

## Which Threshold Values Should be Recommended in Ambulatory Blood Pressure Monitoring and Self Blood Pressure Monitoring?

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New methods to evaluate blood pressure – such as ambulatory blood pressure monitoring (ABPM) and home monitoring of blood pressure (HMBP), have been increasingly more used in clinical practice as key source of additional information to the traditional evaluation of blood pressure measuring at the doctor's office. There is a growing body of evidence available to show that both methods are strong predictors of both substitute or intermediate cardiovascular outcomes such as cardiovascular morbidity and mortality<sup>1</sup>. In addition, both methods can also evaluate conditions so far under less extensive research, such as the white coat syndrome, blood pressure behavior during sleep, masked hypertension, and early morning surge.<sup>2</sup>

Blood pressure “normal” threshold values have been kept a topic under extensive debate. The JOINT-VII – recognizing the continuous correlation between blood pressure systolic and diastolic values – (measured through the traditional sphygmomanometer) and cardiovascular risk – has defined the concept of pre-hypertension<sup>3</sup>. The body of cohort studies that pooled data from one million individuals shows that such correlation is true starting at 115/75 mmHg. Likewise, the risk has shown to be twofold for every 20 mmHg increase in systolic pressure and for every 10 mmHg increase in diastolic pressure<sup>4</sup>.

Such finding indicates that defining thresholds when considering a continuous variable such as blood pressure may be regarded as arbitrary, irrespective of the method used for measuring it. However, in the clinical assistance environment, doctors' decision making follows a dichotomy. The definition of threshold values is crucial.

The purpose of this review is to analyze the body of evidence currently available to define threshold values for mean blood pressure values through AMBP and HMBP.

### Thresholds for AMBP

#### Normal < >common

Normal values are many times considered to be those close to most frequently found values in a given population. Such strategy may lead to errors<sup>5</sup>. Firstly: low, infrequent values may not be associated to disease or risk. Secondly: frequent values may be associated to risk, and even define interventions. This is what occurred in the serum cholesterol example in Framingham's adult population (Fig. 1). Today, the most commonly found values are known to be associated to cardiovascular risk, and to determine therapeutic intervention. Despite such limitations, this was the first strategy used to define AMBP threshold values (Table I)<sup>6,7</sup>.

#### Normal values are those not associated to risk

A more consistent approach is based on the use of cohort studies to define as normal values those not

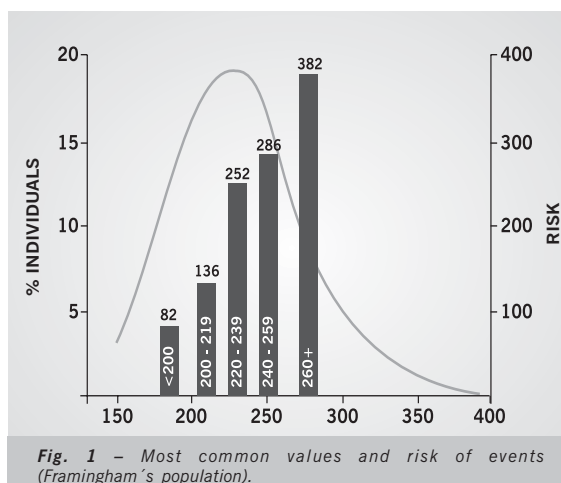


Fig. 1 – Most common values and risk of events (Framingham's population).

**Table I - "Normal" values obtained from mean values of different samples**

Blood Pressure	International Record <sup>6</sup>	PAMELA Study <sup>7</sup>
<b>Systolic pressure</b>		
24-hour AMBP	116 ± 10	118 ± 11
Day time AMBP	122 ± 11	123 ± 11
Sleep AMBP	106 ± 11	108 ± 11
<b>Diastolic Pressure</b>		
24-hour AMBP	70 ± 7	74 ± 7
Day time AMBP	75 ± 7	79 ± 8
Sleep AMBP	61 ± 8	65 ± 8

associated to risk (which for AMBP is to be understood as cardiovascular risk). Longitudinal studies have been carried out, but results obtained from different populations may turn generalization difficult.

In a cohort comprising 1,187 patients under follow-up for 3.2 years in average, Verdecchia et al. found that men and women showing AMBP awake values under 136/87 mmHg and 131/86 mmHg, respectively, reported cardiovascular prognosis similar to individuals screened as normotensive based on recordings at the doctor's office. A later analysis of the same population showed that awake values under 130/80 mmHg – irrespective of gender – would be associated to lower cardiovascular risk<sup>8</sup>. It should be pointed out that this cohort does present limitations as to external validity, since hypertensives were those with medical visits at the clinic, and normotensives were "added in" based on the sample of health centers employees or patients that had been assisted at outpatient units for other reasons.

The Japanese cohort at Ohasama community studied 1,542 individuals over forty years old under mean follow-up time of 6.2 years. AMBP values associated to best cardiovascular prognosis during the 24-hour period ranged from 120 to 133 mmHg, with systolic and diastolic blood pressure ranging from 65 to 78 mmHg respectively<sup>9</sup>.

Follow-up was carried out by Clement et al<sup>10</sup> on close to 2,000 hypertensives for five years in average. They identified AMBP systolic and diastolic blood pressure increase to be a risk factor for cardiovascular events, irrespective of other risk factors, blood pressure values measured at the doctor's office included. A secondary analysis showed that 24-hour AMBP systolic values at 135 mmHg reported lower cardiovascular risk, irrespective

of systolic pressure values at the doctor's office. After adjusted for potential confusion bias such finding was not given statistic significance.

### **Normal value is taken to be that reached by those who have benefitted from some intervention**

It must be kept in mind that not all risk factors can be treated successfully. As new knowledge is acquired from clinical trials results, normal values may be changed. Therefore, normal values are defined based on the extent to which intervention can revert risk. Very few clinical trials have analyzed the benefits of anti-hypertensives in samples under AMBP.

In a sub-sample of the Syst-Eur clinical trial – that analyzed the benefits of anti-hypertensive based on the use of nitrendipine as compared to placebo in elderly patients with systolic hypertension – 536 patients had their blood pressure taken by AMBP at baseline and after 4.4 years of follow up. Systolic AMBP values in the group on anti-hypertensive medication (who also had benefits in regard to reduction of events) was 140 mmHg, 135 mmHg, and 124 mmHg, respectively, for both awake and sleep 24-hour pressure<sup>11</sup>.

Normal values obtained based on the results of studies referred to are summarized in table II. Those are compared with normal values, as recommended by the European Society of Hypertension.

### **HMBP Normal Values**

As for home monitoring of blood pressure, values below 135/85 mmHg have been recommended as normal, based on AMBP awake value as reference for normal values.

The cutting points were analyzed in a longitudinal study at Ohasama community, with follow-up of 1,491 adults in a 10-year period timeframe. Considering lower than 115/70 mmHg as reference value, values above 135/85 mmHg posed a nearly three-fold risk for the development of cerebrovascular events (RR 2.86; CI 95%: 1.55-5.30 for systolic, and RR 2.81; CI 95%: 1.64-4.77 for diastolic)<sup>12</sup>. The same value was analyzed by Bobrie et al<sup>13</sup> in a cohort with nearly 5,000 elderly hypertensives. Considering the group with blood pressure control by doctor's office measure (< 140/90 mmHg) and HMBP

**Table II - Values proposed by the different studies and by the European Society of Hypertension Guideline**

	24-hour SBP	24-hour DBP	Daytime SBP	Daytime DBP	Sleep SBP	Sleep DBP
PAMELA <sup>7</sup>	118 ± 11	74 ± 7	123 ± 11	79 ± 8	108 ± 11	65 ± 8
Verdecchia et al. <sup>8</sup>	-	-	131-137	86-87	-	-
Japanese <sup>9</sup>	120-133	65-78	-	-	-	-
Sys-Eur <sup>11</sup>	135	-	140	-	124	-
Verdecchia et al. <sup>8</sup>	-	-	<130	<80	-	-
Hypertensives <sup>10</sup>	< 135	-	-	-	-	-
Guideline <sup>2</sup>	-	-	<135*	<85*	<120*	<70*

\*Optimal values - awake: 130/80 mmHg; sleep: 115/65 mmHg.

as reference, individuals with HMBP values above 135/85 mmHg presented a nearly two-fold risk for the occurrence of events, irrespective of blood pressure control when measured at the doctor's office.

## Conclusions

Although it is recognized that there is a continuous correlation between blood pressure and cardiovascular

risk, irrespective of the measuring method, the use of normal values helps doctors at the point of clinical decision making. Longitudinal studies have helped detect values above which risks become significant. Twenty-four hour AMBP values at 130/80 mmHg and HMBP values at 135/85 mmHg are the figures obtained by the body of evidence. Results from clinical trials where blood pressure is measured by automatic methods may define our therapeutic objectives more accurately.

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