



Current perspective on seasonal variation in blood pressure

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Current perspective on seasonal variation in blood pressure

Short title: Seasonal BP variation

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ABSTRACT

Blood pressure (BP) fluctuates with an annual cycle, with BP levels generally lower in summer and higher in winter. In this narrative review with a quasi-systematic literature search, we aim to summarise current evidence from a wide variety of research fields on seasonal BP variability, and to present our findings to stimulate interest in this largely unexplored area. Environmental temperature would be the key driver of seasonal BP variation, while other external and internal factors mediate this variation; quantifying these effects is difficult because of the various factors and their interactions. Self-measured home BP would be the most favorable information for evaluating long-term seasonal BP changes. Nocturnal home BP reduction is lower in summer than in winter, leading to a higher prevalence of a riser BP pattern in summer; we need to pay attention

to the various risk factors associated with higher BP across seasons. Temperature obviously affects BP; therefore, it seems reasonable to assume that seasonal BP changes linearly contribute to seasonal mortality variation. However, our patients database showed that there are >10% of patients whose home BP is higher in summer than in winter, and the cardiovascular risk was significantly higher in patients with such inverse seasonal variation as well as those with contrarily large-sized seasonal variation in home BP (≥ 9.1 mm Hg in systolic or ≥ 4.5 mm Hg in diastolic measurements) than in those with the other small- to middle-sized seasonal variation. The inverse seasonal BP pattern is not rare in patients under antihypertensive drug treatment, and the mechanisms warrant investigation. Although the importance of BP level as a dominant and modifiable risk factor should be emphasized, assessing seasonal BP variation through long-term BP measurement, particularly based on home BP monitoring, has clinical benefits and should be widely promoted.

Key words: cardiovascular risk, home blood pressure, indoor and outdoor temperature, seasonal blood pressure variation

INTRODUCTION

As a result of the widespread practice of continual blood pressure (BP) measurement, the significance of seasonal BP variation and its impact on cardiovascular complications and mortality have been recognized. Various factors should be considered comprehensively to investigate such long-term BP changes. BP levels are generally lower in summer and higher in winter, and environmental temperature is widely accepted as the key driver of BP variation [1, 2]. Furthermore, seasonal changes in other external factors such as daylight hours [3], corresponding solar ultraviolet light exposure [4], atmospheric pressure [5], weather changes [6], temperature variability [7], and availability of central heating [8], as well as internal factors such as circadian rhythms, dietary habits [9, 10], physical activity [10], body height [11] and weight status [9, 10, 12], sleep duration [12], and concomitant diseases [13], would mediate seasonal BP variation [2]. Genetic factors may also affect seasonal changes, as familial aggregation of seasonal changes has been suggested [14]. Furthermore, endocrine substances such as epinephrine [15], aldosterone [15], and normetanephrine [16] also fluctuate on a yearly cycle in individuals. Seasonal affective disorder, variation of mood, might also affect BP changes [12, 14]. Seasonal BP

variation eventually affects the prevalence of hypertension [17, 18] and is associated with cardiovascular risk, but occurs simultaneously in other risk factors [1].

The great diversity of seasonal BP changes across populations and settings in previous studies makes it difficult to integrate the reports and provide an unbiased quantification of the impact of each contributor. To reinforce this narrative review, we performed a systematic literature search at the PubMed database using the following term strategy: (blood pressure) AND (seasonal*). We limited the publication date between June 1, 2018 and December 31, 2025 because our previous publication regarding seasonal home BP variability was published in 2018 [19] and because the cited meta-analysis by Kollias et al. [20] conducted the literature search using the same term until May 2018. We screened 215 eligible English-language articles, and integrated their insights into this narrative review.

DEFINITION AND CALCULATION OF SEASONAL BLOOD PRESSURE CHANGES

A simple and clear definition of seasonal BP changes encompasses the difference in BP between winter and summer [21, 22]. BP levels in spring and autumn can also be assessed. More details, monthly or bimonthly BP levels have been assessed in some reports [23–25]. Whereas, real-world data on long-term BPs often appear outside these simple seasonal or monthly summaries, and precise analysis of their impact on outcomes has been demanded. Based on recent advances in analysis, several investigators have developed a specific calculation formula to assess BP values and potential contributors regarding seasonal changes. Within these formulae, key models use trigonometric functions to show seasonal patterns [13, 24, 26]. By applying a trigonometric spline, we can simultaneously assess changes in seasonal BP and other seasonal factors, such as outdoor temperature. However, recorded outdoor temperatures are sometimes not well fit by a developed trigonometric spline due to the effects of rainy and dry seasons or the length difference of the seasons. The interaction between indoor and outdoor temperatures further complicates the model. To assess the effects of temperature and irregularly repeated factors, we should be deliberate in the observed measurements well before modeling.

FACTORS AFFECTING SEASONAL BLOOD PRESSURE CHANGES

Even though heterogeneity remained high regarding seasonal BP changes, Kollias et al. [20] colleagues accomplished the feat of conducting a meta-analysis of seasonal BP variation. They classified reports into prospective and cross-sectional designs, as those including the same individuals assessed in different seasons and those including different individuals assessed in different seasons, respectively. The pooled difference of office BP between winter and summer among 29 studies was 5.6/3.3 mm Hg, and that of home BP among 9 studies was 6.1/3.1 mm Hg. Meanwhile, in meta-regression analysis of prospective studies, age was marginally, but not significantly, associated with seasonal variation ($P = 0.07$). It should be noted that the classification of the study design, prospective or cross-sectional, cannot be definitive because some studies were conducted based on a mixed design, i.e., repeated measurements by the same individuals and different measurements by different people were combined. Although sensitivity analysis limited to prospective studies yielded similar findings, assessing the impact of each factor remains burdensome. A meta-analysis focuses on a single variable (e.g., the mean difference of BP) and loses information regarding confounders that were duly considered in the individual studies. Additional meta-regression analysis can evaluate the influence of individual variables, though adequately adjusting for multiple variables remains difficult. Nevertheless, our quasi-systematic literature search did not fundamentally amend the primary finding of the meta-analysis [20].

As the marginal association was demonstrated in the aforementioned meta-analysis [20], whether seasonal BP variation would be enhanced by advancing age remains under debate. Among UK patients with mild hypertension, men aged 55–64 years had systolic/diastolic BPs 6–7/3–4 mm Hg higher on a cold winter day than on a warm summer day, and the BP rise was 2–4/2–3 mm Hg in men aged 35–44 years [23]. The report was not a person-to-person comparison but rather a trial-registered BP-based analysis of multiple individuals [23]. Seasonal variation of BP among 96 patients from a single general UK practice (mean age 69 years; women 51.0%) was 12.0 (95% confidence interval [CI], 9.7–14.3)/5.5 (95% CI, 4.4–6.7) mm Hg [24]. Among 182 treated Israeli outpatients with hypertension (mean age 74.1 years; age range 65–92; women 46.2%), winter-summer BP differences during 3–5 years observation were 31 (standard deviation 19.4)/15 (14.1) mm Hg in systolic/diastolic measurement [22]; however, within this study, there was no correlation between BP changes and the age of the patients [22]. In 11 440 South Africans (by a multilevel model based on 3 times BP measurements; mean age 35

years; women 60.9%), the magnitude of overall seasonal BP changes was 4.21/4.01 mm Hg in women and 4.25/4.00 mm Hg in men [26]. Impact of age was observed in those aged 55–64 years, but only in systolic measures, and there was no statistically significant difference among age groups in diastolic measures [26].

It is well established that environmental temperature is inversely associated with BP [27], and seasonal BP changes are mainly influenced by temperature [1, 2]. The impact of indoor and outdoor temperatures on BP measurements was reported. Using the World Health Organization MONICA project database, a 1-degree increase in indoor and outdoor temperature reduced systolic BP by an average of 0.31 mm Hg and 0.19 mm Hg, respectively, and these effects were independent [28]. In 2016, Wang et al. [29] published a meta-analysis on temperature and BP, in which a 1-degree increase in outdoor and indoor temperature was associated with a 0.26 (95% CI, 0.18–0.33) mm Hg and a 0.38 (0.18–0.58) mm Hg decrease in systolic BP, respectively. However, as the authors stated [29], data on temperature and BP measurements in previous studies were not sufficiently accurate. Improving the accuracy of office BP would also be challenging. Kinuta et al. [30] evaluated the impact of temperature on self-measured home BP, as the association was stronger for indoor temperatures among Japanese community-dwelling residents in the western region of Japan. After adjusted for outdoor temperature, a 1-degree increase in indoor temperature reduced systolic/diastolic BP by 0.33/0.12 mm Hg in the morning and 0.45/0.26 mm Hg in the evening home BP measurements [30].

The increase in BP along with a lowering of outdoor temperature was reported to be attenuated below 10°C [31], and the attenuation of the BP increase in winter might be explained by heating system-modified room temperatures. A recent Chinese study reported that the effect of inter- and intra-day temperature variability on BP was also attenuated in November to March when the heating system is commonly running [32]. Among inhabitants in Tromsø, Norway, the peak systolic/diastolic BP was observed in September/February, the bottom in June/June to August, and the seasonal differences were 3.4/1.6 mm Hg [33]. The similar magnitude of the seasonal BP difference was observed in Italy and Japan, as 3.5/2.2 mm Hg (compared with different populations matched for sex, age, and body mass index) [34] and 4.7/3.3 mm Hg ($n = 50$; 64% receiving antihypertensive treatment) [35], respectively. In contrast, populations living closer to the equator showed larger seasonal variations in BP [28], e.g., a difference was 15.1/7.6 mm Hg in Iraqi ($n = 120$; 58% patients) [36], where the mean daytime temperature was 14.7°C even in January. The dissociation between outdoor and indoor

temperatures in winter is likely to be weaker in comparably hot areas. The wide differences in climate would contribute to differences in seasonal variations in BP [13, 37].

HOME BLOOD PRESSURE AND SEASONAL VARIATION

Accurate BP measurement is a prerequisite for the assessment and management of risk factors [38]. Although the recommended conditions for home BP differ across practice guidelines for the management of hypertension, home measurement enables people to regularly monitor their BP, resulting in multiple readings obtained under consistent measurement conditions. Home BP is considered the most favorable information for evaluating BP changes over a long period, i.e., seasonal BP variation [39–41]. Frequent home BP measurements, even day-by-day continual monitoring, are feasible [42], and long-term home BP data can be matched with daily environmental changes, e.g., both indoor and outdoor temperatures as well as various weather conditions [43].

Based on a dataset from a multicenter clinical trial Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure (HOMED-BP) [42], we investigated 1649 hypertensive patients with morning home BP data for a total of ≈ 2 years or more since randomization [13]. Multivariable-adjusted models showed that significant factors for changes in seasonal variation were sex (different from the within-day ambulatory BP variability as recently reported among the Polish population [44], women showed 0.57/0.22 mm Hg lower seasonal changes than men), age, body mass index, and diabetes mellitus, as well as tobacco smoking for systolic measurement and hypercholesterolemia for diastolic measurement [13]. Patients living in the northern part of Japan (Hokkaido and Tohoku regions) had 1.48/0.99 mm Hg lower BP variation than that in the other regions of Japan. A unique finding of the subsequent HOMED-BP analysis was that more than 10% of patients (13.3% and 19.3% in systolic and diastolic measurements, respectively) demonstrated higher BP in summer than in winter [19]. Such a high proportion of patients with inverse BP variation might explain the conflicting reports regarding seasonal BP variation. For example, BPs in cold 6 months and those in warm 6 months were statistically the same level among 78 people aged around 80 years old, as 143.8/85.9 mm Hg and 143.7/85.1 mm Hg, respectively [21]. Woodhouse et al. [24] reviewed these results [21], as this might be because half of the participants lived in sheltered housing or residential homes and were relatively protected from seasonal changes in their environment [24].

A cross-classification by office and home BP identifies people with white-coat and masked hypertension [40, 45], even though the difference in out-of-office BP, i.e., home and ambulatory BP values, should be noted [46]. Prevalence of masked hypertension, assessed by office and home BPs, was low in the summer, whereas that of white-coat hypertension was higher [47]. Among 70 949 nationwide Brazilian individuals (61% women, 51% under antihypertensive medication), a 1-degree decrease in outdoor temperature was associated with 3.9% (95% CI, 3.6%–4.9%) higher and 1.3% (95% CI, 0.4%–2.1%) lower prevalence of masked and white-coat hypertension, respectively [43]. However, as Kollias et al. [48] commented, the study [43] assessed different individuals across different seasons, and the definitions of winter and summer should be clarified [48], particularly because Brazil straddles the equator. The merged assessment of 2 studies demonstrated that the differences between office and home BPs were similar in both winter and summer [48], implying that seasonal differences affected office and home BPs equally. A further report from the same Greek group demonstrated that day-to-day home BP variability did not differ between winter and summer, in contrast to average BP levels, which were higher in winter than in summer as well [49].

Nocturnal BP during sleep can be measured by home devices, as can be performed by intentionally wearing a cuff before sleeping alone [50, 51]. Nocturnal BP dipping can also be assessed by home BP difference between waking (morning and evening) and nighttime measurements. In a Japanese community-based population in mid Japan [52], nocturnal systolic home BP reduction was significantly lower when BP was measured during the summer season (July and August, –5.8%) than during the winter (November to March, –11.0%). This seasonal variation was contradicted by home BP variation upon awakening, with an average of morning and evening measurements. Thus, the prevalence of those with a riser (inverted) BP dipping pattern, i.e., nocturnal BP being higher than awakening BP, was significantly higher in the summer (19.9%) than in the winter (7.8%). Such large seasonal variations in nocturnal BP fall and its dipping pattern in a large general population [52] warrant careful attention when assessing BP dipping. Based on ambulatory BP monitoring, multivariable-adjusted (though different population) mean nighttime systolic/diastolic BP in summer was 5.6/4.2 mm Hg higher than in winter [53]. Narita et al. [54] reported that the prevalence of nocturnal hypertension (nocturnal home BP ≥ 120 mmHg while awake home BP < 135 mm Hg in systolic measurement) was highest in summer (45.6%) compared with the other 3 seasons (24.9%–27.2%) among 1565 outpatients with 1 or more cardiovascular risk factors. Meanwhile, BP values can

be altered by a cold-induced BP response, as the impact of a home BP increase from getting up is more pronounced in winter than in summer [55]. Changes in BP dipping pattern across seasons would be influenced by corresponding lifestyle modifications in individuals.

Seasonal BP variation in a special population remains a frontier for investigation. We first reported seasonal home BP variation during pregnancy [56]; in northern Japan, outdoor temperature was associated with home BP in pregnant women ($n = 117$). February and August were the seasons of the largest and smallest estimated home BPs at term, respectively, and the difference was almost 6 mm Hg (Figure 1). A similar finding was recently reported among pregnant women living in a comparably southern part of Japan ($n = 603$) [57], with a difference of 4.6/3.4 mm Hg between summer and winter in systolic/diastolic home measurements. In contrast, data on seasonal home BP variation in children are lacking, despite a synthesis office systolic BP changed by 3.4–5.9 mm Hg between summer and fall or winter across 7 pediatric studies [58]. Similarly, the prognostic impact of seasonal home BP variation among patients with chronic kidney disease (CKD) has also been scarcely investigated. A Taiwanese study reported that 507 CKD patients who reduced home BP in winter had better renal outcomes, whereas consistent home BP elevation was associated with worse outcomes [59]. Home BP is a useful tool for patients with CKD, including those with end-stage renal failure and on hemodialysis [59, 60], and further investigation of seasonal variation in home BP is warranted.

SEASONAL VARIATION OF BLOOD PRESSURE TOWARD CARDIOVASCULAR COMPLICATIONS

Over the seasonal BP changes, seasonal temperature variation is associated with cardiovascular diseases worldwide [2, 61–65]. In the Israeli study, >40% of cardiovascular diseases (8 of 17 myocardial infarctions and 4 of 10 strokes) occurred in the winter season [22]. Näyhä [66] summarized that mortality is usually lowest in the region of 15–20°C, and mortality from coronary heart disease increases by $\approx 1\%$ per 1°C fall in temperature [5, 66]. Seasonal variation would eventually affect cardiovascular risk prediction models, though it has not been sufficiently considered [67]. An excess Framingham risk score [68] between winter and summer increased with age, and was higher among men, smokers, and people with low household income, even though small differences in seasonal BP change with age were observed [26]. Seasonal variation in

multiple risk factors contributed to differences in SCORE risk [69, 70] between winter and summer, which may reflect the seasonality of cardiovascular mortality [71]. Based on data from 384 worldwide locations, non-optimal temperature accounted for 7.71% of mortality (95% empirical CI, 7.43–7.91) [63]. Although temperature-attributable deaths were predominantly caused by cold (7.29%; 95% empirical CI, 7.02–7.49), they were also significantly observed by heat (0.42%; 95% empirical CI, 0.39–0.44) [63]. A recent meta-analysis suggested that hypoxia in the hot season can induce ischemic cardiovascular events [65]. More interestingly, minimum mortality temperatures as estimated optimal temperatures differed greatly, from $\approx 60^{\text{th}}$ percentile in tropical areas to $\approx 80\text{--}90^{\text{th}}$ percentile in temperate regions; for example, the minimum mortality temperature in Stockholm and London was $\approx 19^{\circ}\text{C}$, while those in Rome and Madrid were $21\text{--}22^{\circ}\text{C}$ [63]. Although a meta-analysis warned that indoor temperatures below 18°C result in adverse health effects [72], geological heterogeneity should be considered when applying the consensus.

It would be a reasonable assumption that temperature affects BP, and therefore that seasonal BP changes linearly contribute to seasonal mortality variation. In a longitudinal Scottish study [73], when patients ($n = 16\,010$; 53% women; mean age 50.8 years) were classified according to monthly weather variables, patients demonstrating an opposite direction between temperature changes and BP response showed higher all-cause mortality than those with a concordant BP response to temperature. However, the outcome of the aforementioned HOMED-BP study called that assumption into question [19]. When 2787 eligible HOMED-BP patients were classified into 4 categories according to the magnitude of their seasonal home BP changes, the cardiovascular risk was significantly higher in patients with inverse and, contrarily, large-sized seasonal variation in home BP (≥ 9.1 mm Hg in systolic or ≥ 4.5 mm Hg in diastolic measurements) than in those with the other 2, small- and middle-sized seasonal variation (**Figure 2**). Based on estimates from previous reports derived from their standard deviation ranges [11, 35, 41], the inverse seasonal variation in BP would not be rare in patients under antihypertensive drug treatment, possibly reflecting an abnormal response of biological pathways to outdoor temperature [19]. Otherwise, inverse seasonal variation in BP may partially be attributable to medication nonadherence or to hard labor during the summer; identification of the factors contributing to inverse seasonal variation remains open to investigation.

Other factors affect seasonal variation in BP and cardiovascular events. Based on a morbidity registry (Lille-WHO MONICA Project) monitoring 257 000 men from 25 to 64 years of age, it was showed that atmospheric pressure was independently associated with coronary heart disease events, as a 10-hPa decrease and a 10-hPa increase from 1016 hPa was associated with 12% and 11% event rate increase, respectively [5]. Relative humidity would be another major factor in the seasonal variation of cardiovascular dysfunction [74], and is also related to preeclampsia [75]. Short-term increases in pollen concentration are associated with BP elevations in people with pollen allergies, suggesting pollen and other allergic reactions may trigger cardiovascular events [76]. Research is also ongoing on the impact of exposure to air pollutants, such as particulate matter [77] and ozone [78], on seasonal changes in BP and cardiovascular disease [74, 79, 80].

STRANGE PHASE SHIFT OF SYNCHRONIZING BLOOD PRESSURE AND TEMPERATURE

A close relationship between BP and temperature has been reported for more than a century [1]. Even based on home BP measurements, a monthly assessment showed a nonmisaligned, convincing inverse association between home BP in the morning and both indoor and outdoor temperatures [81]. However, causality has been observed oddly when assessed in detail using day-to-day home BP measurements. In the HOMED-BP study, the highest and lowest home BP values in the population were observed in mid-January and mid-July. In contrast, the highest and lowest temperatures in Japan are generally observed at the end of January and early August, respectively [13]. In other words, temperature followed BP changes in both the summer and winter seasons. Although this might be due to the BP variability models, which consist of a simple trigonometric function, the observed average home BP values reached the highest level even in December [13]. Furthermore, another Japanese study comprising 87 535 home BP records from 106 community-dwelling residents demonstrated that both indoor and outdoor temperatures were highest in August and lowest in January, despite the fact that the lowest BP was observed in July, and March was the month showing the highest BP (Figure 3) [25].

These findings suggest that temperature should not be the sole determinant of seasonal BP variation — they would not be completely synchronous — and that it is also mediated by meteorological, environmental factors, as well as in-body contributors [82].

Setting sunshine duration as the primary cause of seasonal BP variability is a compelling hypothesis, as a causal relationship can be explained as changes in sunshine duration precede the change in home BP [13, 25]. In a UK Biobank study conducted at a temperate latitude, cardiovascular mortality synchronized with BP, inflammatory markers, and body mass index, and was significantly related to day length [83]. Weller et al. [4] recently reported that predialysis systolic BP was inversely associated with environmental ultraviolet exposure independent of temperature. Increased sun exposure reduced cardiovascular complications [84], suggesting a protective effect of vitamin D [85]; however, recent randomized controlled trials have failed to prove the causal relationship between vitamin D supplementation and beneficial effects on BP and cardiovascular outcomes [86–88]. Instead, an increase in circulating nitric oxide from sunlight exposure may vasodilate the arterial vasculature, thereby lowering BP [85, 88, 89].

PERSPECTIVES

It is very likely that a simple model or a single factor cannot explain seasonal changes in BP. The statistical models are therefore generally very complicated; nevertheless, simplifying the modeling is required to apply the findings on seasonal BP variation in clinical practice. As a comprehensive integrated index, the Universal Thermal Climate Index is a bio-meteorological indicator for managing thermal stress and environmental conditions on the human organism, and the Universal Thermal Climate Index would also be useful for assessing the relationship between atmospheric conditions and BP values [90]. Meanwhile, antihypertensive medication modifies seasonal BP changes, and it differs according to the drug regimen [19, 91]. Although robust evidence on the prognostic significance of seasonal BP changes is still lacking, earlier adjustments of antihypertensive drug regimens according to the upcoming season reduced the summer-winter difference in home BP, which may improve BP control, particularly in the winter season [19]. Furthermore, a recent report from Iran showed that there was a sex difference in BP response to the outdoor temperature, with higher vulnerability among women [92], which urges us to pay attention to sex differences in seasonal variation in BP. Although the importance of BP level as a dominant and modifiable risk factor should be emphasized, assessing seasonal BP variation through continual long-term BP measurement, particularly self-measurement at home, has clinical benefits and should be widely promoted.

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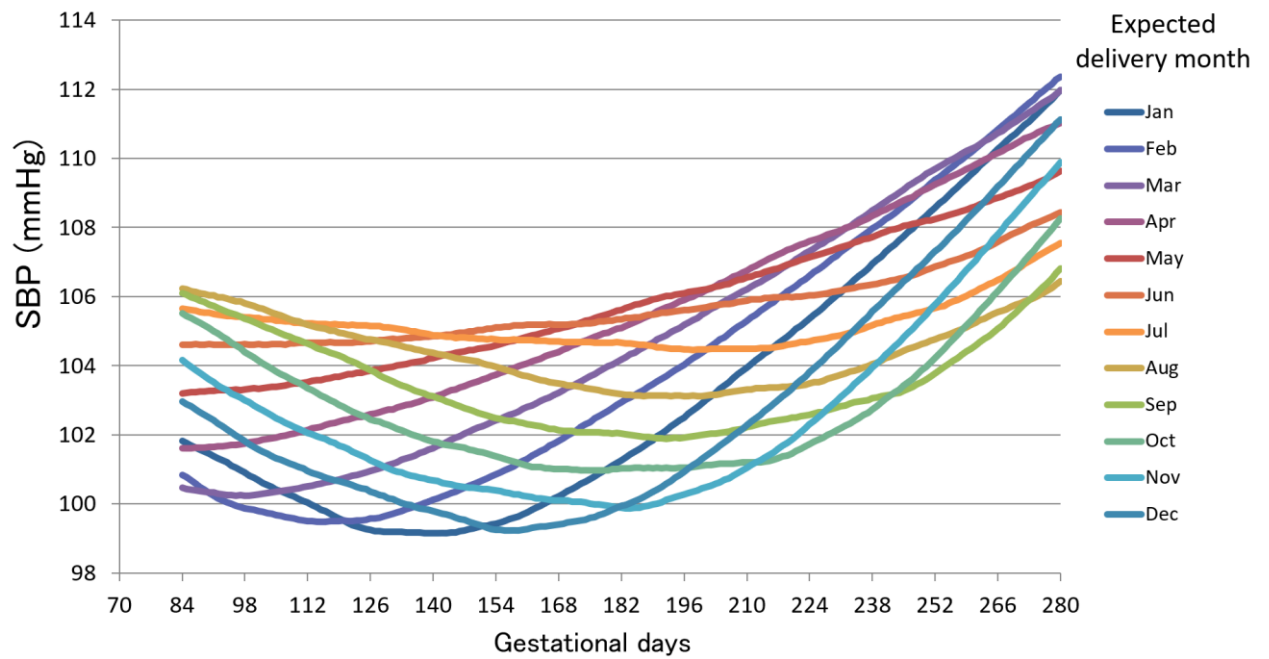


Figure 1. Changes in systolic home blood pressure (BP) during pregnancy by the expected delivery month

Twelve lines show estimated systolic home BP values for gestational age according to the expected date of birth, e.g., “Jan” denotes estimated BPs for pregnant women due in January. Each value was adjusted by the normal value of the daily minimum outside temperature. The figure was reproduced from Metoki et al [56]

Abbreviation: SBP, systolic blood pressure

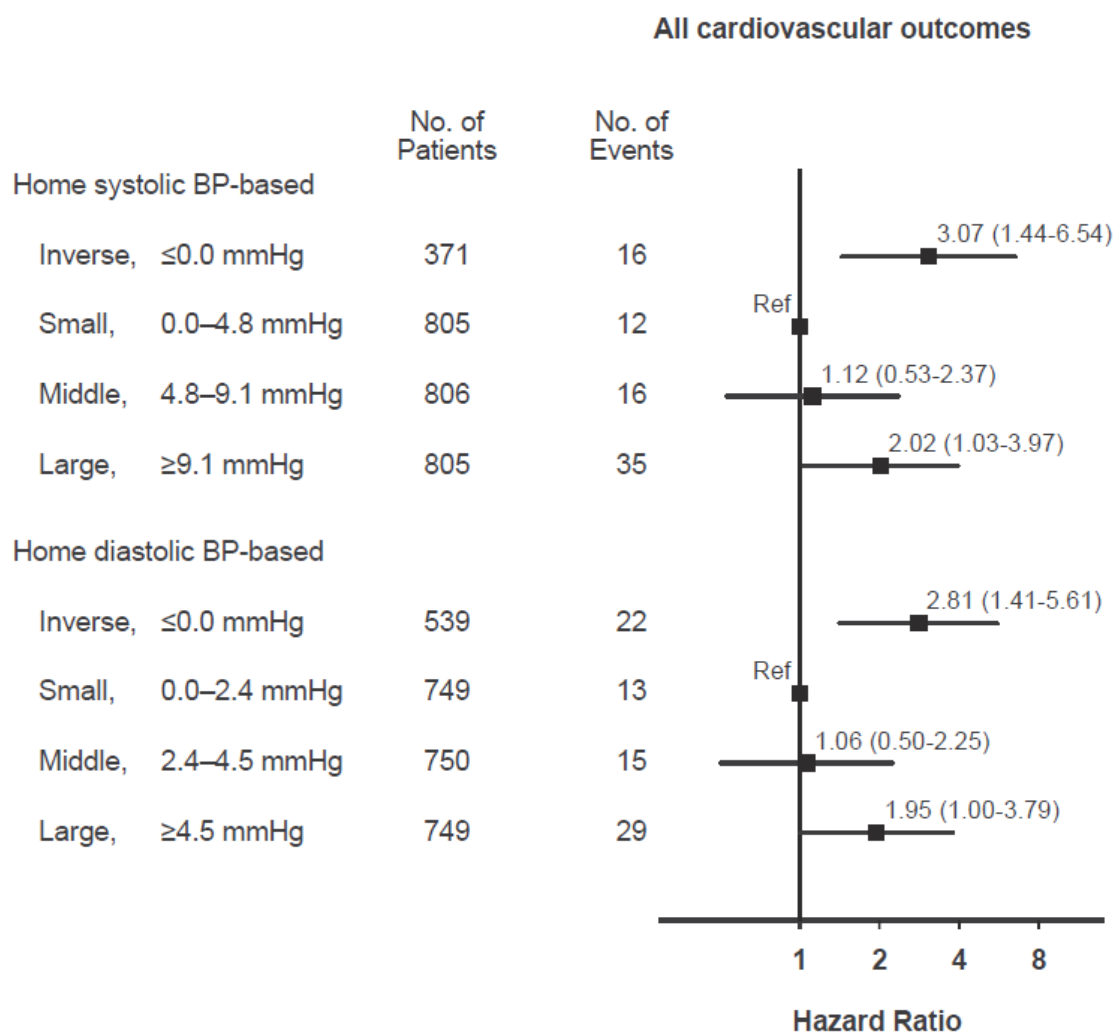


Figure 2. Multivariable-adjusted hazard ratios for all cardiovascular outcomes

The box (vertical bar) shows the hazard ratio (95% confidence interval) in each variation group compared with the group of the lowest cardiovascular risk (shown as Ref). The values were adjusted by sex, age, body mass index, current smoking, current habitual drinking, diabetes mellitus, hypercholesterolemia, history of cardiovascular disease, baseline home BP, on-treatment home BP (either systolic or diastolic BP according to the seasonal BP information), and the randomized groups in the HOMED-BP study. Follow-up was initiated at 1 year (day 365) after randomization in the Cox model. The figure was reproduced from Hanazawa et al. [19]

Abbreviations: BP, blood pressure; HOMED-BP, Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure

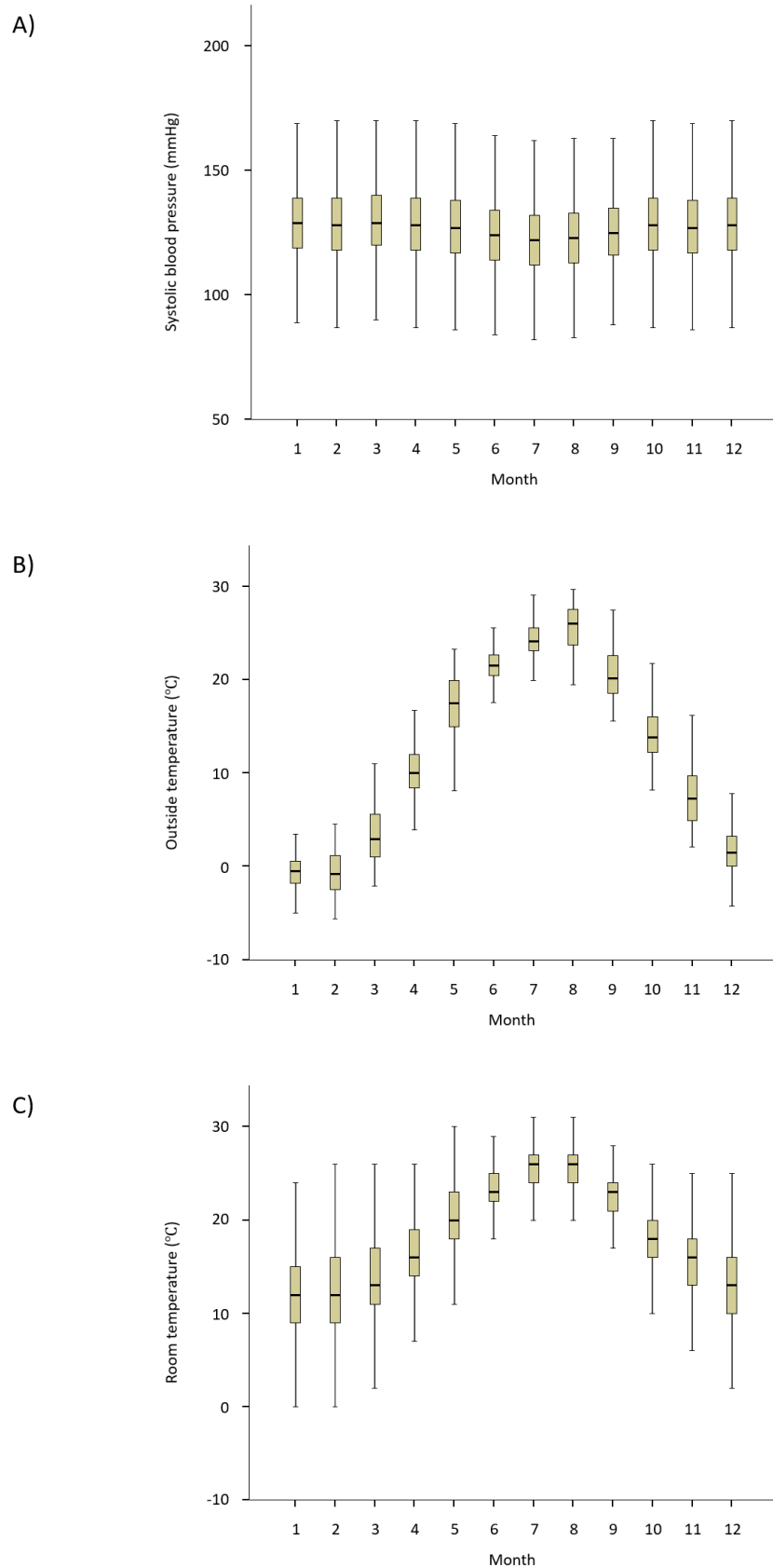


Figure 3. Monthly trend of systolic home BP (A), outside temperature (B), and inside (room) temperature (C) among residents in Aizumisato Town, Japan

All panels are expressed as box-and-whisker plots. The figure was reproduced from Yatabe et al. [25]