ATTENDED VS. UNATTENDED BLOOD PRESSURE – LEARNINGS BEYOND SPRINT

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Blood pressure (BP) has been measured as office BP, usually taken after 5 minutes of quiet rest, in all clinical outcome trials in hypertension until recently, when the Systolic Blood Pressure Intervention Trial (SPRINT) was carried out. In the publication of the main SPRINT results it was not evident how BP had been measured (1). Following some literature search (2) it became visible that BP in SPRINT was taken as unattended automated office blood pressure (unattended-AOBP). The more than 100 sites participating in the SPRINT Study in the U.S.A. used the Omron 907 automated device. Personal were additionally trained to use the full capacity of this device by leaving the room prior to the 5 minutes period of rest followed by the preset unattended automated measurements at 5, 6 and 7 minutes. This is properly described in later publications including the article reporting the subgroup data in the elderly participants (3). However, a post hoc investigation in response to the debate suggested that not all investigators had followed the protocol and left the room prior to BP measurement (4). Alternatively, some of the SPRINT investigators years later may in fact not remember how their personal had performed the BP measurement.

The SPRINT study was designed to compare outcomes in hypertensive people with high cardiovascular risk who were randomized to target office systolic BP <120 vs. <140 mmHg. However, until the method for BP measurement in SPRINT was clarified in detail, i.e. the unattended approach, there was uncertainty which BP had been compared in the SPRINT Study. A 24-hour ambulatory BP (ABPM) sub-study in SPRINT participants was particularly useful in this context; it could be calculated that in SPRINT the investigators compared office systolic BP of approximately 132 vs. 144 mmHg when translated from the unattended-AOBP. This calculation was done, as recommended in European Hypertension Guidelines, by adding 5 mmHg to the daytime ambulatory systolic BP measured in the SPRINT sub-study.

The controversy regarding which method had been used for office BP measurement in such a large outcome trial such as SPRINT initiated further investigations of the relationships between BP taken in the office manually or with semi-automated or automated devices, e.g. the Omron 907 device, unattended-AOBP and ABPM. Seo J et al. reported a study from South Korea, which aimed to compare unattended-AOBP with ABPM in patients with a high cardiovascular risk (5). Participants (n=1208) were recruited from a prospective cohort study and they had successfully undergone both unattended-AOBP and ABPM within 7 days of enrollment. Unattended-AOBP was taken with a validated device and so was 24-hour ABPM. The 95% limits of agreement between systolic unattended-AOBP and daytime systolic ABPM were -34.8 and 20.2 mmHg (mean difference= -7.3±14.0). The mean differences in quintiles of unattended-AOBP distributions increased with decreasing systolic unattended-AOBP. The prevalence of masked hypertension was 25.7% and that of white-coat hypertension was 8.4%. Cut-offs here were < or ≥ 135/85 mmHg and the terms "masked" and "white-coat" hypertension were used because no better terms are available to characterize the differences between unattended-AOBP and ABPM. The lower range of systolic unattended-AOBP exhibited a large discrepancy with daytime systolic ABPM. Moreover, higher cardiovascular risk and history of asymptomatic cardiovascular disease were independently associated with larger discrepancy between unattended-AOBP and ABPM. The authors concluded that the status of BP control should be confirmed using out-of-office BP measurements, even when using unattended-AOBP as a clinical BP reference in high-risk patients.

The key finding in this study was the relatively large difference and poor limits of agreements compared with similar data in early reports. The inconsistent findings may be due to differences in populations; the early studies may to a large extend have investigated people with mild hypertension referred for ABPM while the present (6) and some other recent studies have included people with high risk hypertension and hypertensive people being well treated with antihypertensive drugs. The present study thus showed that the discrepancy was larger in people with higher cardiovascular risk and more asymptomatic cardiovascular disease. The lower the unattended-AOBP, the larger the discrepancy and it may be tempting to speculate that the BP reactivity is larger in people with more advanced cardiovascular disease. In other words, the higher cardiovascular risk and the more subclinical disease, the larger is the potential for these people to have a decrease in BP when they are seated completely unattended and by themselves during standard quiet conditions in the clinic to have their BP taken with a preset automated device. Such conditions may be extended beyond the clinic or the physician’s office: “Being alone and not location is what matters most” (7).

Thus, it matters how BP is measured. Office BP taken manually, with semi-automated or even with automated device has been the standard in all outcomes trials in hypertension research until the SPRINT study (8) came about. Typically, study participants have been seated quietly for 5 minutes before measurements. This standardization of BP measurements has been a major achievement for research. There are minor differences in the way measurements have been done and reference values have been extracted (waiting time, average of 3 measurements, average of last two measurements, etc.), but basically the same method has been used all over the world.
which is a treasure for hypertension research. We can just imagine what it will mean in the future to have papers adopting SPRINT and other classical measurements, with no possibility to compare.

The novelty with BP measurements in SPRINT was the unattended approach which was a part of the protocol followed by a large group of investigators but not necessarily by all. SPRINT was an outcome trial, which searched for the optimal target systolic BP in high risk hypertensive people. SPRINT, like the more recent study by Seo J et al., showed a large discrepancy between unattended-AOBP and ABPM probably because patients were of the high risk category and thus similar to the patients in the study by Seo J and colleagues. We have been critical to an approach like this in the investigation of the optimal target office BP in the treatment of hypertension. The main reason for our criticism is that many patients will be treated to unexpectedly low target BPs when unattended-AOBP is used; they may develop adverse events because of hypotension and subsequently they may discontinue treatment remaining unprotected from antihypertensive treatment.

Besides, unattended-AOBP has limited evidence in predicting cardiovascular disease. To our knowledge, observational data is limited to one prospective study in Canada in which unattended-AOBP was taken in pharmacies. There was a relationship with cardiovascular disease but the relationship was not very strong. Because of widespread use of unattended-AOBP it could even cause a concern that BP is underestimated in the Canadian population. It could then be argued that BP could rather be taken during a short (6 minutes) bicycle exercise test at a moderate load like 100 watts; an early rise in systolic BP in this setting is a strong predictor of coronary disease and cardiovascular death even when adjusted for BP at rest and other cardiovascular risk factors. However, there is no randomized intervention trial to support using exercise BP as basis for treatment in clinical practice – much like as for ABPM, home BP and the unattended-AOBP. For the time being, the conclusion is then that in clinical practice we should still measure BP in office with physician or personal being present during measurements, using the manual technique, or semi-automated or automated devices. All other methods for measurements of BP should be supplementary whichever method we may believe in when we assess cardiovascular risk.

**CONFLICT OF INTEREST**
The authors report no relevant conflict of interest to this newsletter.