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Out-of-office blood pressure: do we have enough evidence to recommend routine implementation?

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ABSTRACT

There is a widespread implementation of out-of-office blood pressure (BP) measurements in the usual clinical practice in different countries across the globe. The diagnosis of hypertension with out-of-office BP was, for the first time, strongly recommended by the 2011 National Institute for Health and Care Excellence (NICE) guidelines. More recently, the 2017 American Heart Association / American College of Cardiology (AHA/ACC) and the 2018 European Society of Cardiology / European Society of Hypertension (ESC/ESH) both encouraged physicians to adopt out-of-office BP measurements for the diagnosis of hypertension and evaluation of BP control of hypertensive patients. In the 2023 ESH guidelines, out-of-office BP measurements are strongly advised, especially to avoid misclassification of patients with white-coat or masked hypertension, and may also be helpful in special populations with nocturnal BP increases. Although out-of-office BP evaluation in the usual clinical practice represents a revolution in hypertension, some barriers limit its widespread implementation. Indeed, the higher cost compared with office BP measurements, the reduced availability, and sometimes patient unwillingness may lead doctors to pursue repeated office BP measurements for hypertension diagnosis. Another largely unconfessed issue is whether or not enough clinical evidence supports a recommendation for routine use of out-of-office BP measurements).

Key-words: *Home blood pressure, ambulatory blood pressure, out-of-office blood pressure, hypertension, hypertension guidelines*

Following the era of the 2011 National Institute for Health and Care Excellence Hypertension guidelines[1] suggesting that out-of-office blood pressure (BP) measurements are necessary to confirm the diagnosis of hypertension, the latest release of the 2017 American Heart Association/American College of Cardiology[2] also recommended that out-of-office BP measurements should be prescribed for the diagnosis of hypertension and titration of BP-lowering medication. A systematic review supplementing the 2017 American hypertension guidelines was undertaken by an independent Evidence Review Committee suggesting that for selected patients and their providers, self-measured (i.e., at home) BP may be a helpful adjunct to routine office care[3]. By contrast, the 2018 European Hypertension guidelines[4], based on expert opinion level of evidence, were somewhat more conservative, recommending the out-of-office BP measurement alternatively to repeated office BP measurements whenever logistically and economically feasible. Although differences between the last version of the American and the European Hypertension guidelines are minor[2,4], the former supports slightly more the use of home BP than ambulatory BP measurements mainly because of some relative advantages for treatment adherence. At the same time, the latter expresses the opinion that ideally, physicians may draw information from both home and ambulatory BP mea-

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surements because in several observational studies [e.g., the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study][5] it has been observed a discordance on BP levels between home and ambulatory measurements (i.e., increased ambulatory against normal home BP and *vice-versa*). Although out-of-office BP measurements have become popular and largely available in many countries, the current evidence to support their routine use seems at least controversial.

Out-of-office BP over office BP is characterized by better reproducibility of the value[6], little or no placebo[7] and white-coat effect[8] and by better prediction of cardiovascular outcomes, mainly based on two different sets of evidence: the steeper relationship with outcomes compared with office BP[9,10] and the fact that this relationship survives adjustment for office BP[11]. However, the relationship of out-of-office BP with cardiovascular outcomes is expected *a priori* to be steeper because of the restricted distribution in the general population compared to office BP[9]. It has been repeatably demonstrated that the prediction of the events by out-of-office BP remains unchangeable after adjustment for office BP[11-13]. Again, this kind of "evidence by adjustment" is somewhat tricky because it relies upon a statistical exercise of confounder removal and not upon real-world direct evidence. It is clear that whenever an adjustment on outcome risk estimates is attempted, no information on how much adding ambulatory or home BP to office BP improves prediction. The comparative predictive value of office and out-of-office BP measurements can also statistically be examined through the "goodness of fit" evaluation against outcome incidence. In the PAMELA study[9], which is the only available study with office, home, and ambulatory BP measurements, systolic BP measured at home demonstrated a better "goodness of fit" pattern for the prediction of cardiovascular death compared with office BP, at variance with the worse predictive pattern of 24-hour ambulatory BP compared with office BP. Although evaluating the receiver operating curve areas of the out-of-office BP measurements (home and/or ambulatory) when considered on top of office BP indicated an added prediction of cardiovascular death risk, the amount of the resulting prediction change is clinically irrelevant[14].

Previous epidemiological studies of untreated or treated patient cohorts were conducted to compare the predictive value of ambulatory and office BP measurements[9,15]. In these studies, only one session of ambulatory BP monitoring was available at variance with office BP, which has been consistently measured several times (i.e., usual or ongoing BP)[12]. Thus, it seems rather unrealistic that one single initial out-of-office BP value may represent the prevailing BP over many years to predict outcomes compared with several serial office BP values obtained, especially in treated patient cohorts in which the variability of adherence to treatment over large periods relegates the predictive role of a single baseline BP value.

In the European Lacidipine Study on Atherosclerosis (ELSA) study, decisions to titrate treatment were based on office BP only. However, this is the only available study in which ambulatory BP was serially evaluated year after year for 4 years[16]. The low annual replication rate of different BP phenotypes (e.g., sustained, masked, and white-coat hypertension) observed in a non-randomized fashion in the ELSA study suggests that ambulatory BP measurements are characterized by increased long-term variability in individual patients under treatment.

To date, no randomized outcome trial using ambulatory or home as the main BP measurement is available, and no trial was designed to compare office with out-of-office BP estimates to guide BP-lowering treatment. Consequently, BP thresholds and targets for out-of-office BP have never been established. The suggested ambulatory or home BP levels achieved during treatment are indirectly inferred from correspondence with the office's ongoing BP in untreated observational cohorts.

The 2018 European Hypertension guidelines[4] acknowledge gaps in the evidence for implementing out-of-office BP measurements in the usual clinical practice. More specifically, the added cardiovascular risk prediction of ambulatory or home BP measurements to office BP measurements has not been established, the optimal treatment targets for ambulatory or home BP measurements are lacking, and the outcome-based comparison between office and out-of-office BP-guided treatment has not been approached. Since many years are needed to bridge the evidence gaps mentioned above, the best policy for routine clinical practice is the improvement in the quality of office BP measurements instead of the widespread use of out-of-office BP for the diagnosis of hypertension and treatment monitoring.

At the bottom line, all of these properties (i.e., risk prediction, reproducibility, prognostic value) of out-of-office BP measurements are largely based on huge patient cohorts. If, for example, you have a co-

hort of 50-100 patients undergoing ABPM today, and two or three months later, the mean cohort BP is almost identical to that of the baseline. However, individual patients demonstrate great variability with the same out-of-office technique at different times.

Therefore, it is difficult to give a definite answer regarding the question of what to do with individual patient ambulatory BP monitoring. The criticism of (unstandardized) ambulatory monitoring is that the patient under monitoring makes different activities from a usual day without the monitor (e.g., a salty meal or sitting in an armed chair for 24 hours gives you different results). By contrast, home BP measurements are more standardized and close to office BP measurement techniques, though they also produce different BP values.

Where do we stand now?

Although a recommendation for routine implementation of out-of-office BP measurement cannot be made, home and/or ambulatory BP may be used in the case of specific conditions in which the diagnosis of hypertension is problematic. Finally, out-of-office measurements may refine the evaluation of BP control during treatment and prevent adverse events related to profuse BP-lowering in special circumstances. Again, the 2023 European Hypertension guidelines[17] propose specific recommendations and statements accompanied by different levels of evidence for out-of-office BP measurements (Table 1).

Table 1. Specific recommendations and statements of out-of-office blood pressure measurements according to the 2023 European Hypertension guidelines[17].

Recommendations	Class of recommendation	Level of evidence
HBPM is recommended in addition to OBPM to improve CV risk prediction due to better reproducibility and prognostic value than OBPM, although lacking data on treatment benefit from RCTs	II	B
ABPM is recommended in addition to OBPM to improve CV risk prediction due to better reproducibility and prognostic value than OBPM, although lacking data on treatment benefit from RCTs	II	B
HBPM is recommended to identify white-coat hypertension or masked hypertension	I	B
ABPM is recommended to identify white-coat hypertension, masked hypertension and nocturnal BP phenotypes. Repeated ABPM may be necessary because these phenotypes have a limited reproducibility	I	B
HBPM is recommended for long-term follow-up of treated hypertension because it improves BP control, especially when combined with education and counselling	I	B
ABPM should be used to diagnose true resistant hypertension	I	B

ABPM, ambulatory blood pressure monitoring; CV, cardiovascular; HBPM, home blood pressure monitoring; OBPM, office blood pressure monitoring; RCTs, randomized clinical trials.

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