



## The association of out-of-office blood pressure time in target range with clinical outcomes

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High blood pressure (BP) remains the overriding modifiable risk factor for cardiovascular disease and associated mortality throughout the world. In 2015, hypertension caused 8.5 million deaths [1]. In addressing the epidemic of non-communicable disease directly attributable to hypertension, the timely recognition of the BP-related risk and treatment to the lowest BP pressure target that is reasonably achievable is of paramount importance. A review of randomized clinical trials highlighted that the definition of a fixed BP target generalizable to all hypertensive patients remains enigmatic. Instead, the target BP should be personalized and be based on the best trade-off between efficacy and safety [2]. Control of the office BP should also be confirmed by out-of-office BP monitoring. BP time in target range (TTR) is a metric designed to quantify the proportion of time spent within the established therapeutic range, thereby reflecting both BP levels and BP diurnal variation [3].

Current guidelines for the diagnosis and management of hypertension unanimously recommend the use of 24-h ambulatory BP monitoring as the state-of-the-art technique for hypertension management [4]. In an inspiring article, Tian and coworkers investigated the association of 24-h systolic BP TTR at baseline with incident heart failure (HF) in the general population [5]. The study included 5152 participants (27.0% women; mean age, 49.87 years). The systolic BP TTR was set from  $\geq 110$  to  $\leq 140$  mm Hg and derived using the Rosendaal

linear interpolation between BP readings [5]. Compared with systolic BP TTR of 0–25%, systolic BP TTR of 75% to 100% was associated with lower risk of incident HF resulting in a multivariable-adjusted hazard ratio (HR) of 0.53 (95% CI, 0.32–0.89) [5]. Similarly, in 3077 patients with uncontrolled hypertension, enrolled in the Global SYMPLICITY Registry (42.2% women; mean age, 60.5 years) [6], TTR was derived over 6 months after renal denervation from both office BP ( $\leq 140$  mm Hg) and the 24-h BP ( $\leq 130$  mm Hg) [6]. Over further follow-up from 6 to 36 months, the HRs expressing the risk per 10% lengthier TTR were 0.85 (0.79–0.91) for major cardiovascular events, 0.89 (0.81–0.97) for cardiovascular mortality, 0.85 (0.75–0.98) for myocardial infarction, and 0.77 (0.68–0.88) for stroke [6].

The BP TTR is a risk indicator with potential clinical implications. Post-hoc analyses of clinical trials and observational studies demonstrated that higher BP TTR is associated a reduced risk of adverse health outcomes in the general population [5, 7], in patients with hypertension [6, 8–11], diabetes mellitus [12], acute ischemic stroke [13], and HF [14, 15], and in participants with at least one cardiovascular risk factor [16]. Of four reviewed studies focusing on out-of-office BP TTR (Table 1), three applied ambulatory [5, 6, 13] and one home BP monitoring [16]. However, a drawback of most studies is that diastolic BP was ignored and that the target range of systolic BP on 24-h ambulatory monitoring was often arbitrarily determined with similar limits for the awake and sleeping periods of the day. Whether linear interpolation refines the determination of BP TTR or unnecessarily generates interpolated data that inflate the associations between adverse outcomes and BP TTR should be considered. Simple time weighting of the office or out-of-office BP readings might produce similar and easier understandable results. Furthermore, whether BP TTR derived from out-of-office BP monitoring is prognostically superior to BP TTR determined from the BP as measured at consecutive office visits and is therefore cost-

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**Table 1** Four reviewed studies focusing on out-of-office blood pressure time in target range

Studies, year	Design	Participants	Duration of follow-up	BP type and range	Endpoints
Tian et al. 2024 [5]	Observational	5152	6.96 years	Ambulatory SBP 110–140 mm Hg	Incident heart failure
Mahfoud et al. 2022 [6]	Observational	3077	30 months	Ambulatory SBP $\leq$ 130 mm Hg	Composite of cardiovascular death, MI, and stroke
Kakaletsis et al. 2023 [13]	Observational	228	3 months	Ambulatory SBP 90–140 mm Hg; DBP 60–90 mm Hg	Death and disability/death
Kario et al. 2024 [16]	Observational	4070	6.3 years	Home SBP 100–135 mm Hg	Cardiovascular events

SBP systolic blood pressure, DBP diastolic blood pressure, MI myocardial infarction

effective in clinical care remains to be determined. This issue is not trivial, given that ambulatory compared with home BP monitoring is complex, requires trained staff, and is substantially more expensive. Ambulatory BP monitoring is unavailable in most middle- and low-income countries, where hypertension is driving the epidemic of cardiovascular disease with loss of quality of life and years lived affecting individual patients and loss of economic productivity and prosperity at the community level.

## Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

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