winter, BP tends to rise more with the same level of exercise. We define the strength of the BP rise in response to physical activity as 'actisensitivity' **(see Figure 3B)**. When we monitored the BP of the same individuals in both summer and winter using ABPM equipped with high-sensitivity actigraphy, we observed that actisensitivity was enhanced during the winter months.[6] The timing of different types of BP surge waves during seasonal variations and physical activity may lead to resonance, generating more dynamic BP surges and suggesting the potential to act as triggers for CV events (the resonance hypothesis of BP surge).[6]

In Japan, where clear seasonal variations in CV mortality are observed, regions that have made improvements to their living environments to counter the cold during the winter have managed to suppress the increase in CV mortality during the winter.[6] Additionally, in a survey conducted before and after insulation retrofitting, a reduction in morning BP was observed alongside improvements in indoor temperature.[1] Therefore, enhancing living conditions by taking measures to address cold temperature during the winter season can result in improvements in hypertension and BP variabilities.

4. The Greatest Unmet Need: Uncontrolled Hypertension

BP control is still insufficient worldwide, and the control status varies greatly among different countries due to differences in environment, culture, and economic conditions. In Japan, the HIJAMP study, which assessed the control status of hypertensive patients receiving antihypertensive treatment using ABPM, a device also capable of measuring home BP, indicated that over 50% of the patients had not attained control of their morning BP to below 135/85 mmHg.[10] Despite the fact that uncontrolled office BP was observed in only 33% of hypertensive patients taking three or more antihypertensive medications, 54% of them had uncontrolled morning BP. These circumstances highlight the limitations of current antihypertensive medication and underscore the need for new perspectives on hypertension management, including the improvement of clinical inertia, adherence, the comprehensive use of polypills, the development of novel medications, digital therapies, renal denervation, and further enhancements in living conditions.[6]

5. What Are the SDGs of Hypertension Management?

The world is experiencing growing instability. Year after year, the effects of global warming lead to abnormal weather patterns and a surge in natural disasters such as earthquakes and floods worldwide. Furthermore, human-made disasters like wars disrupt conventional living environments, creating many situations where people's daily lives are severely affected. The destabilization of our surroundings impairs the homeostasis of individuals' CV systems, leading to fluctuations in BP. BP is not only an indicator of an individual's stress but also a direct acute risk factor for CV events. Maintaining homeostasis on a global scale, both in terms of the environment and between nations, and preserving local environmental stability, all contribute to an extended healthy lifespan for individuals. Therefore, BP serves as a key biomarker for healthcare in this context. It's crucial to measure BP under various circumstances, comprehend an individual's cardiovascular risk, and actively work towards risk reduction. By improving lifestyle and living environments, stricter control of BP levels can be achieved, maintaining the circadian rhythm of BP, and suppressing excessive BP variabilities. This is the ultimate goal of hypertension management SDGs, referred to as the "Perfect 24-hour BP Control."

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Interrelation between SDGs and Hypertension Zero

 # Category A: Hypertension and Life Environment

Hypertension & Global Warming,
- Disaster (Earthquake, Flood)

Air Pollution, Decarbonization, War

- Housing (light, noise, vibration...)
- Sleep Condition etc.

 # Category B: Hypertension and Diversity

Hypertension & Genetic Ancestry

- Poverty/Economic Disparity
- Food Availability
- Loneliness, Social Isolation etc.

 # Category C: Hypertension and Next Generation

Hypertension & DOHaD (Developmental Origins of Health and Disease)

- Emaciation in Women
- Pregnant Women's Health
- Dietary Education, Taste Flavor etc.